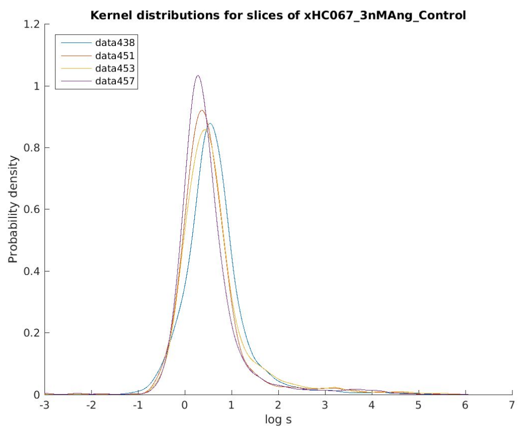
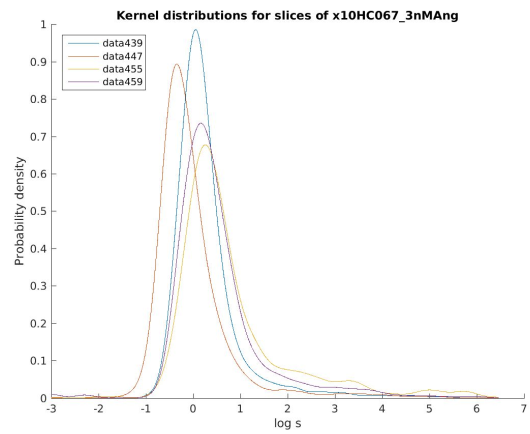
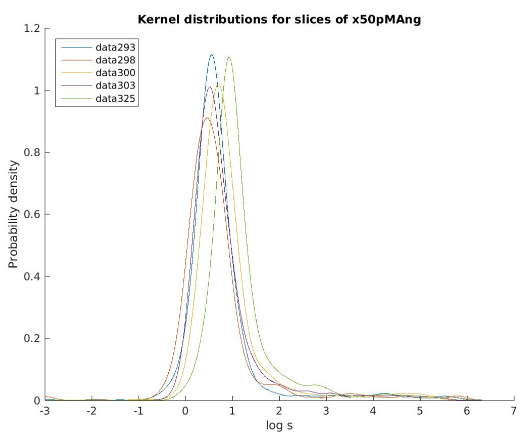
12/11/2017~12/15/2017

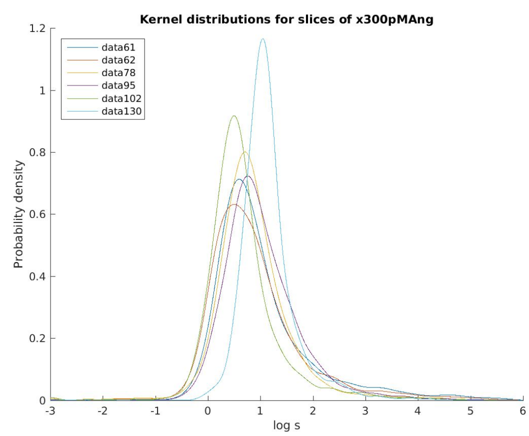
Fitting of Paula's log(IEI) histograms

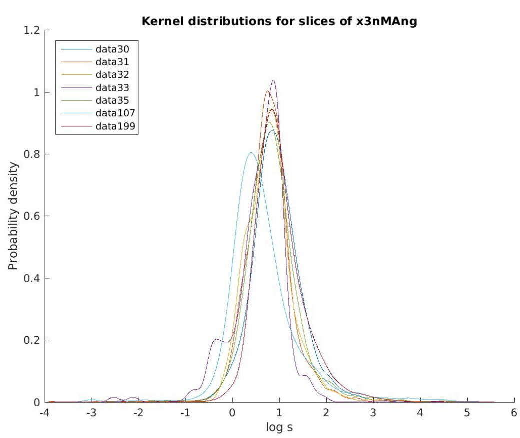
- Overlayed fits of **each slice** of the **same experimen**t on top of each other.
    - Using kernel distributions

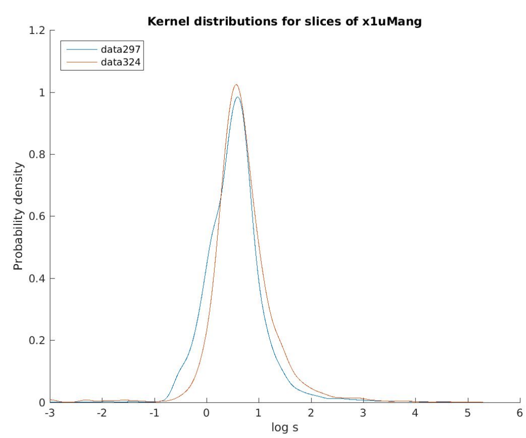




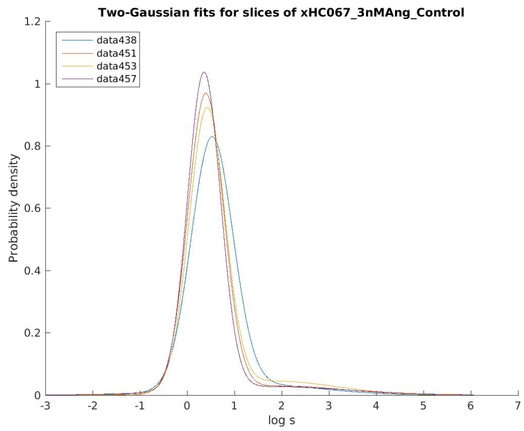


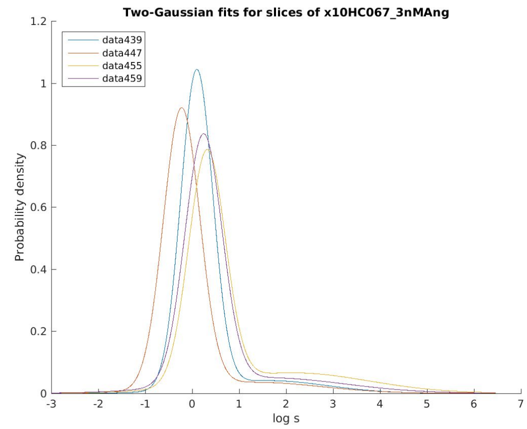


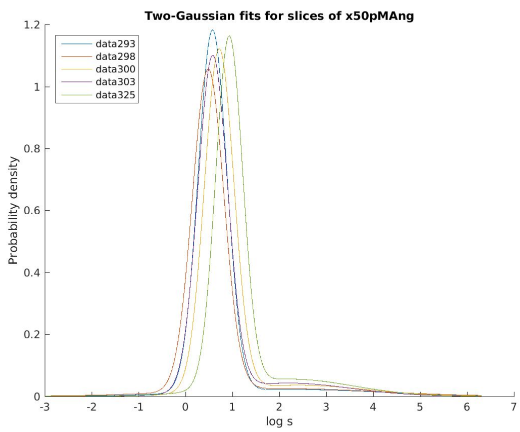


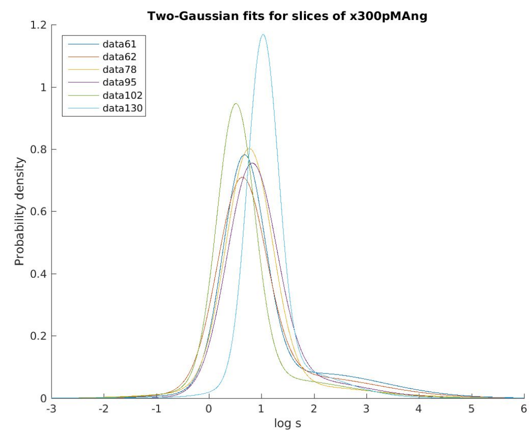


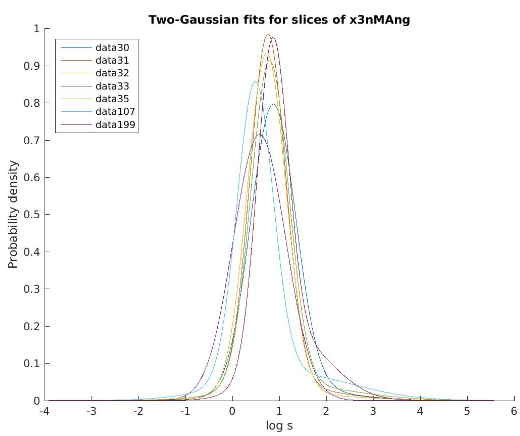
- Using Two-Gaussian distribution fits

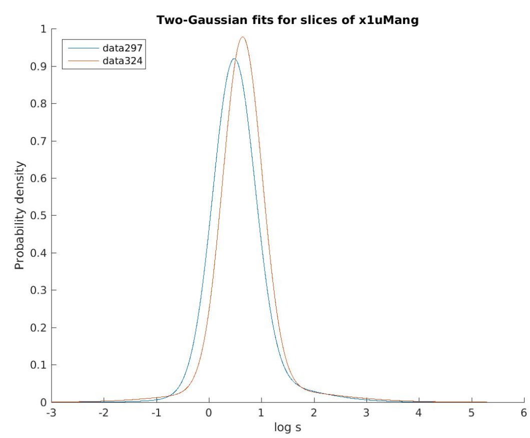




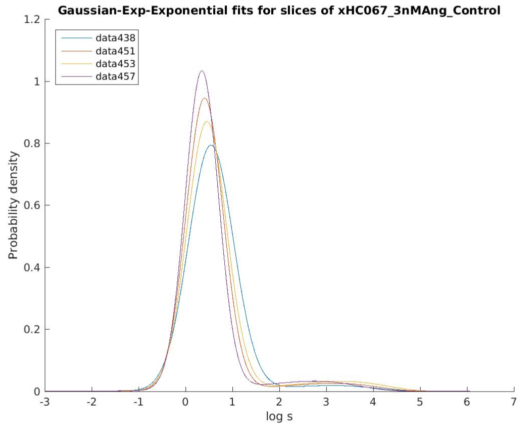


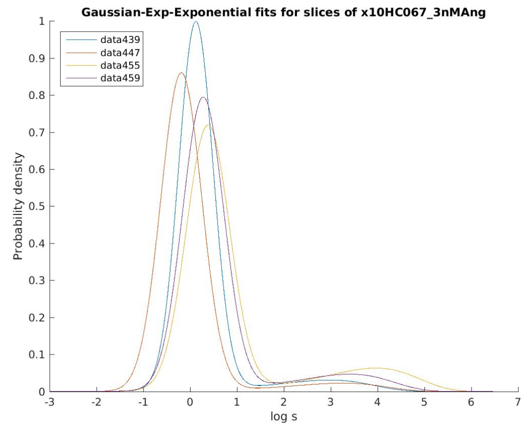


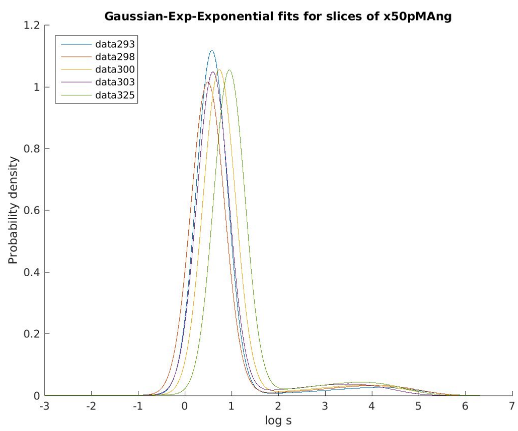


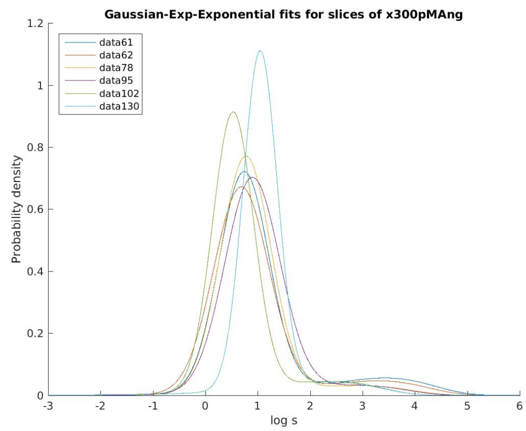


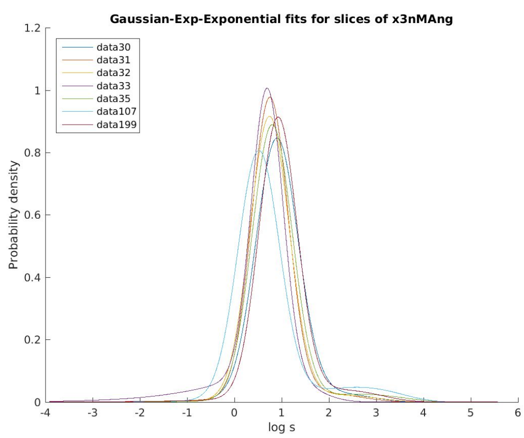
- Using Gaussian-ExpExponential distribution fits

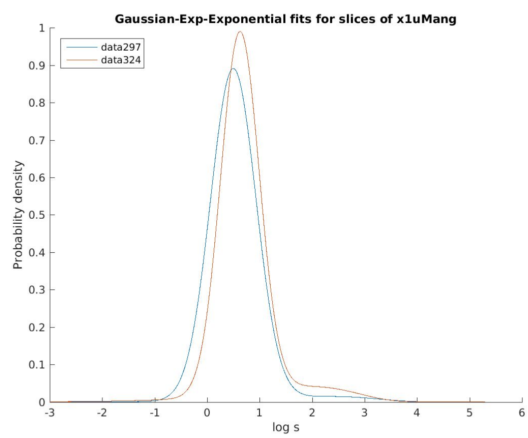




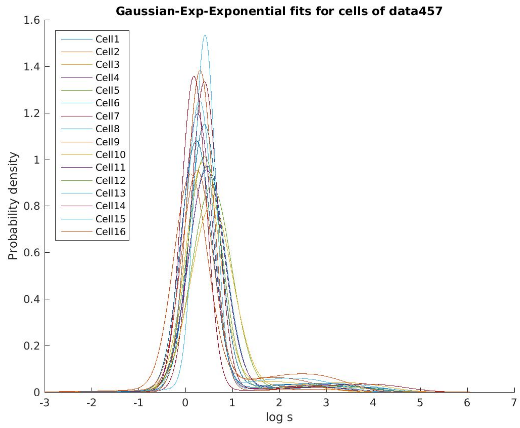


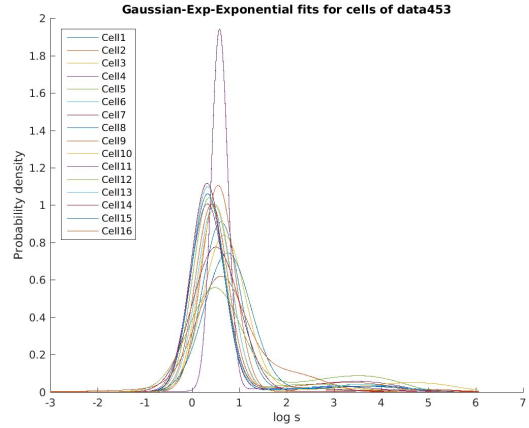


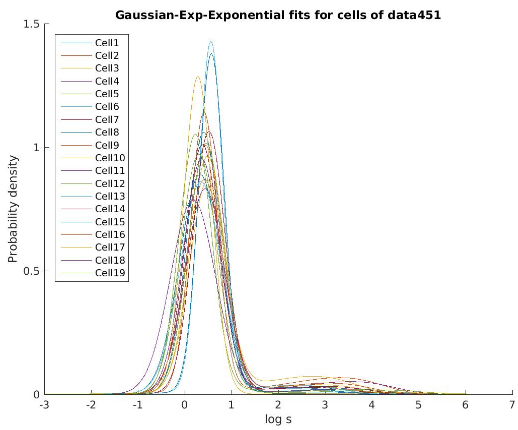


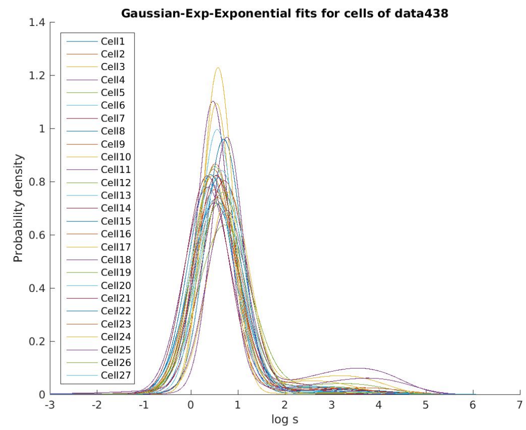


- Overlayed fits of **each cell** of the **same slice** on top of each other
    - **xHC067_3nMAng_Control**

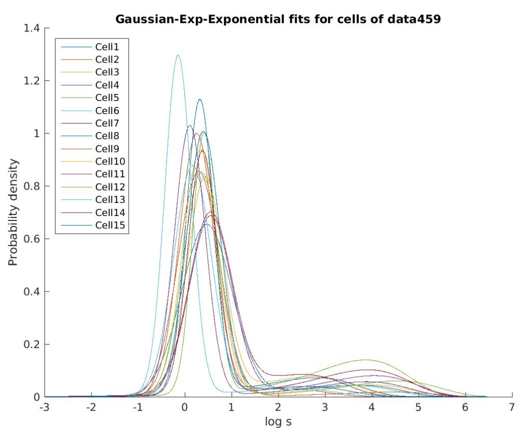


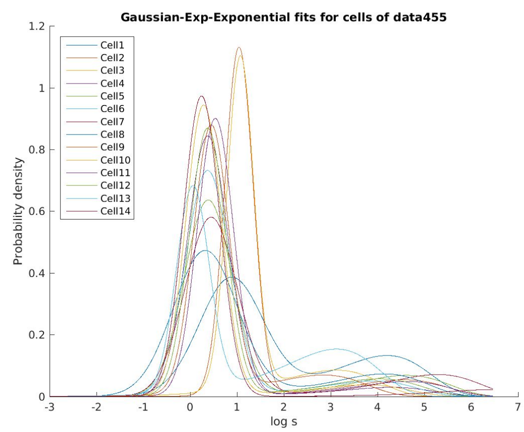


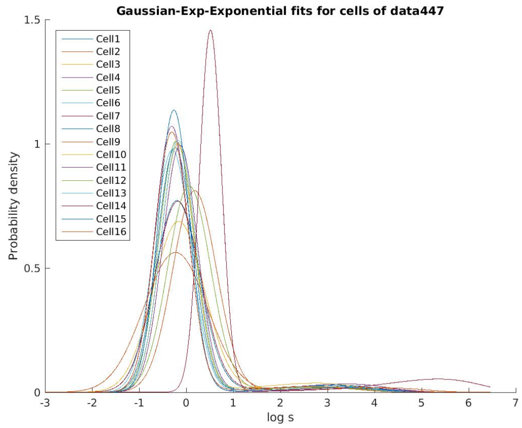


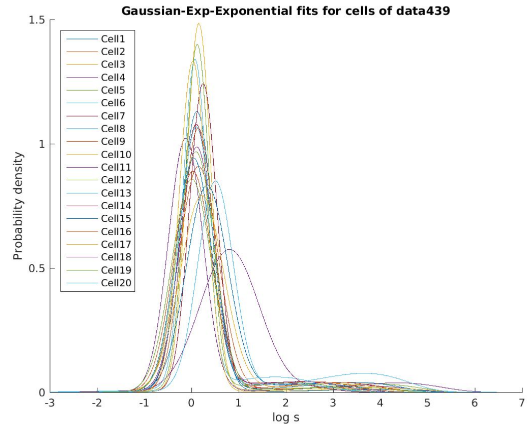


- **x10HC067_3nMAng**

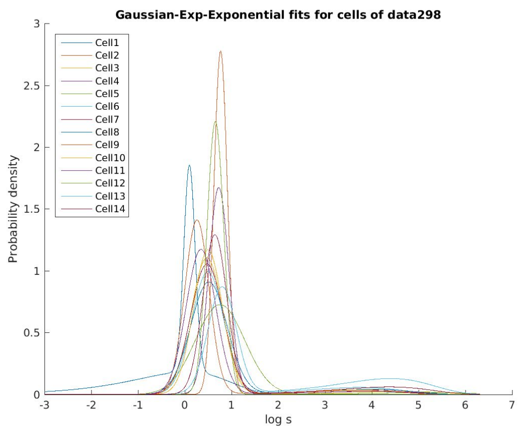


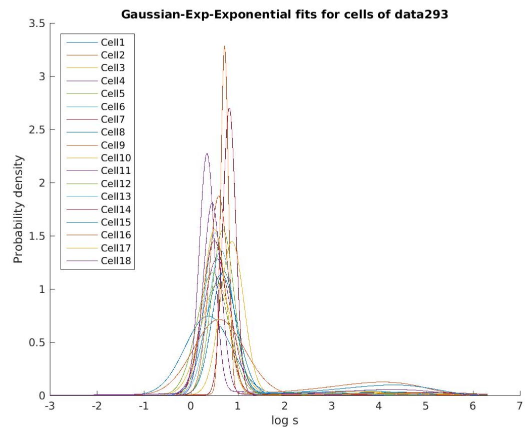


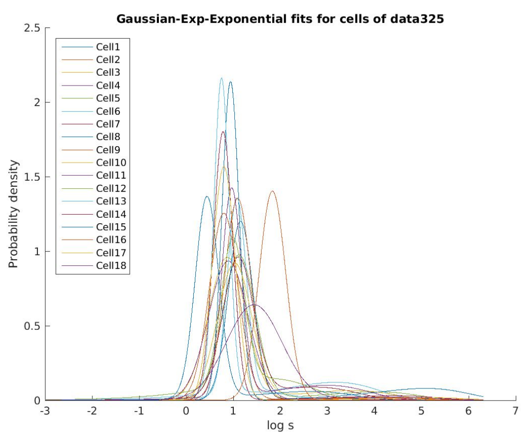

Gaussian-Exp-Exponential fits for cells of data447
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16

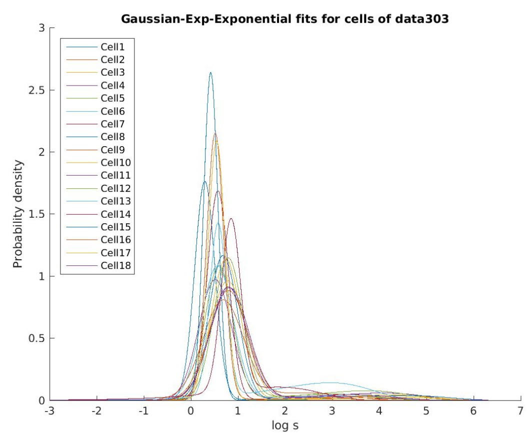

Gaussian-Exp-Exponential fits for cells of data439
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18 Cell19 Cell20

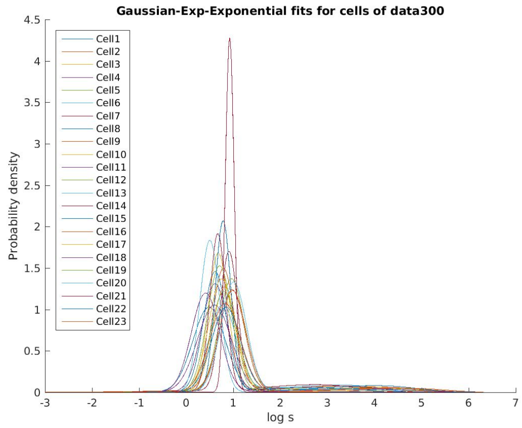
- **x50pMAng**


Gaussian-Exp-Exponential fits for cells of data298
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14

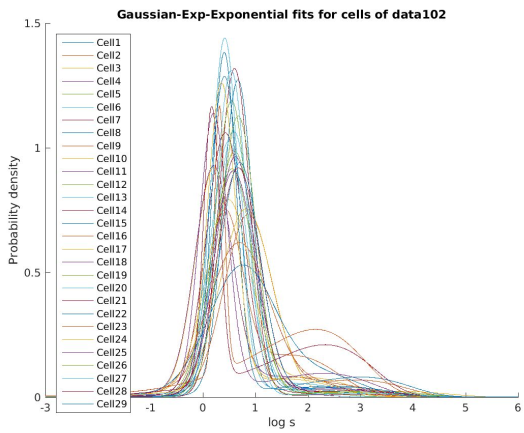

Gaussian-Exp-Exponential fits for cells of data293
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18


Gaussian-Exp-Exponential fits for cells of data325
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18


Gaussian-Exp-Exponential fits for cells of data303
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18


Gaussian-Exp-Exponential fits for cells of data300
Probability density
log s
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
-3
-2
-1
0
1
2
3
4
5
6
7
Cell1
Cell2
Cell3
Cell4
Cell5
Cell6
Cell7
Cell8
Cell9
Cell10
Cell11
Cell12
Cell13
Cell14
Cell15
Cell16
Cell17
Cell18
Cell19
Cell20
Cell21
Cell22
Cell23

- **x300pMAng**


Gaussian-Exp-Exponential fits for cells of data102
Probability density
log s
0
0.5
1
1.5
-3
-1
0
1
2
3
4
5
6
Cell1
Cell2
Cell3
Cell4
Cell5
Cell6
Cell7
Cell8
Cell9
Cell10
Cell11
Cell12
Cell13
Cell14
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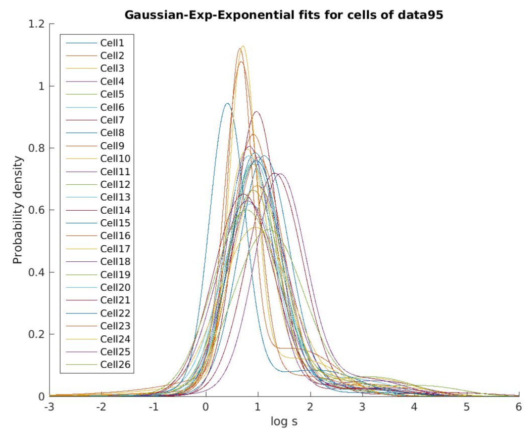
Cell26
Cell27
Cell28
Cell29


Gaussian-Exp-Exponential fits for cells of data95
Probability density
log s
0
0.2
0.4
0.6
0.8
1
1.2
-3
-2
-1
0
1
2
3
4
5
6
Cell1
Cell2
Cell3
Cell4
Cell5
Cell6
Cell7
Cell8
Cell9
Cell10
Cell11
Cell12
Cell13
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Cell15
Cell16
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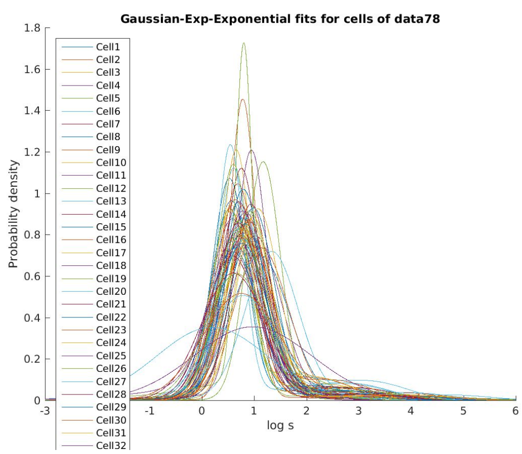
Cell21
Cell22
Cell23
Cell24
Cell25
Cell26


Gaussian-Exp-Exponential fits for cells of data78
Probability density
log s
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
-3
-1
0
1
2
3
4
5
6
Cell1
Cell2
Cell3
Cell4
Cell5
Cell6
Cell7
Cell8
Cell9
Cell10
Cell11
Cell12
Cell13
Cell14
Cell15
Cell16
Cell17
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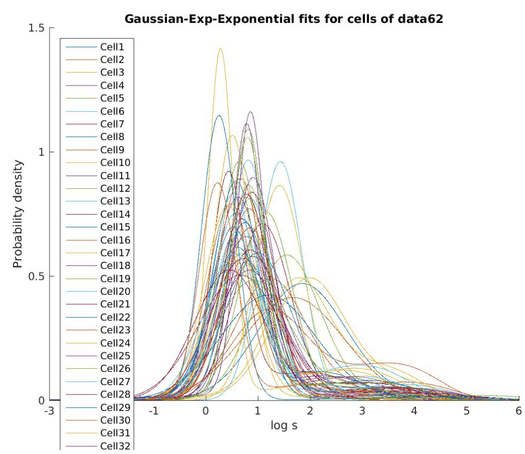
Cell27
Cell28
Cell29
Cell30
Cell31
Cell32


Gaussian-Exp-Exponential fits for cells of data62
Probability density
log s
0
0.5
1
1.5
-3
-1
0
1
2
3
4
5
6
Cell1
Cell2
Cell3
Cell4
Cell5
Cell6
Cell7
Cell8
Cell9
Cell10
Cell11
Cell12
Cell13
Cell14
Cell15
Cell16
Cell17
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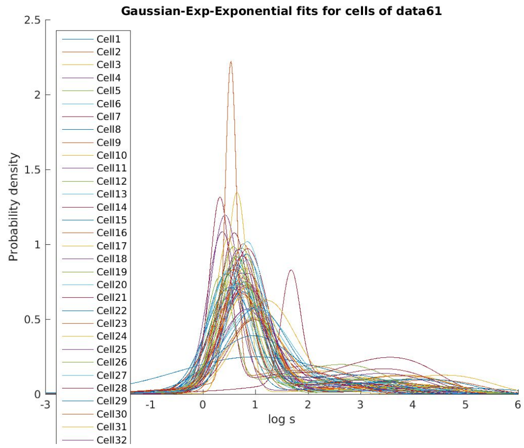
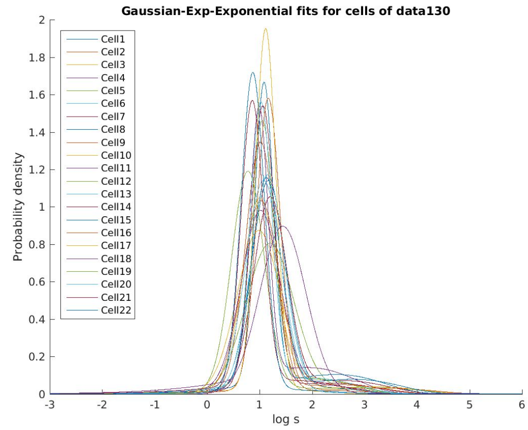
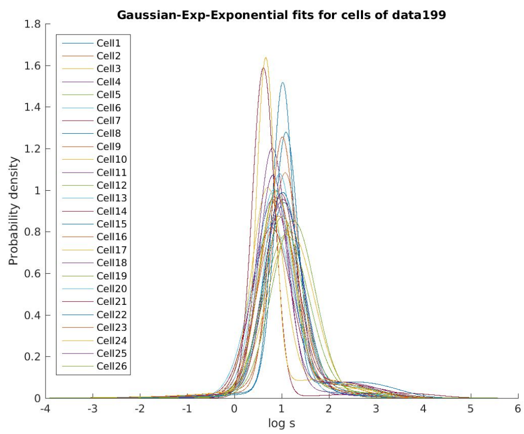
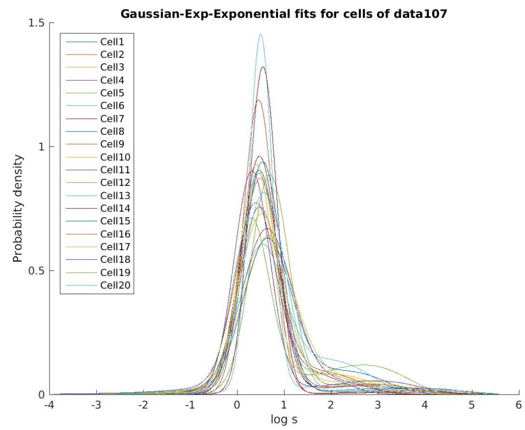
Cell31
Cell32

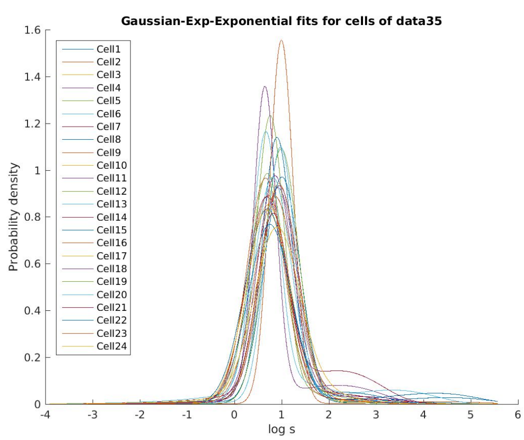

Gaussian-Exp-Exponential fits for cells of data61
Probability density
log s
Cell1 … Cell32

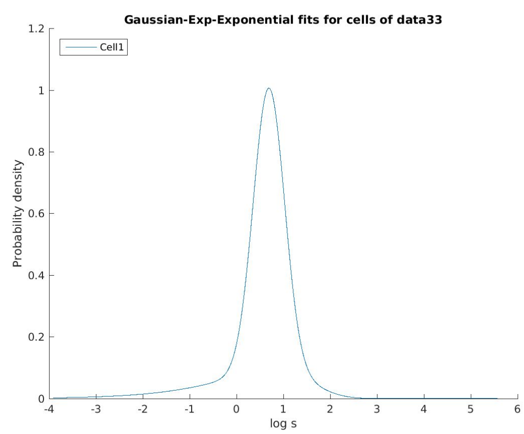

Gaussian-Exp-Exponential fits for cells of data130
Probability density
log s
Cell1 … Cell22

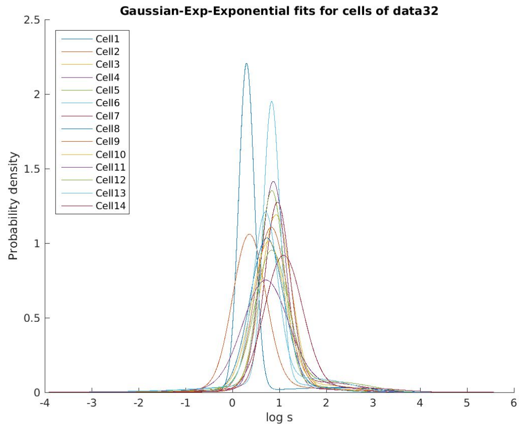
- x3nMAng

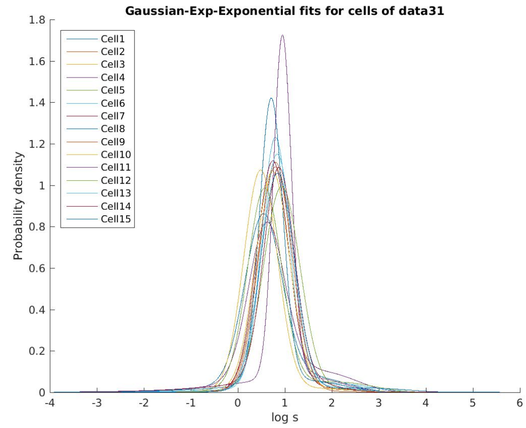

Gaussian-Exp-Exponential fits for cells of data199
Probability density
log s
Cell1 … Cell26

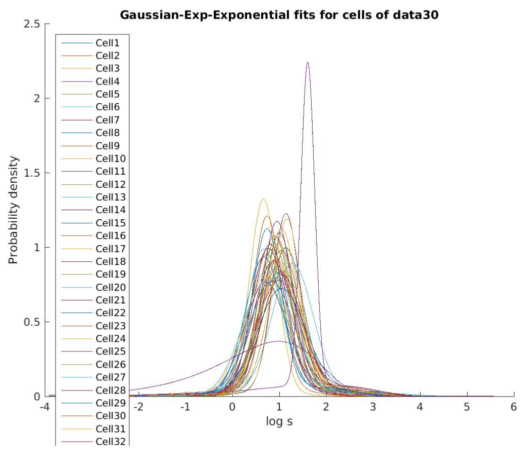

Gaussian-Exp-Exponential fits for cells of data107
Probability density
log s
Cell1 … Cell20


Gaussian-Exp-Exponential fits for cells of data35
Probability density
log s
Cell1 … Cell24

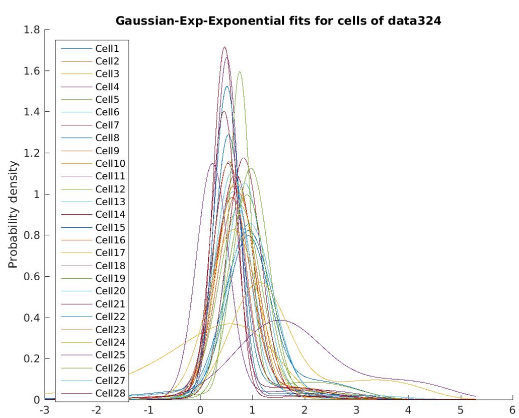

Gaussian-Exp-Exponential fits for cells of data33
Probability density
log s
Cell1

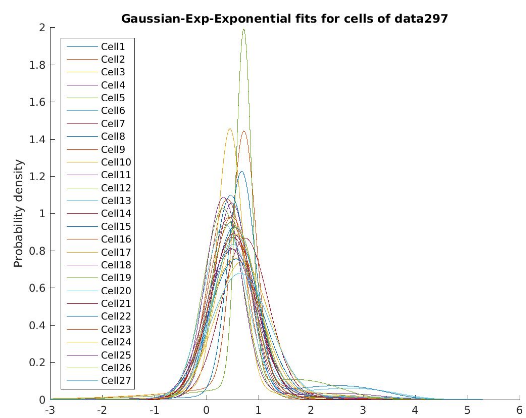

Gaussian-Exp-Exponential fits for cells of data32
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14


Gaussian-Exp-Exponential fits for cells of data31
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15

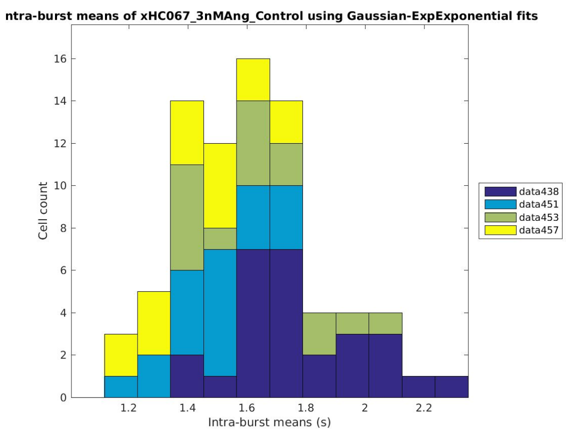

Gaussian-Exp-Exponential fits for cells of data30
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18 Cell19 Cell20 Cell21 Cell22 Cell23 Cell24 Cell25 Cell26 Cell27 Cell28 Cell29 Cell30 Cell31 Cell32

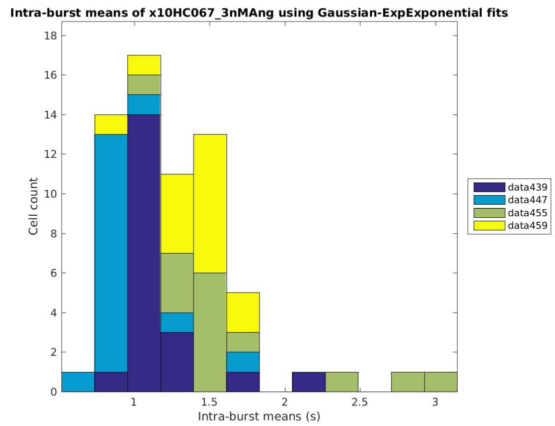
- **x1uMAng**

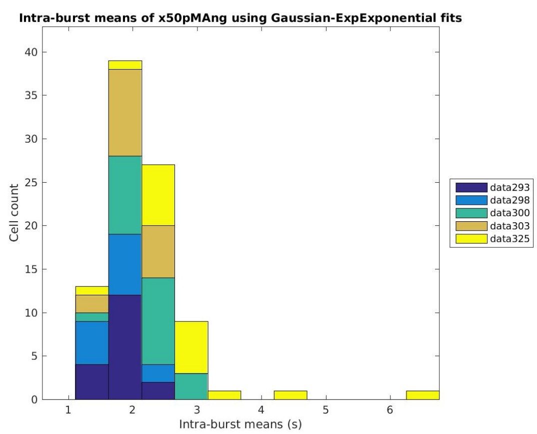

Gaussian-Exp-Exponential fits for cells of data324
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18 Cell19 Cell20 Cell21 Cell22 Cell23 Cell24 Cell25 Cell26 Cell27 Cell28

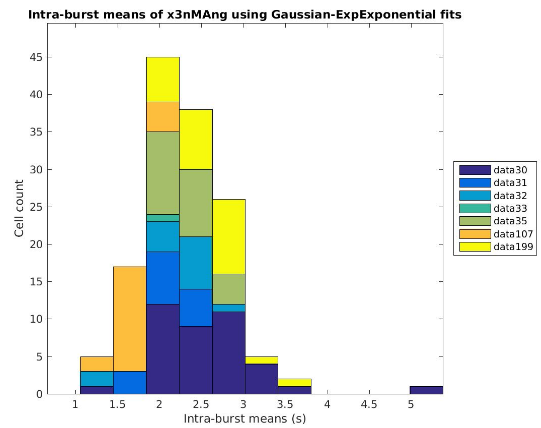

Gaussian-Exp-Exponential fits for cells of data297
Probability density
log s
Cell1 Cell2 Cell3 Cell4 Cell5 Cell6 Cell7 Cell8 Cell9 Cell10 Cell11 Cell12 Cell13 Cell14 Cell15 Cell16 Cell17 Cell18 Cell19 Cell20 Cell21 Cell22 Cell23 Cell24 Cell25 Cell26 Cell27

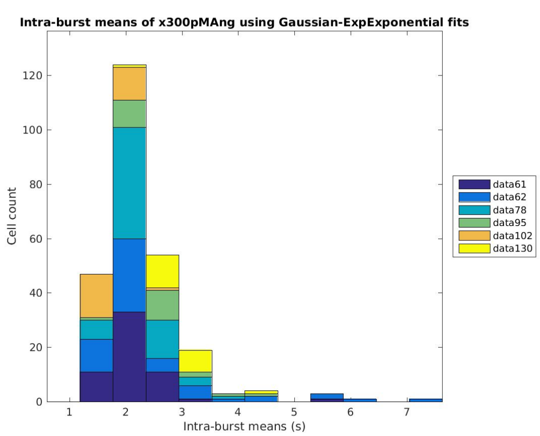
- Plotted **stacked histograms** of intra-burst means, inter-burst means, spacing parameters, thresholds, void parameters **for each cell grouped by slice**
    - **Intra-burst means**

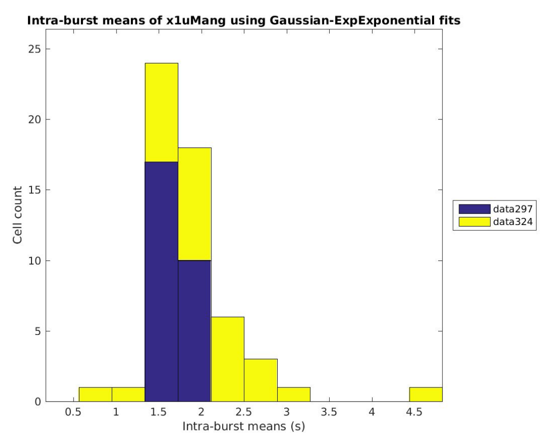




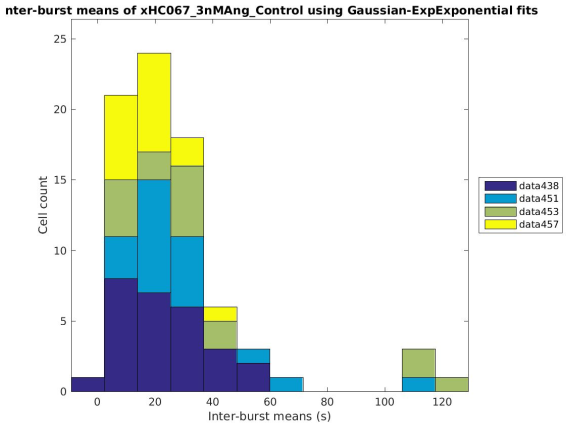


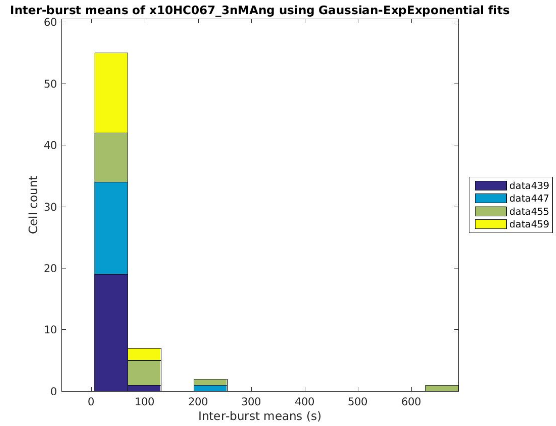


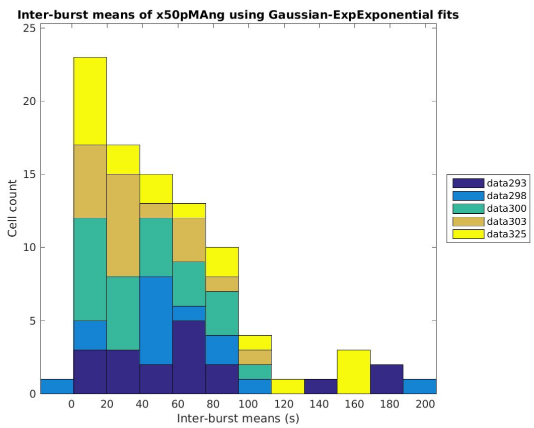


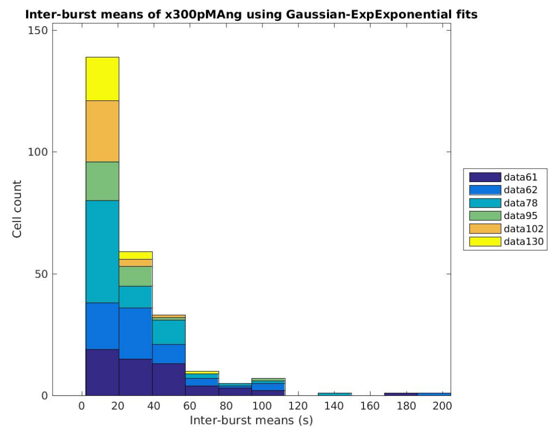


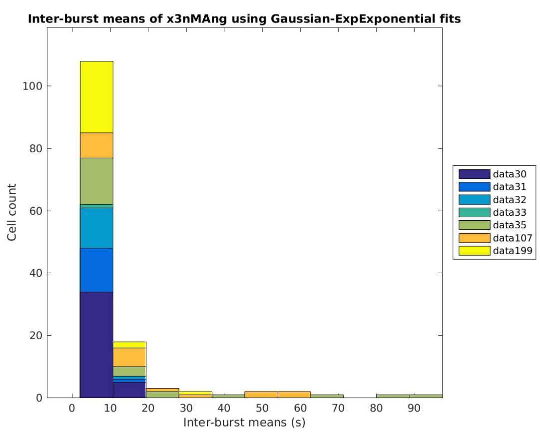
○ Inter-burst means

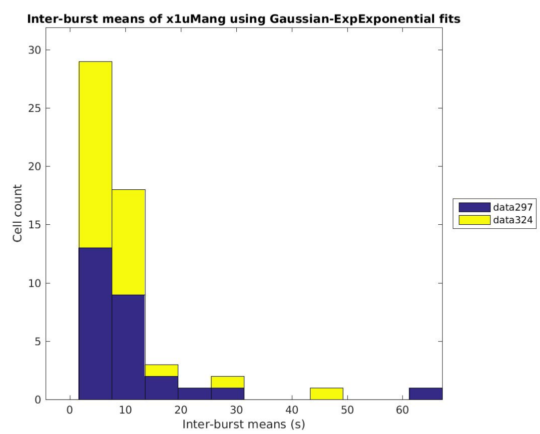




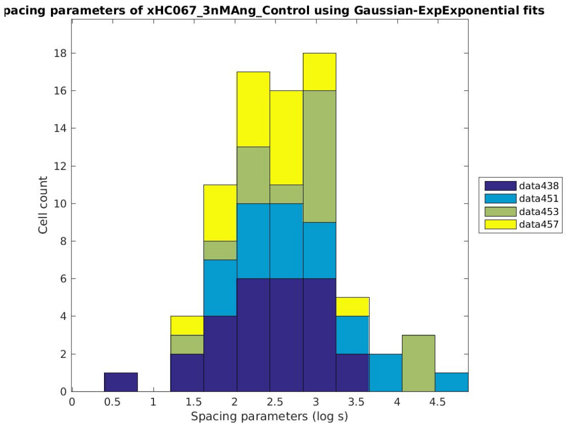


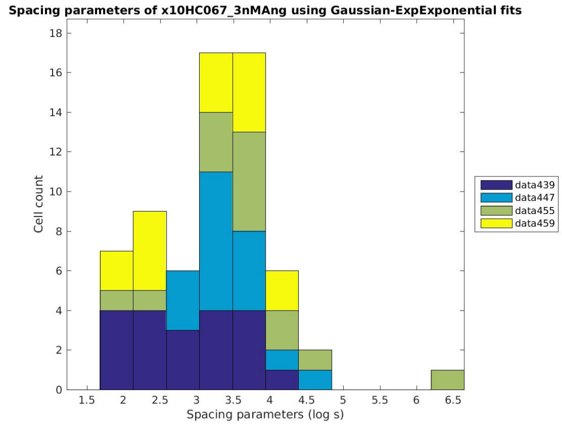


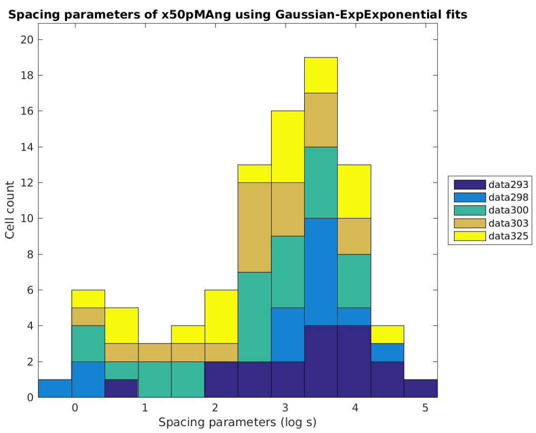


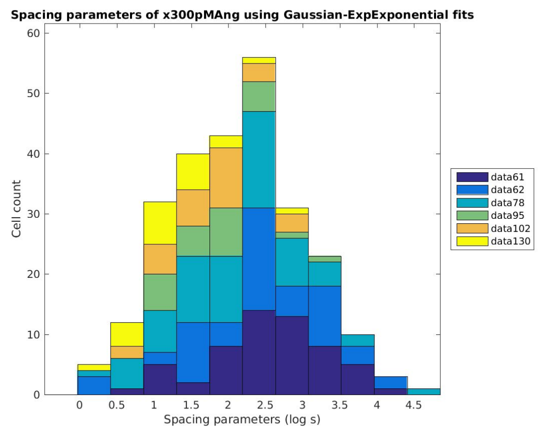


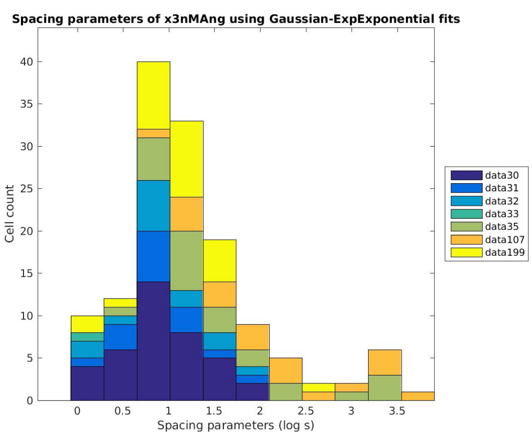
- **Spacing parameters**

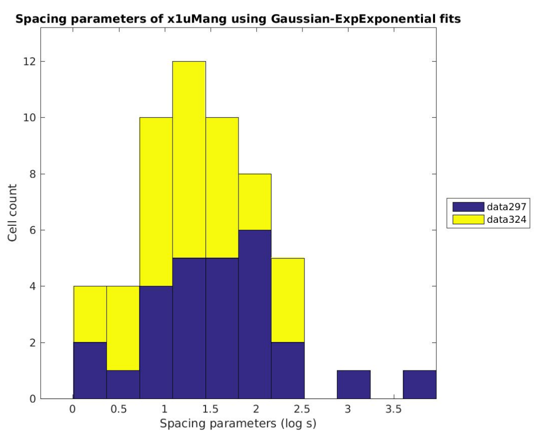




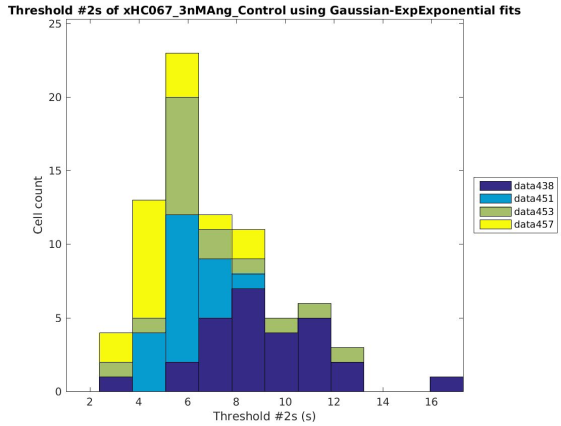


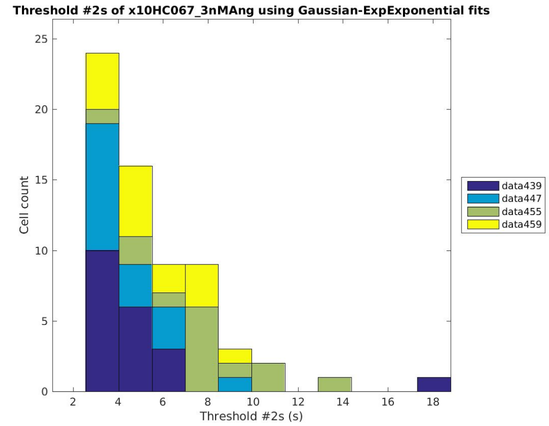


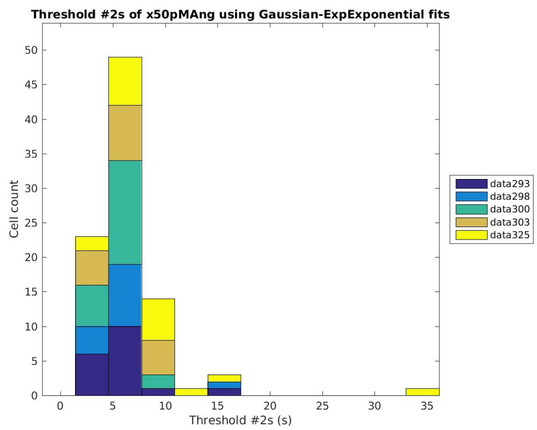


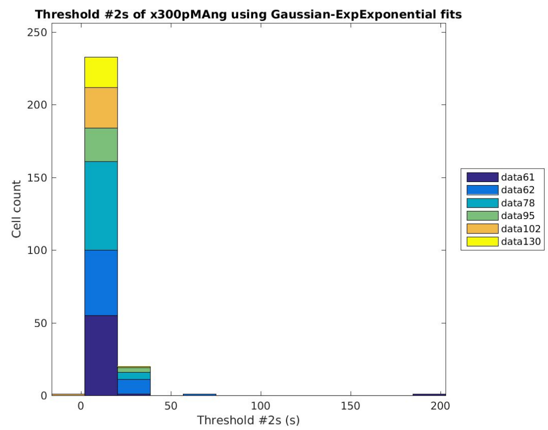


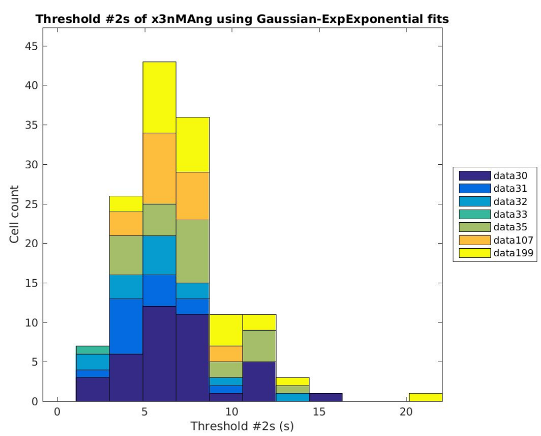
- **Thresholds (minimum between peaks)**

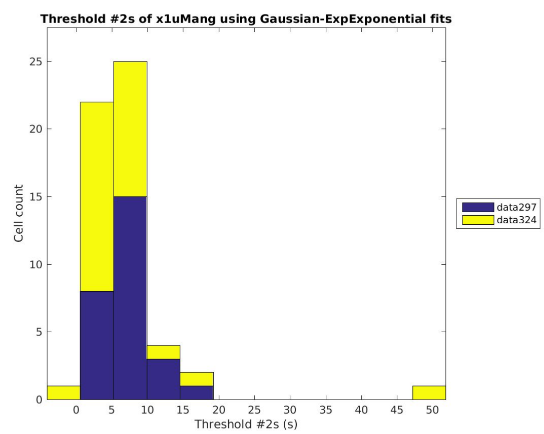




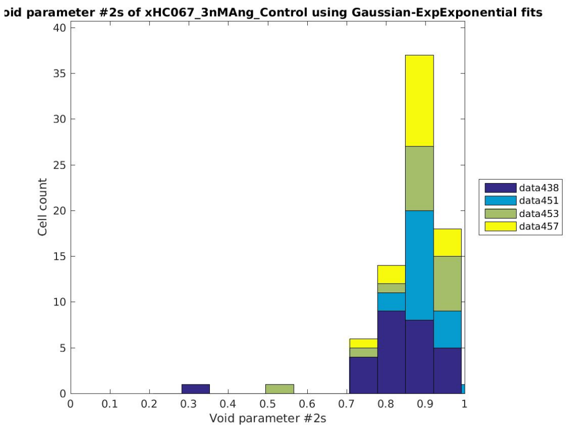


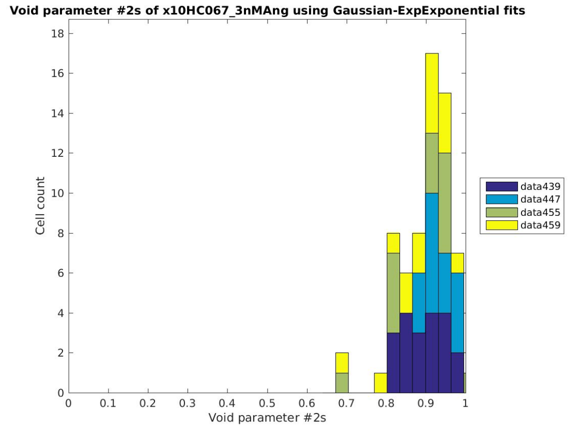


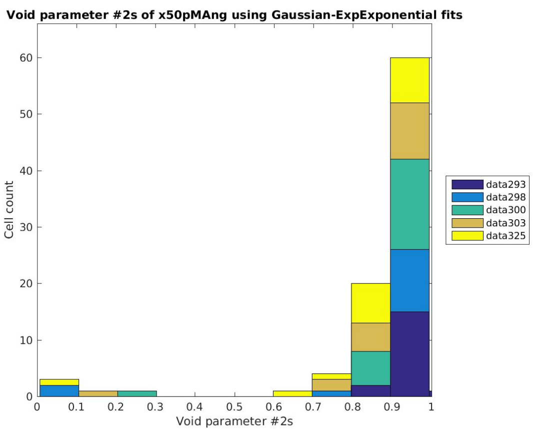


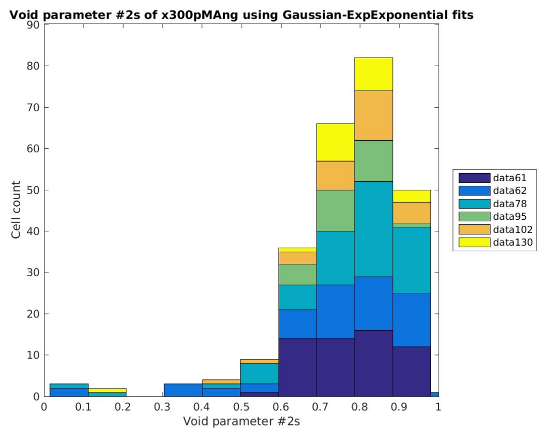


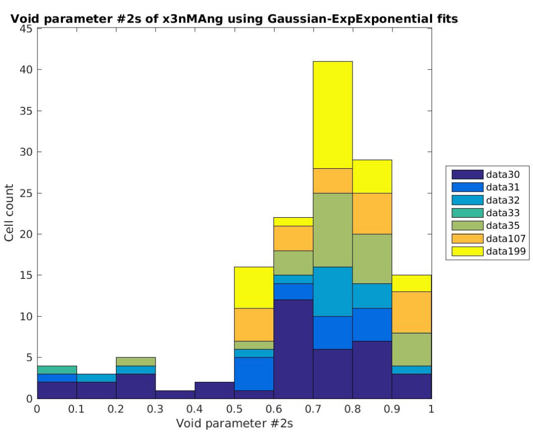
- ### Void parameters

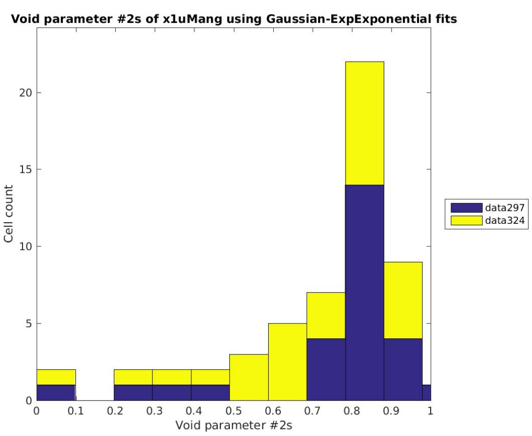




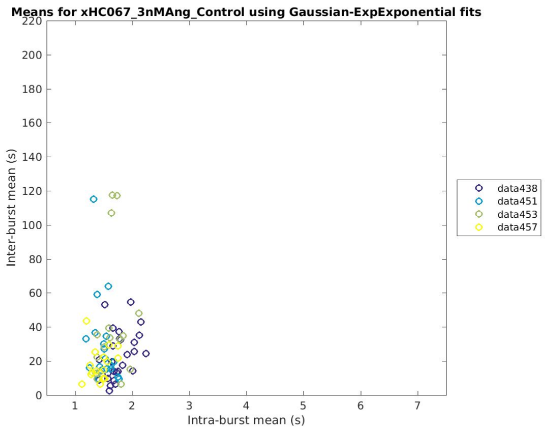


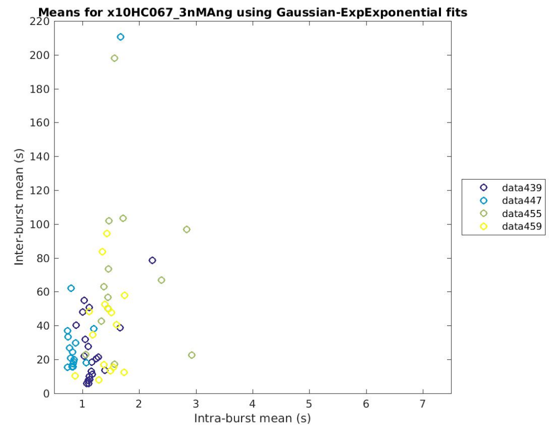


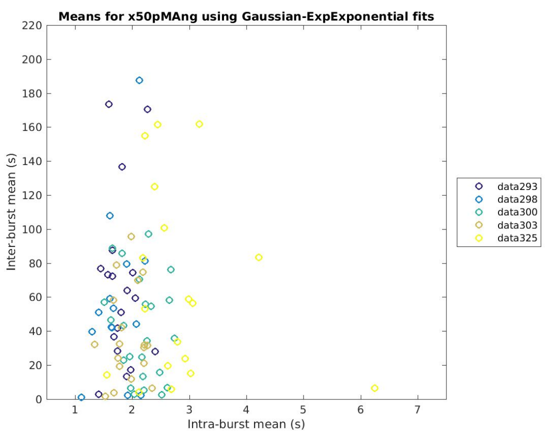


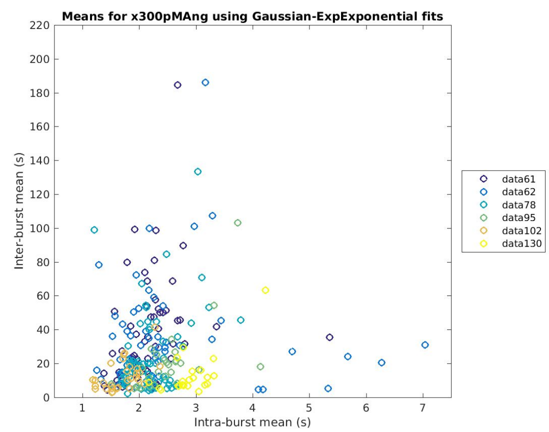


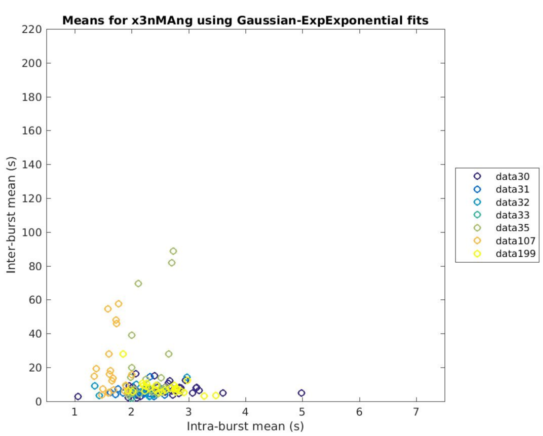
- Scatter plots of statistics taken from each **cell** grouped by **slice**
    - **Inter-burst mean vs. intra-burst mean** (linear scale)

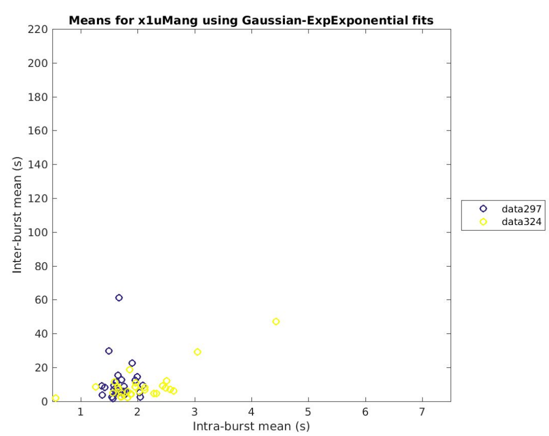




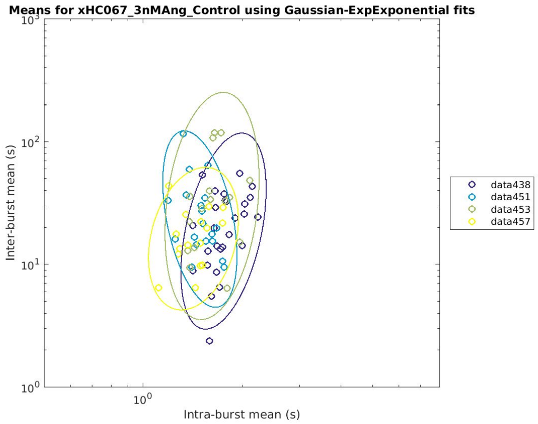


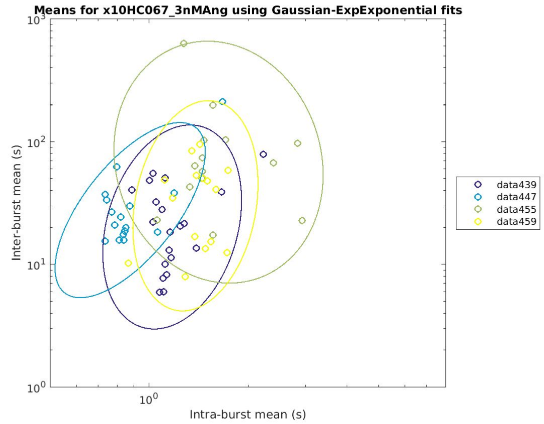


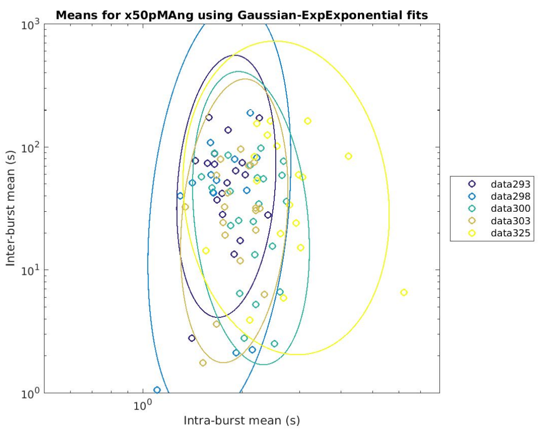


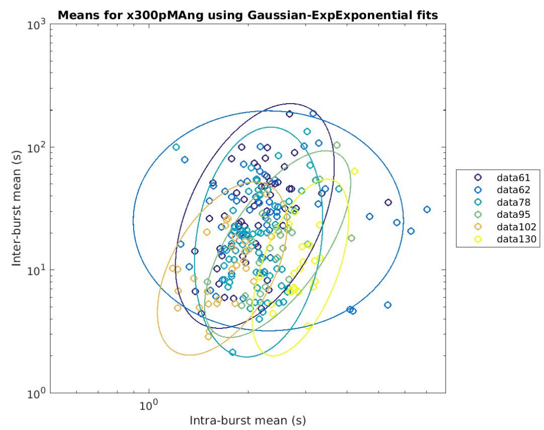


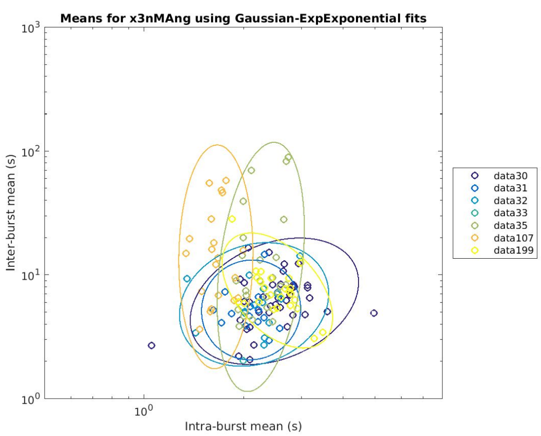
- **Inter-burst mean vs. intra-burst mean** (log scale)

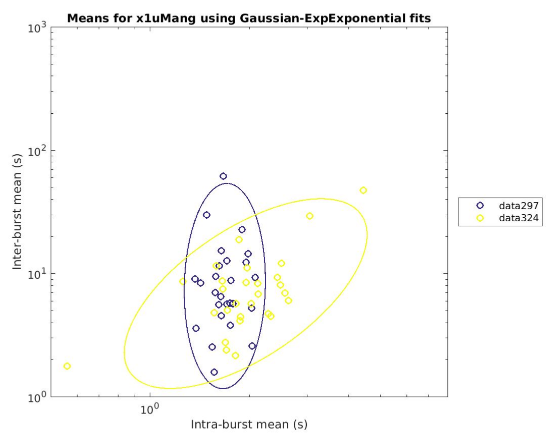




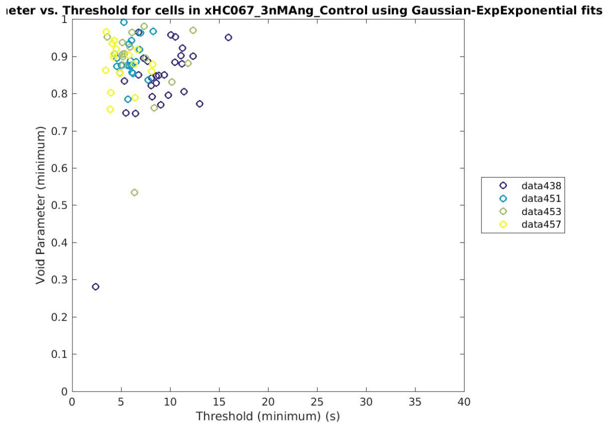


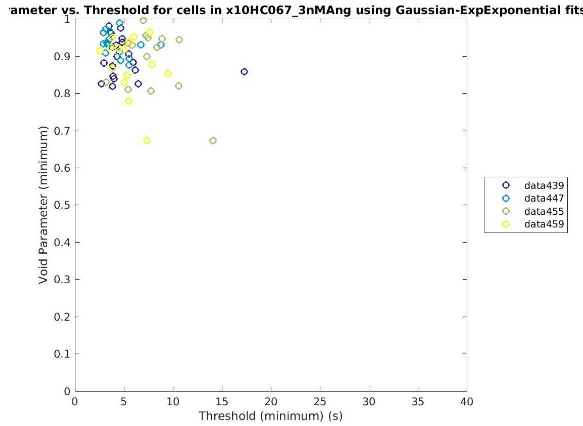


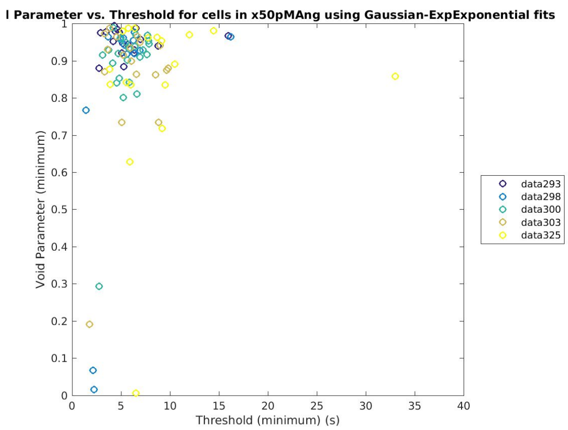


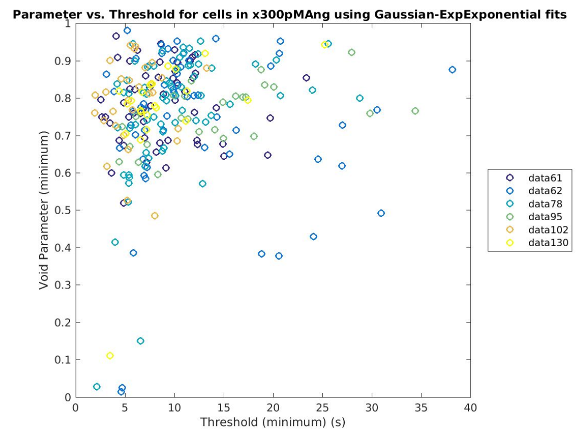


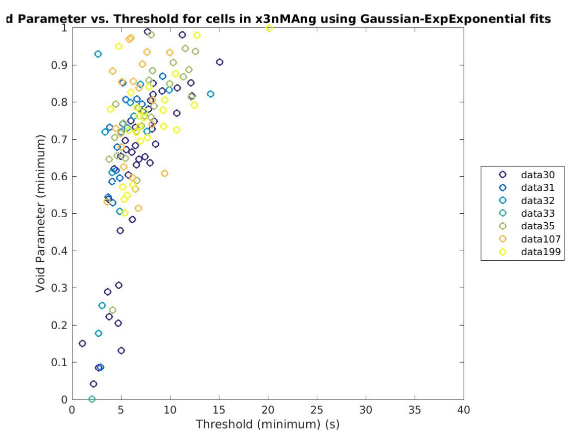
- **Void parameter vs. Threshold** (linear scale)

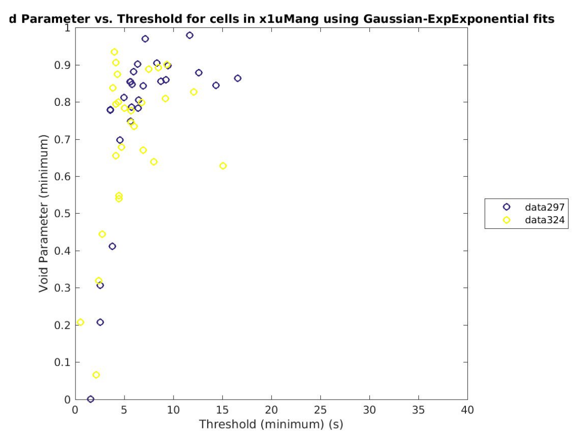




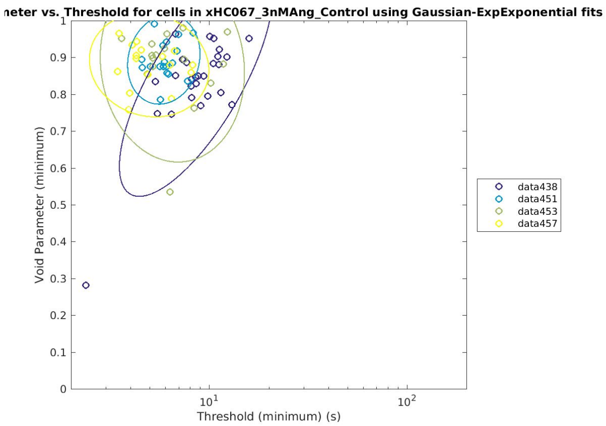


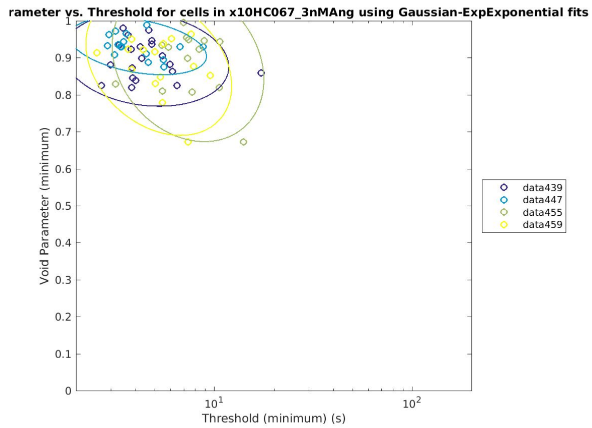


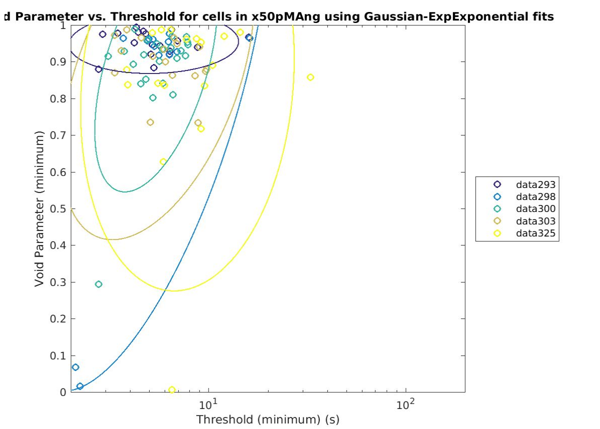


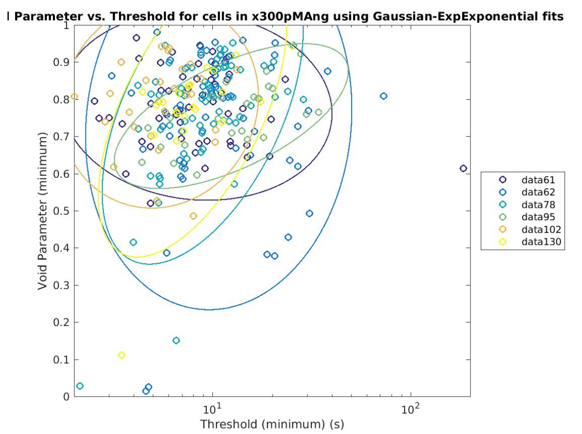


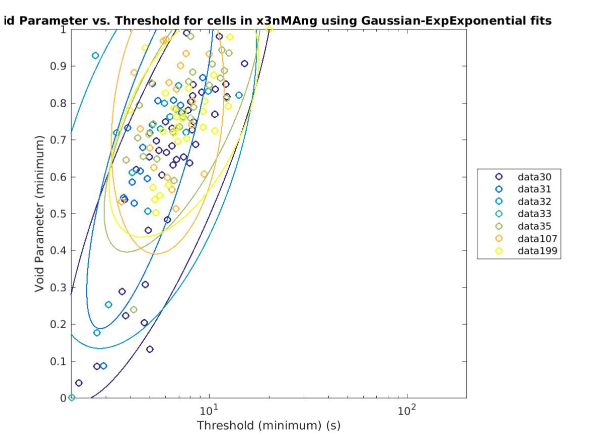
- **Void parameter vs. Threshold** (log scale)

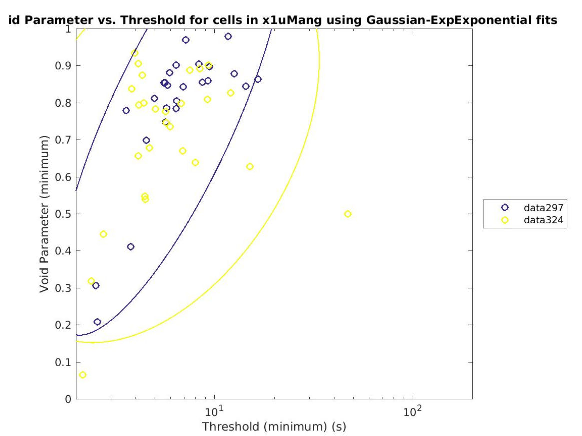




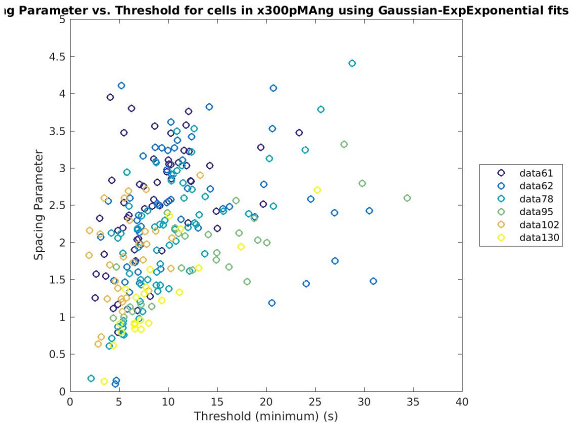


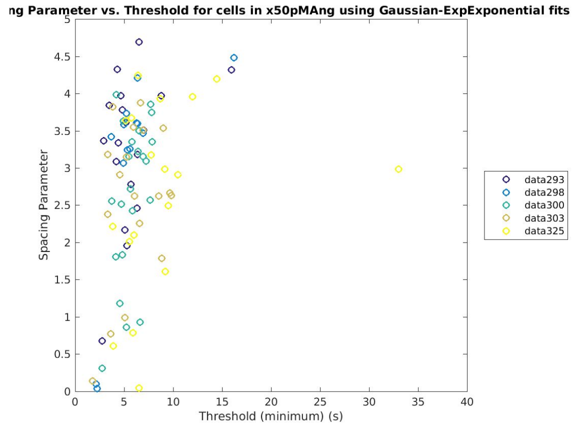


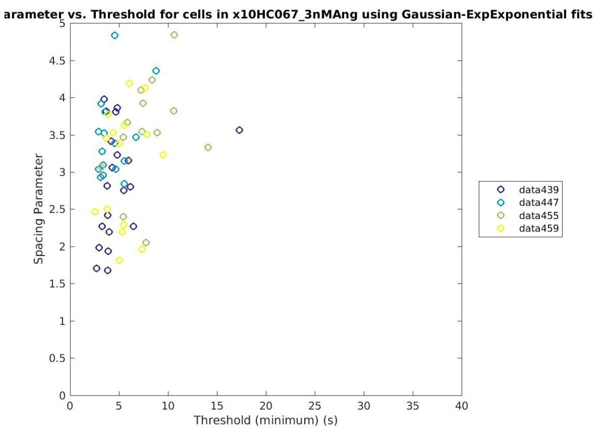


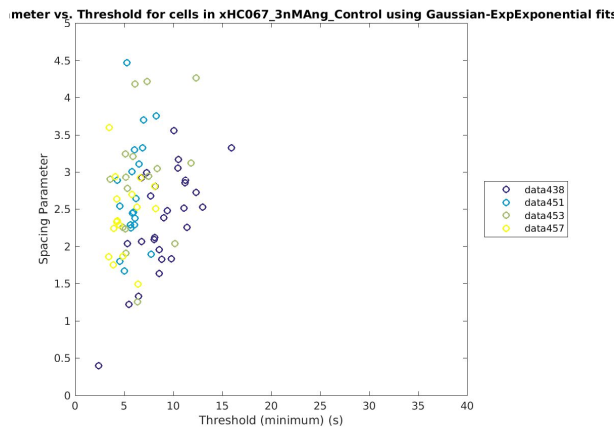


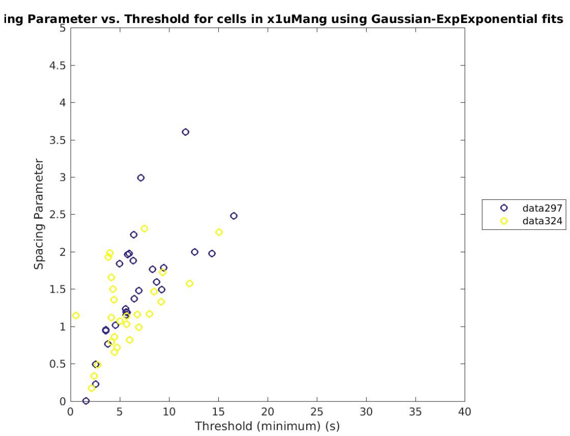
○ **Spacing parameter vs. Threshold** (linear scale)

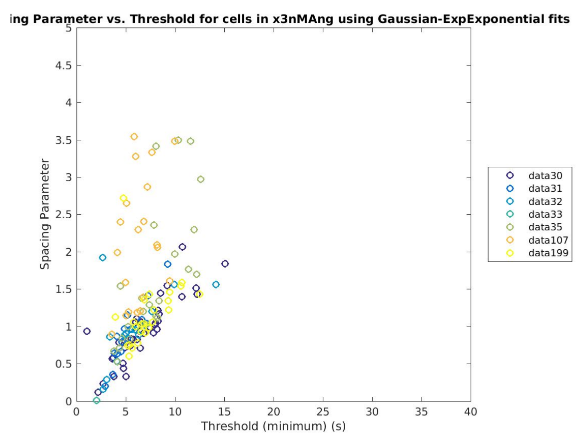




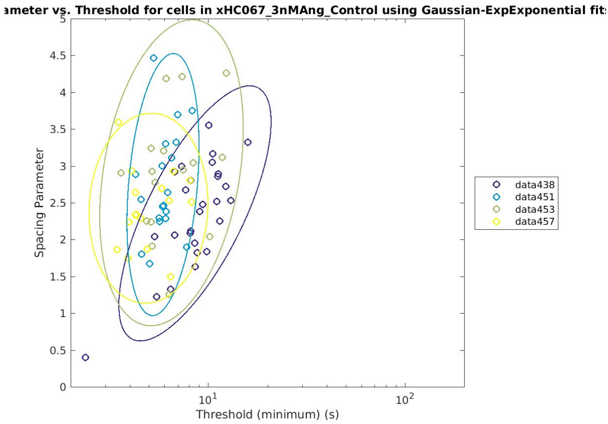


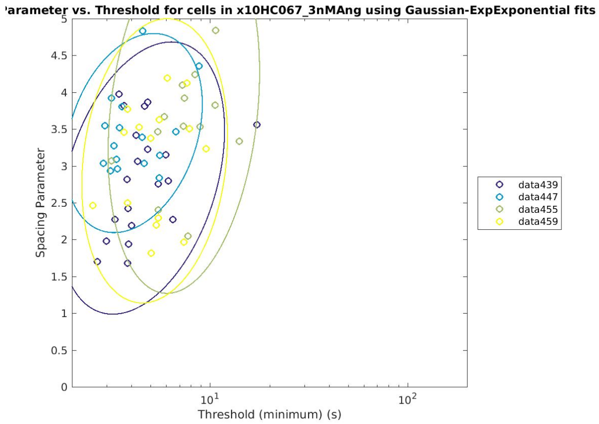


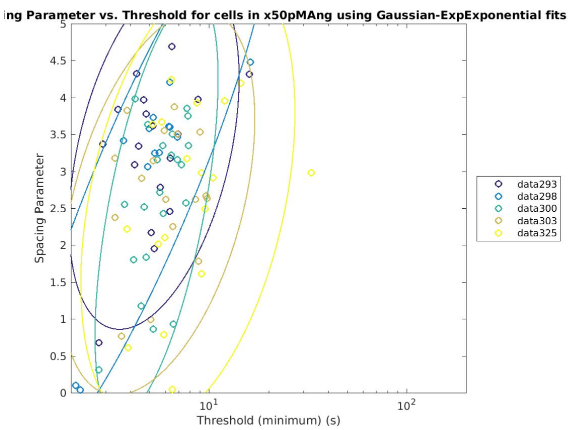


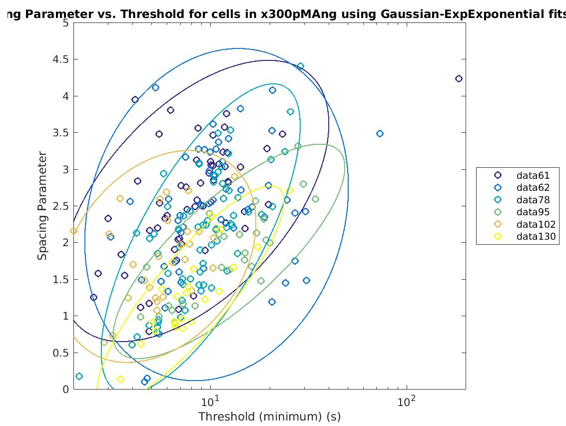


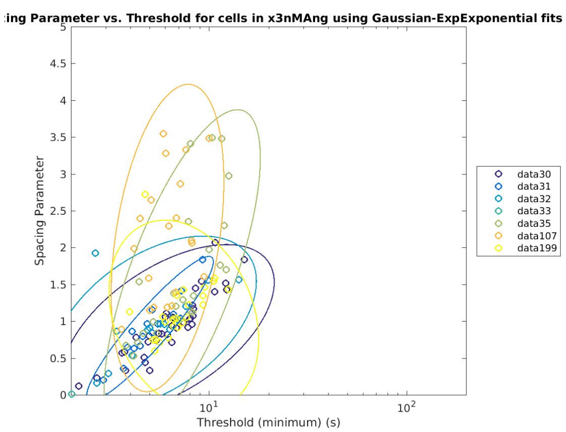
- **Spacing parameter vs. Threshold** (log scale)

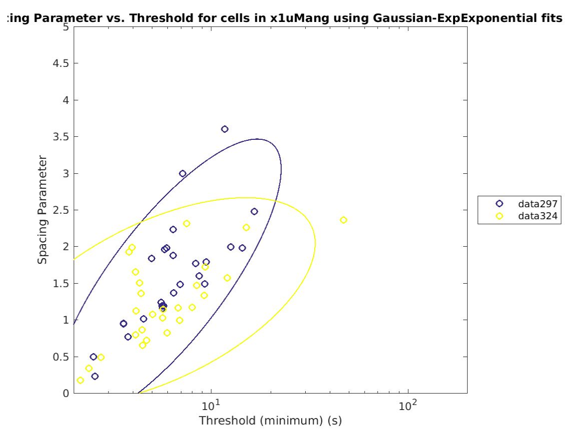




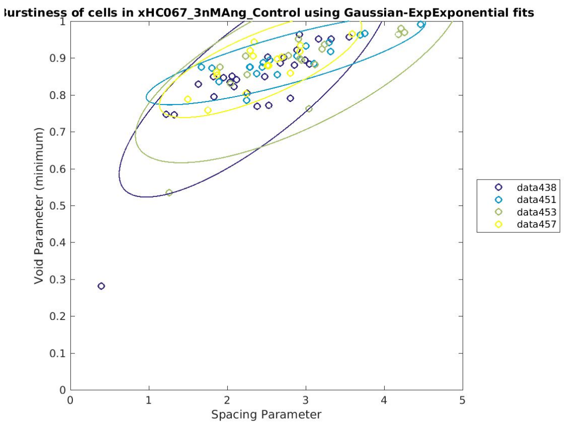


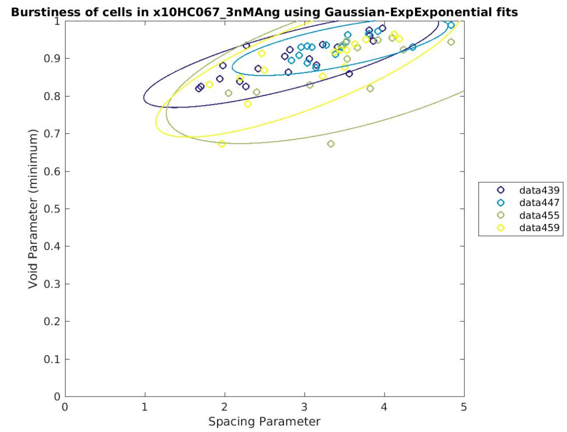


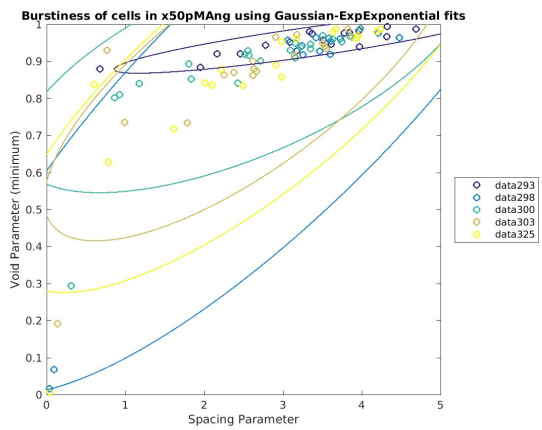


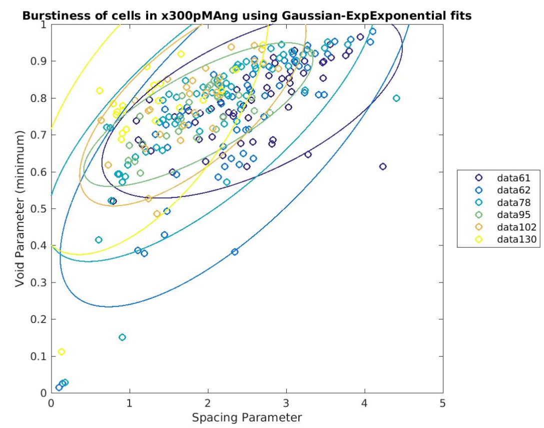


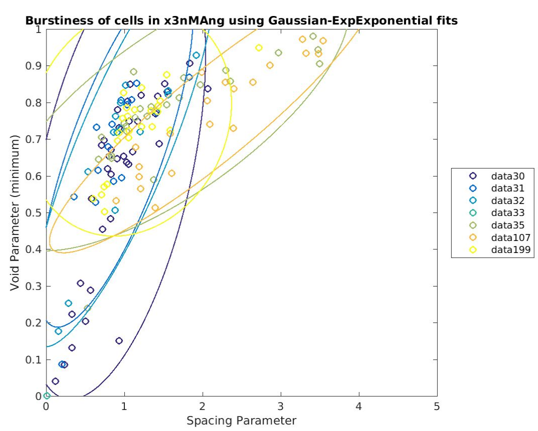
- **Void parameter vs. spacing parameter**

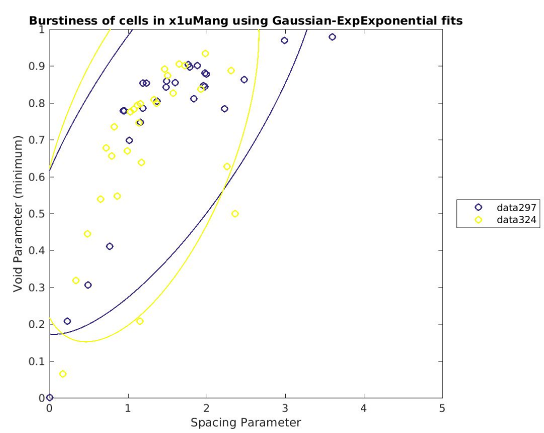












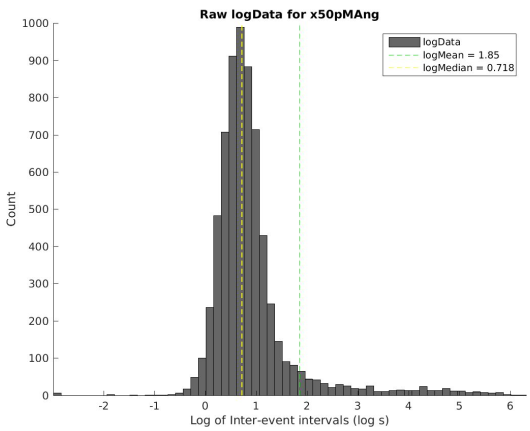
Plan for next week

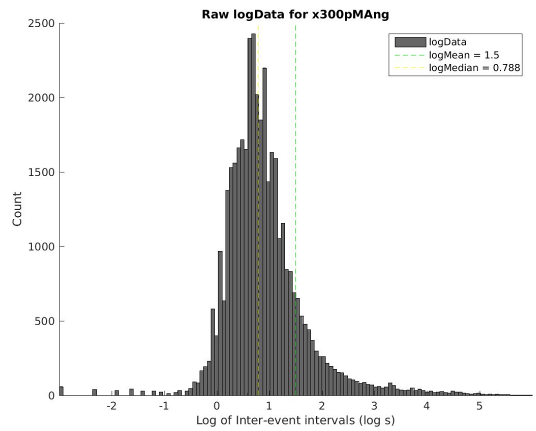
- Dynamic Clamp Data Analysis:
    - Extract **spike threshold** & **maximum slope time**
    - Plot correlation diagrams both ways and perform regression analyses
- Single Neuron Fitting
    - Adapt code so that **parallel MATLAB toolbox** could be called **without using a license**
    - Fit 12 traces (1 trace per condition) for each cell on Rivanna, **20 initial conditions**
    - Fit **all traces (5~15 traces per condition)** for each cell on Rivanna, 20 initial conditions
- Network
    - Implement **network simulations without HH currents** by predicting **burst onset time**, **spikes per burst** & **spike frequency** based on **maximum LTS slope time** and **value**.
    - Plot **autocorrelograms** and compute **oscillatory index**, **oscillation period**.
- Oscillation experiments
    - **Move** Paula's rig?
    - Learn how to perform **oscillation experiments**.

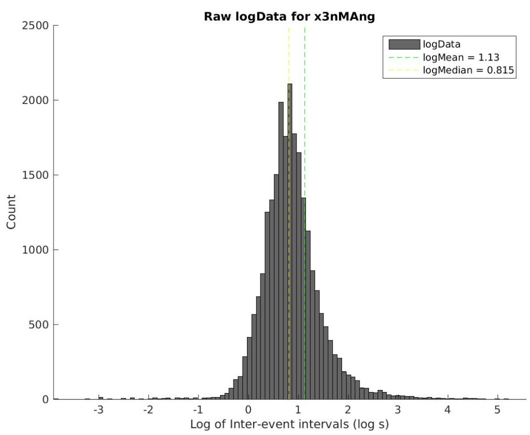
11/29/2017~12/10/2017

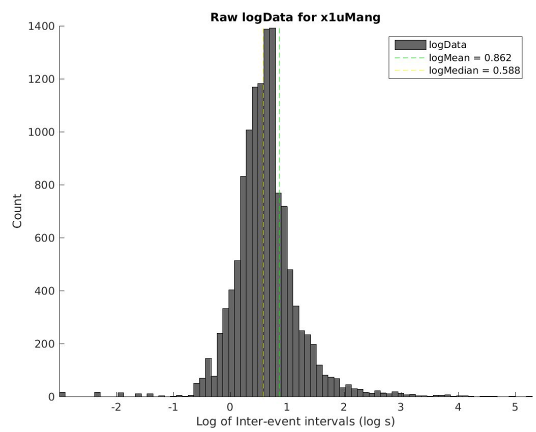
Fitting of Paula’s log(IEI) histograms

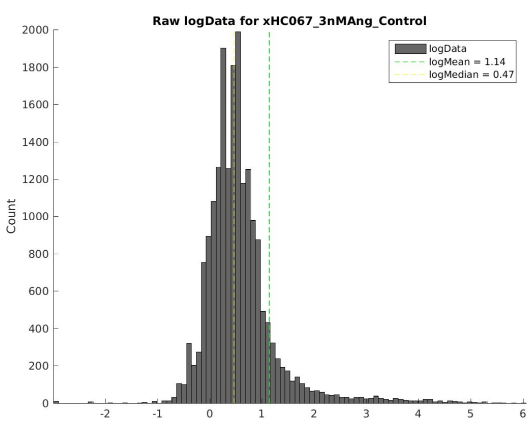
- Raw log(IEI) data
    - By Experiment

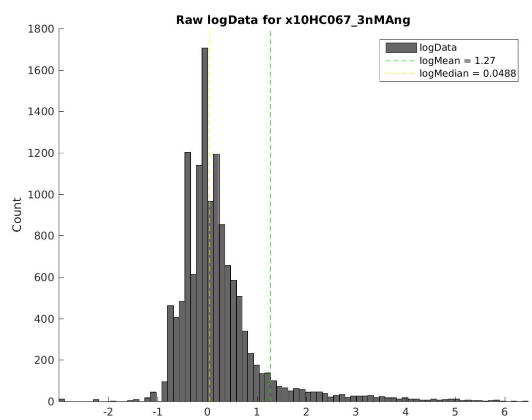




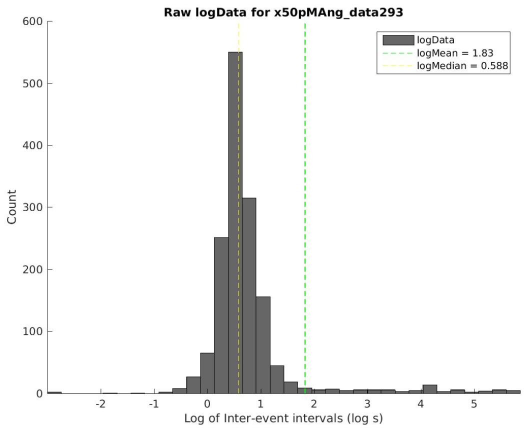


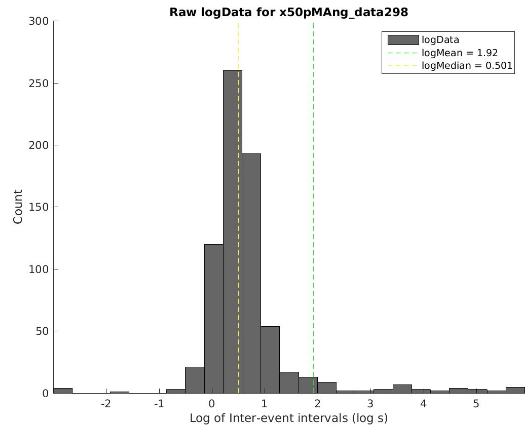


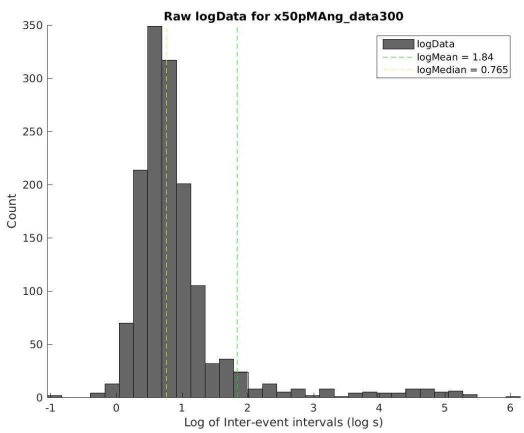


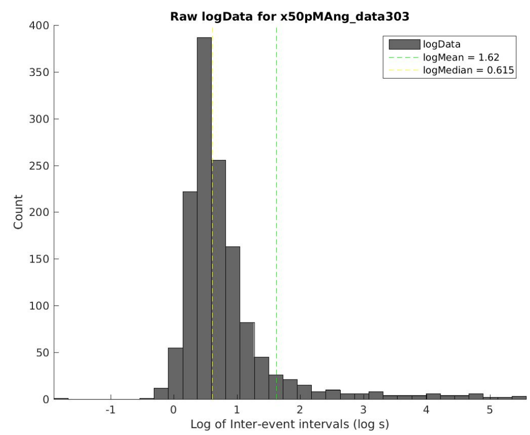


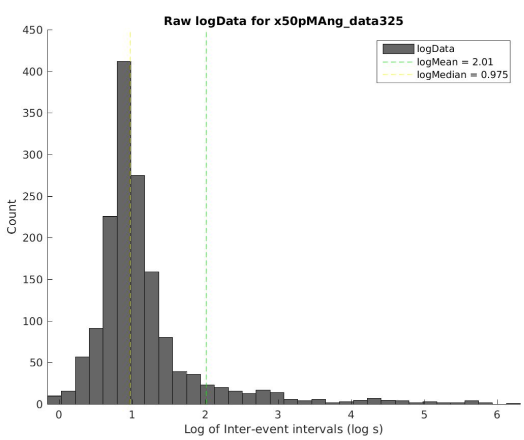
- By Slice


Raw logData for x50pMAng_data293
logData
logMean = 1.83
logMedian = 0.588
Count
Log of Inter-event intervals (log s)

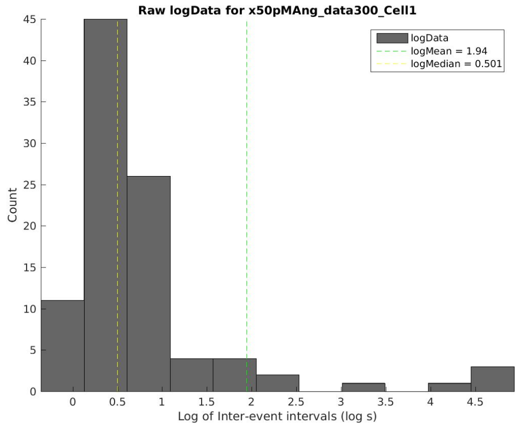

Raw logData for x50pMAng_data298
logData
logMean = 1.92
logMedian = 0.501
Count
Log of Inter-event intervals (log s)

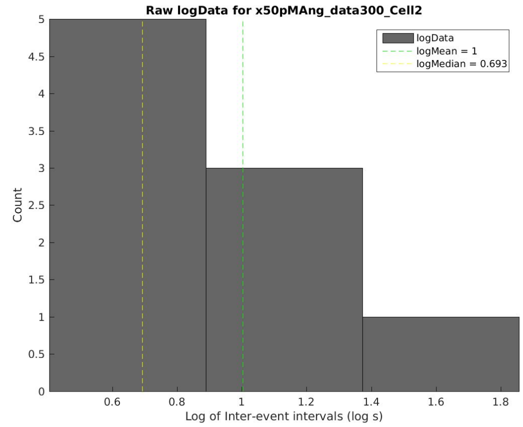

Raw logData for x50pMAng_data300
logData
logMean = 1.84
logMedian = 0.765
Count
Log of Inter-event intervals (log s)

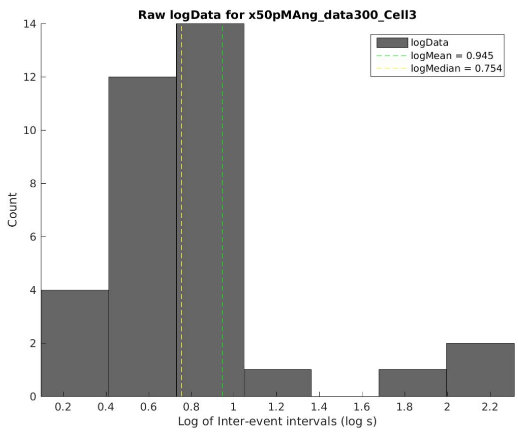

Raw logData for x50pMAng_data303
logData
logMean = 1.62
logMedian = 0.615
Count
Log of Inter-event intervals (log s)

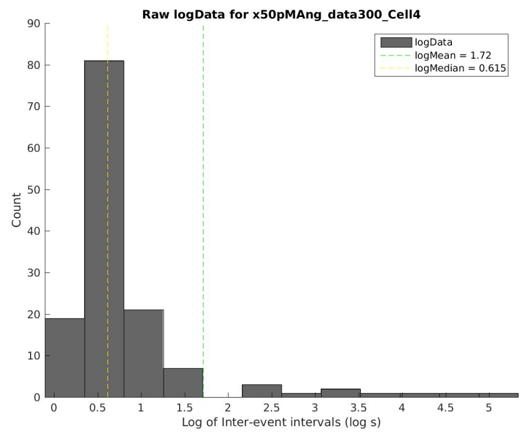

Raw logData for x50pMAng_data325
logData
logMean = 2.01
logMedian = 0.975
Count
Log of Inter-event intervals (log s)

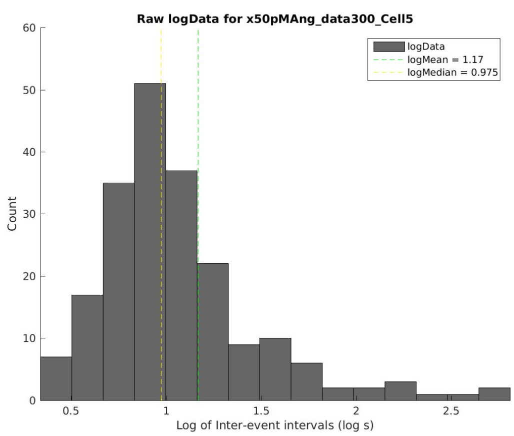
- By Cell

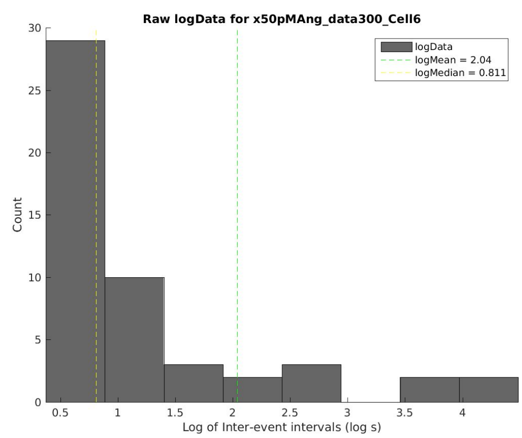

Raw logData for x50pMAng_data300_Cell1
logData
logMean = 1.94
logMedian = 0.501
Count
Log of Inter-event intervals (log s)


Raw logData for x50pMAng_data300_Cell2
logData
logMean = 1
logMedian = 0.693
Count
Log of Inter-event intervals (log s)

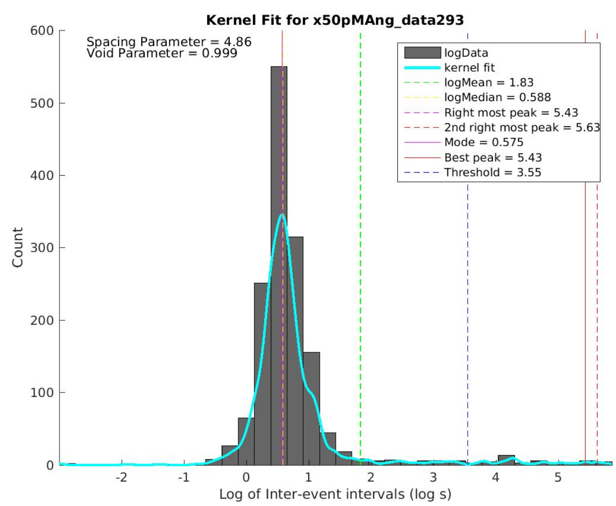

Raw logData for x50pMAng_data300_Cell3
logData
logMean = 0.945
logMedian = 0.754
Count
Log of Inter-event intervals (log s)

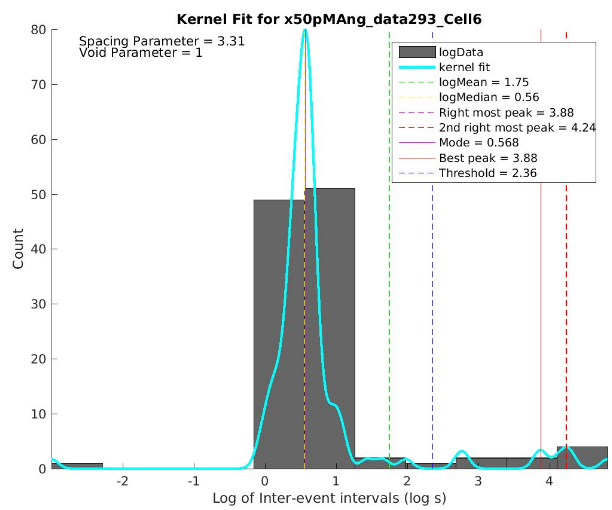

Raw logData for x50pMAng_data300_Cell4
logData
logMean = 1.72
logMedian = 0.615
Count
Log of Inter-event intervals (log s)


Raw logData for x50pMAng_data300_Cell5
logData
logMean = 1.17
logMedian = 0.975
Count
Log of Inter-event intervals (log s)

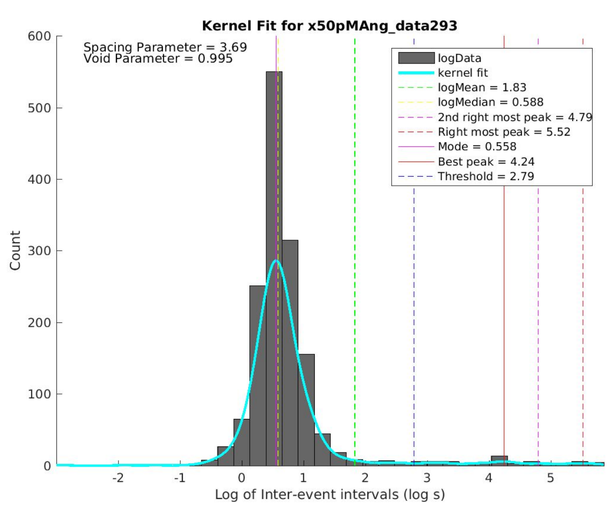

Raw logData for x50pMAng_data300_Cell6
logData
logMean = 2.04
logMedian = 0.811
Count
Log of Inter-event intervals (log s)

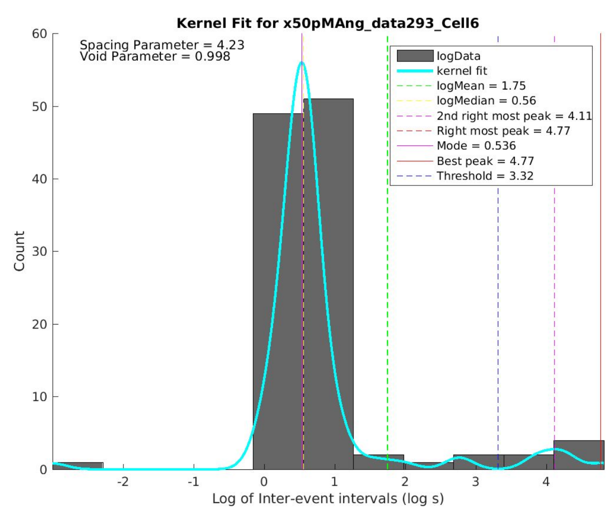
- Determination of intra-burst vs. inter-burst means and threshold:
  - **Method 1**: Compute **kernel distributions** with a **Gaussian kernel**. Choose **mode** as first peak; choose 2nd peak that has the **highest void parameter value** when paired with the mode. Choose **threshold** as the minimum between the two peaks.
    - Note: an Epanechnikov kernel did not change the bar graphs significantly
    - The default bandwidth Matlab uses is “**optimal for normal distributions.**” However, I cannot find how this was computed. Therefore, the newest version forces Gaussian kernels to have a bandwidth equal to **⅛ * standard deviation of the data**.
      - Default bandwidth: “optimal for normal distributions”



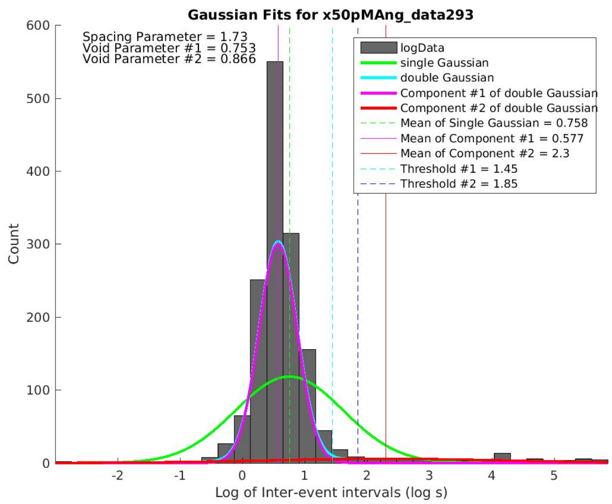


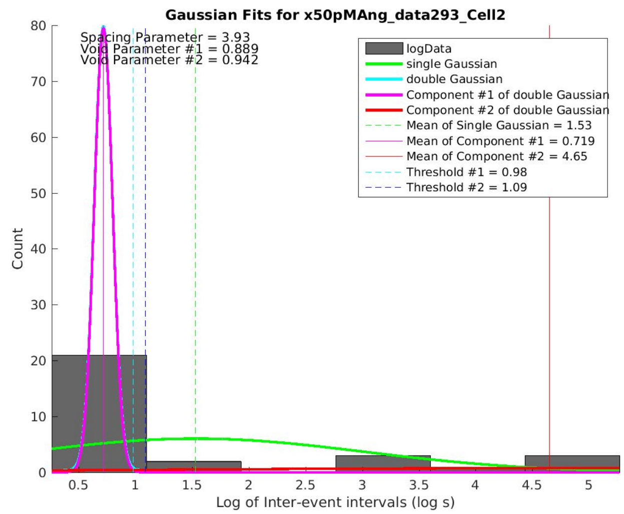
- Bandwidth = **⅛ * standard deviation of the data**



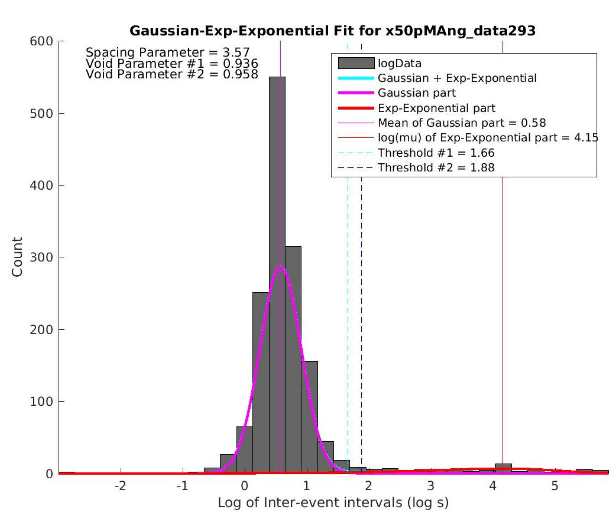


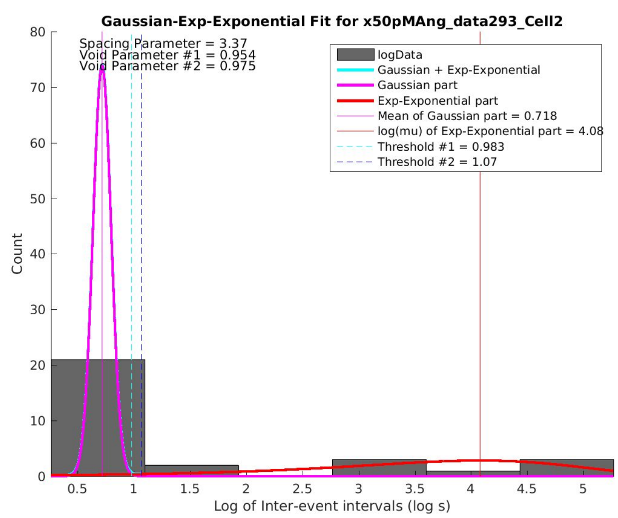
- **Method 2**: Fit with **2 Gaussian distributions** using the **maximum likelihood estimate**. **Threshold #1** is the **intersection** of the two component distributions. **Threshold #2** is the **minimum** between the two peaks in the combined distribution.



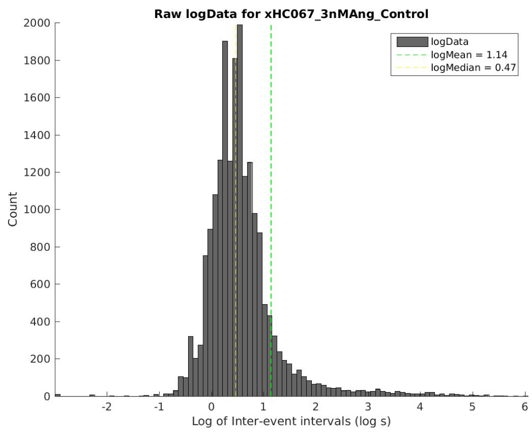


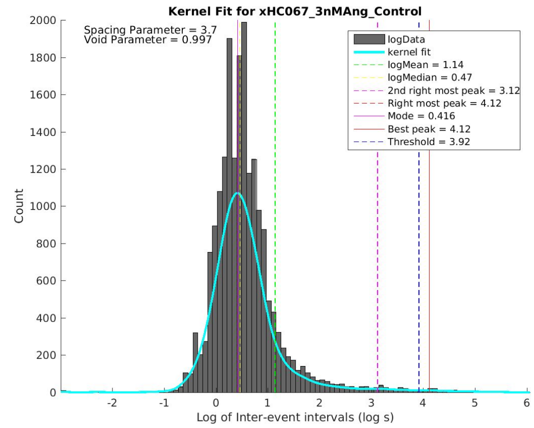
- **Method 3**: Fit with **a Gaussian distribution + an Exp-Exponential distribution** using the **maximum likelihood estimate**. **Threshold #1** is the **intersection** of the two component distributions. **Threshold #2** is the **minimum** between the two peaks in the combined distribution.

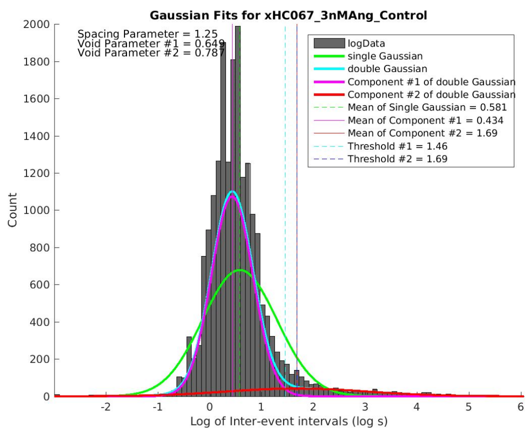


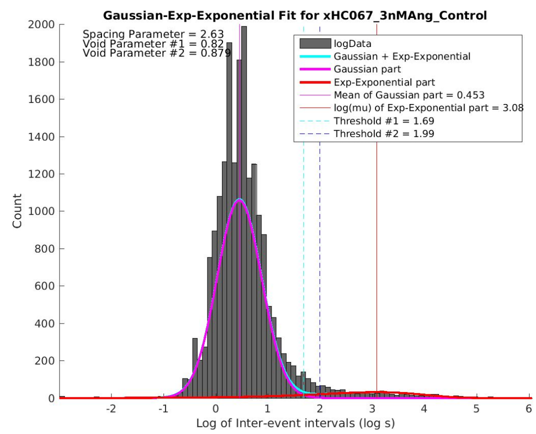


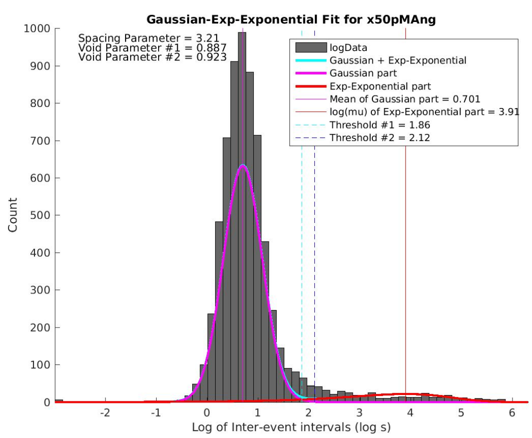
- Examples of fits and threshold determination
    - By Experiment

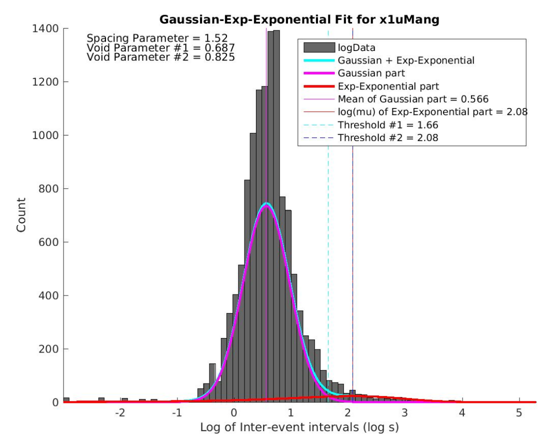




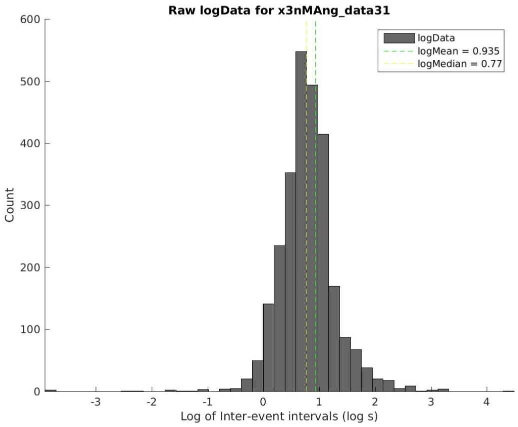


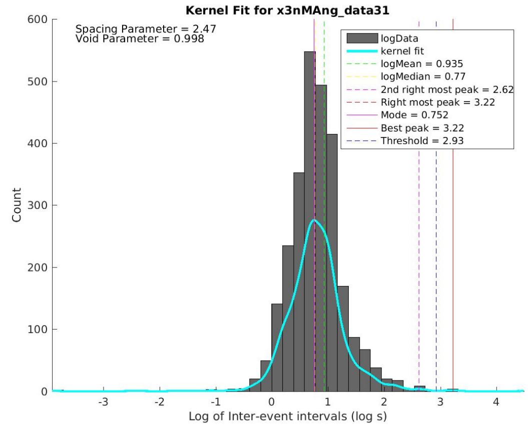


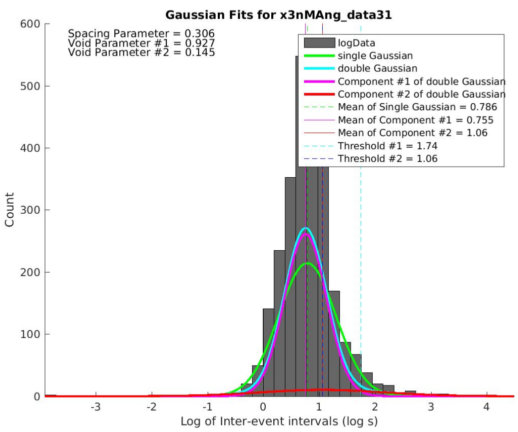


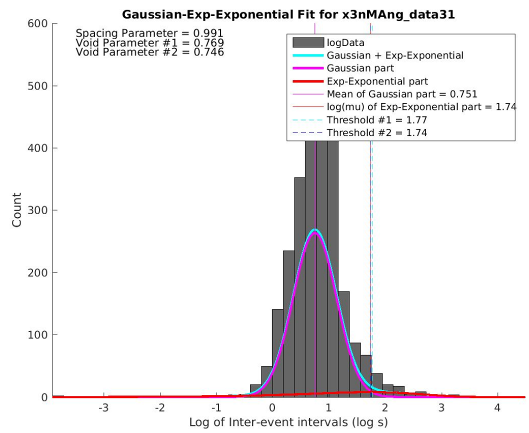


- By Slice

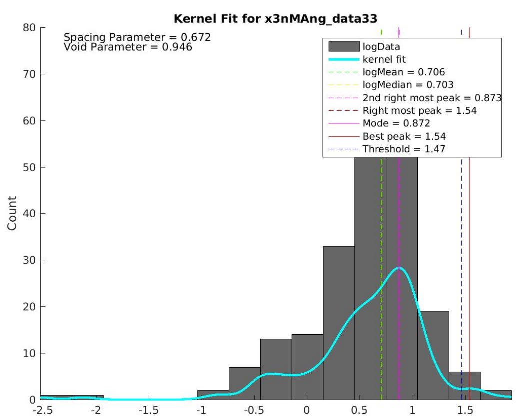


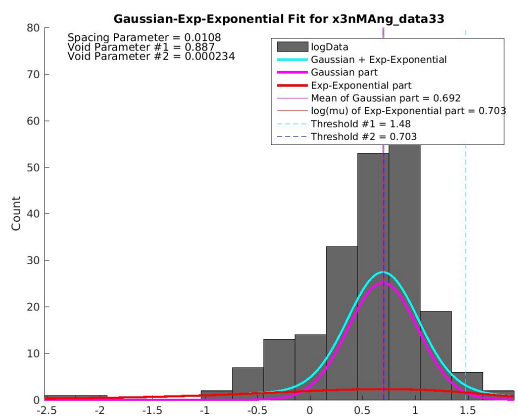




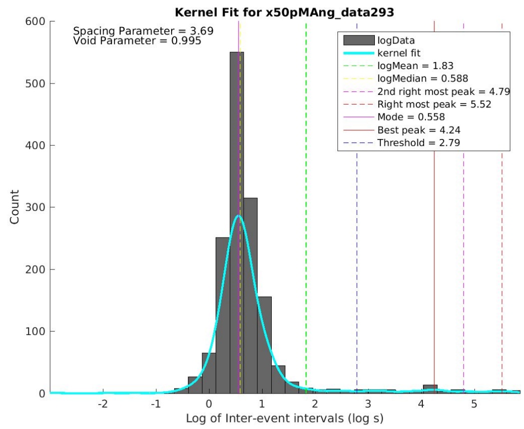


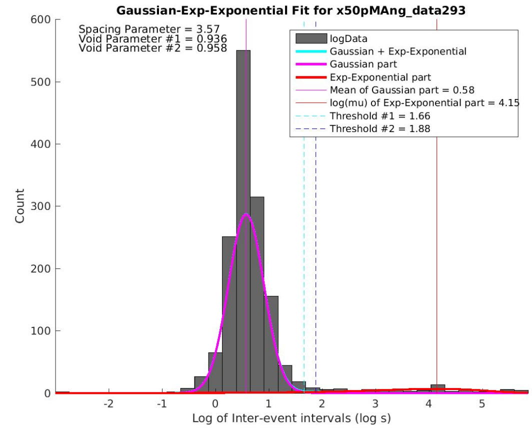
- For some slices, is there really a second peak? Note the difference in void parameter value computed from two different methods. In fact, there is only one cell recorded in this slice.

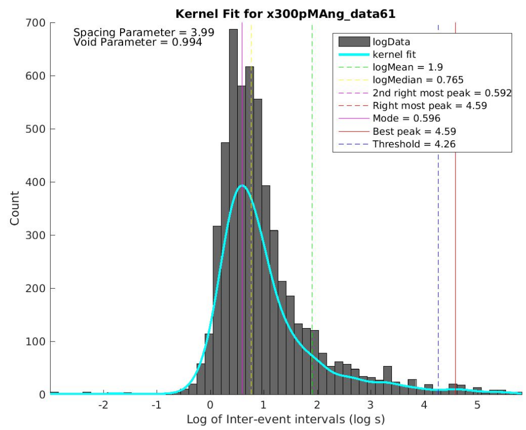


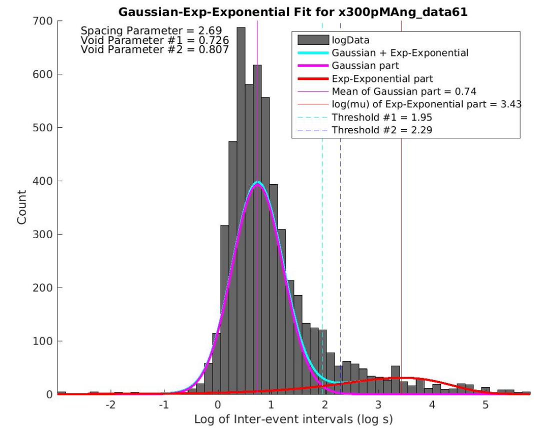


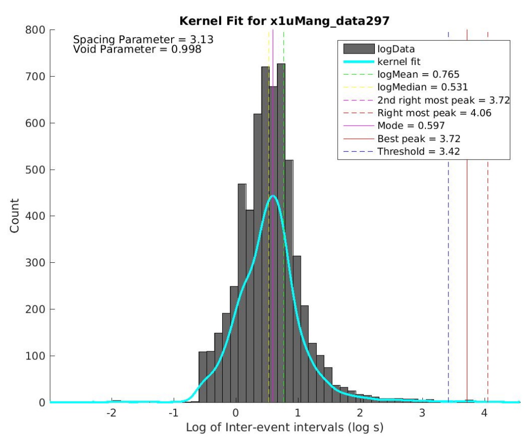
- The trend with increasing drug concentration:

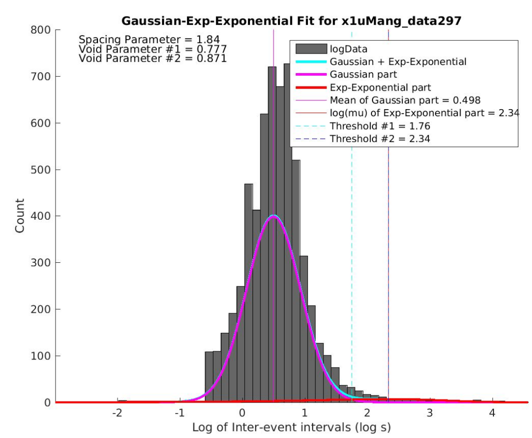




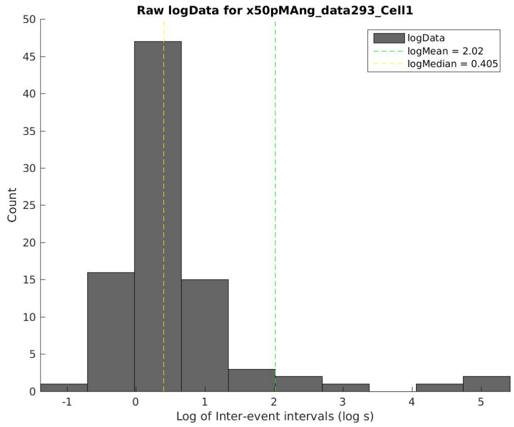


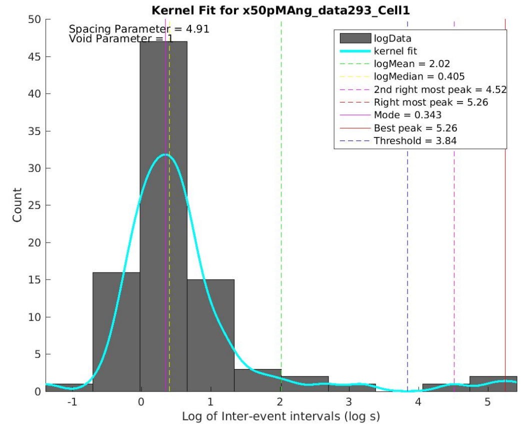


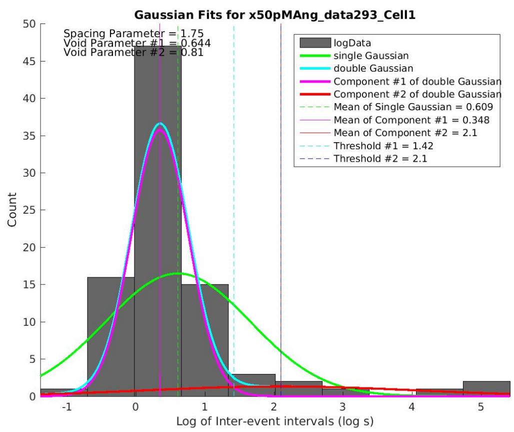


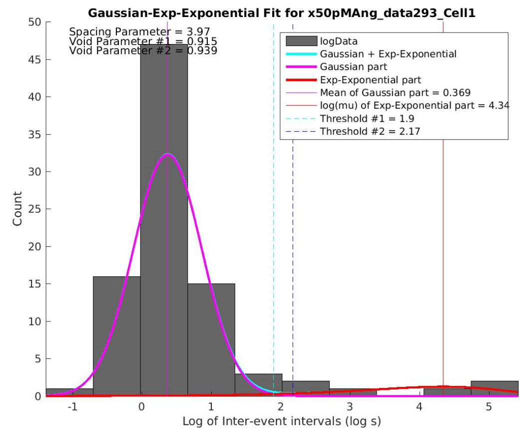


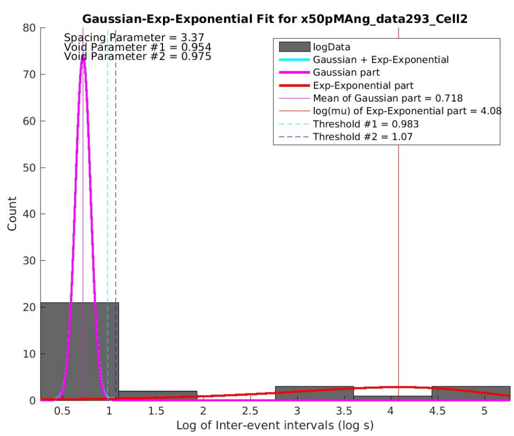
- By Cell

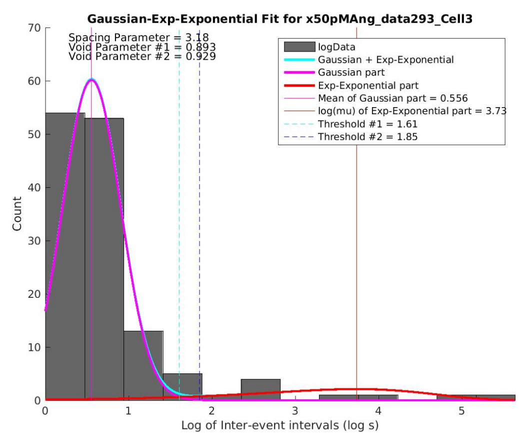

Raw logData for x50pMAng_data293_Cell1
logData
logMean = 2.02
logMedian = 0.405
Count
Log of Inter-event intervals (log s)


Kernel Fit for x50pMAng_data293_Cell1
Spacing Parameter = 4.91
Void Parameter = 1
logData
kernel fit
logMean = 2.02
logMedian = 0.405
2nd right most peak = 4.52
Right most peak = 5.26
Mode = 0.343
Best peak = 5.26
Threshold = 3.84
Count
Log of Inter-event intervals (log s)

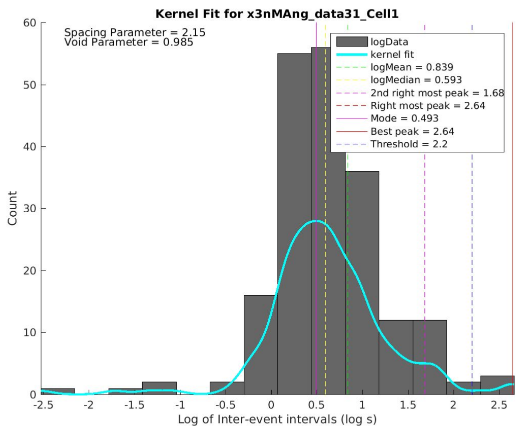

Gaussian Fits for x50pMAng_data293_Cell1
Spacing Parameter = 1.75
Void Parameter #1 = 0.644
Void Parameter #2 = 0.81
logData
single Gaussian
double Gaussian
Component #1 of double Gaussian
Component #2 of double Gaussian
Mean of Single Gaussian = 0.609
Mean of Component #1 = 0.348
Mean of Component #2 = 2.1
Threshold #1 = 1.42
Threshold #2 = 2.1
Count
Log of Inter-event intervals (log s)

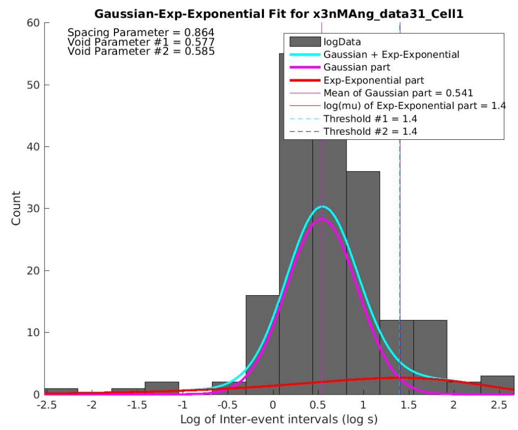

Gaussian-Exp-Exponential Fit for x50pMAng_data293_Cell1
Spacing Parameter = 3.97
Void Parameter #1 = 0.915
Void Parameter #2 = 0.939
logData
Gaussian + Exp-Exponential
Gaussian part
Exp-Exponential part
Mean of Gaussian part = 0.369
log(mu) of Exp-Exponential part = 4.34
Threshold #1 = 1.9
Threshold #2 = 2.17
Count
Log of Inter-event intervals (log s)

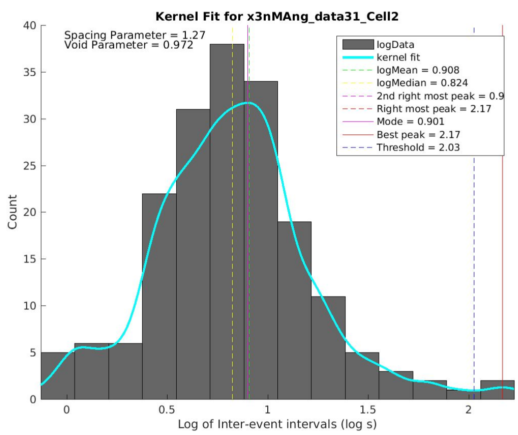

Gaussian-Exp-Exponential Fit for x50pMAng_data293_Cell2
Spacing Parameter = 3.37
Void Parameter #1 = 0.954
Void Parameter #2 = 0.975
logData
Gaussian + Exp-Exponential
Gaussian part
Exp-Exponential part
Mean of Gaussian part = 0.718
log(mu) of Exp-Exponential part = 4.08
Threshold #1 = 0.983
Threshold #2 = 1.07
Count
Log of Inter-event intervals (log s)

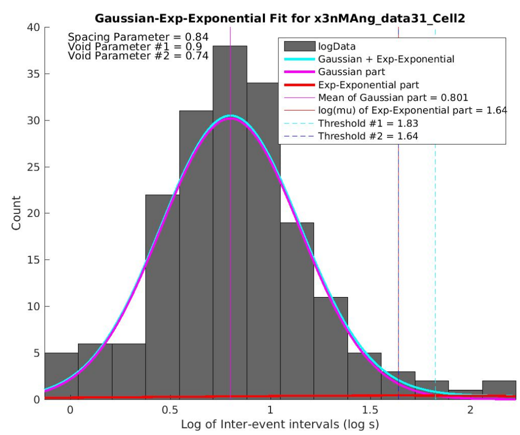

Gaussian-Exp-Exponential Fit for x50pMAng_data293_Cell3
Spacing Parameter = 3.18
Void Parameter #1 = 0.893
Void Parameter #2 = 0.929
logData
Gaussian + Exp-Exponential
Gaussian part
Exp-Exponential part
Mean of Gaussian part = 0.556
log(mu) of Exp-Exponential part = 3.73
Threshold #1 = 1.61
Threshold #2 = 1.85
Count
Log of Inter-event intervals (log s)

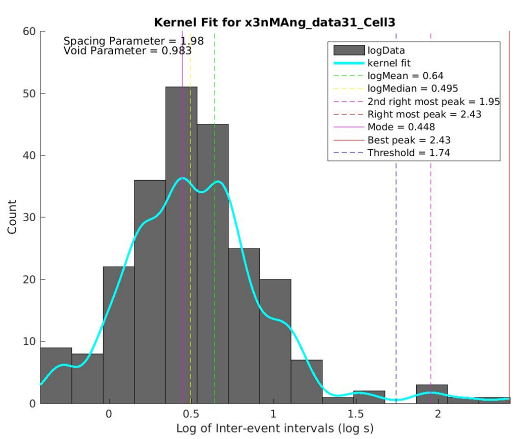
- ○ Did slice **data31** really have a second peak? A look at the distributions for each cell in the slice:

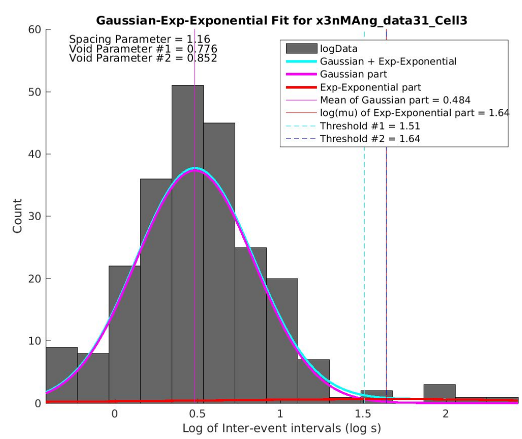




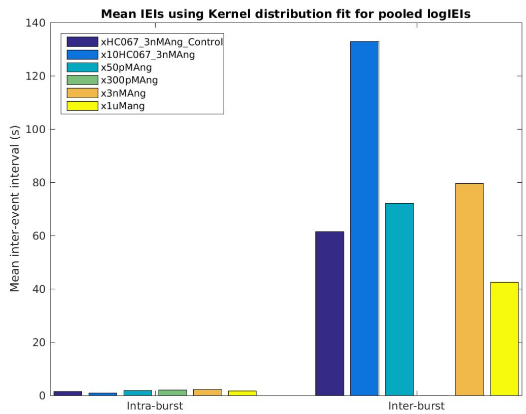


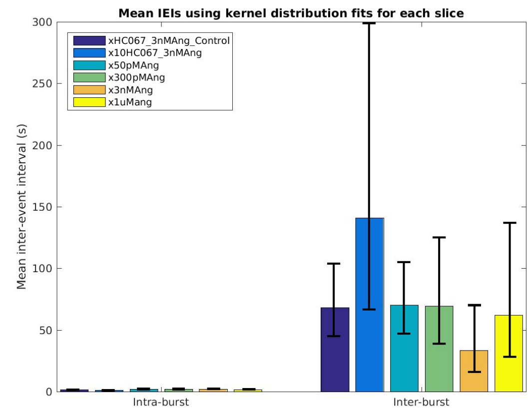


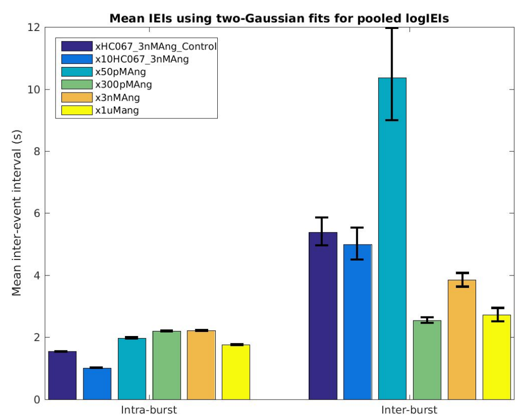


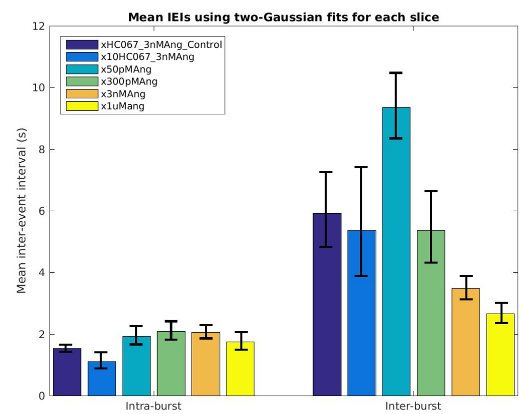


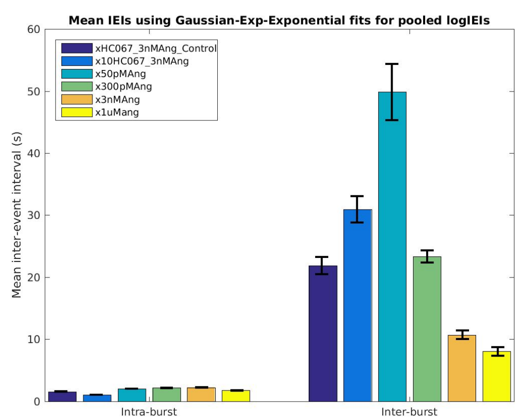
- Statistics of fits and threshold determination
    - Intra-burst means vs. inter-burst means

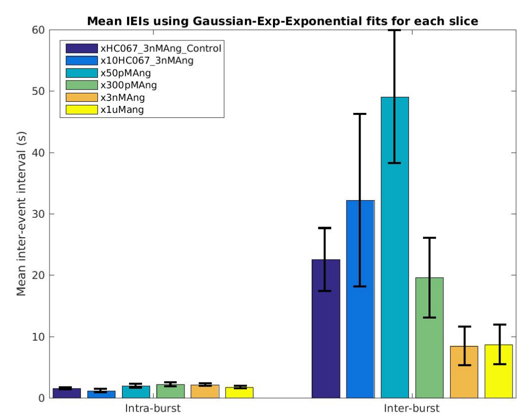


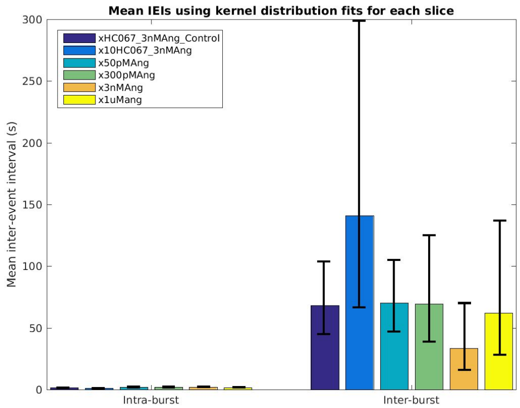


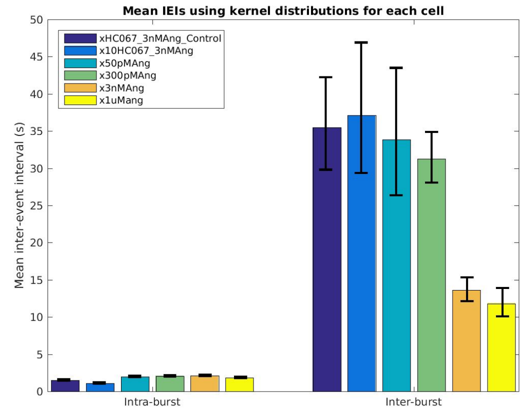


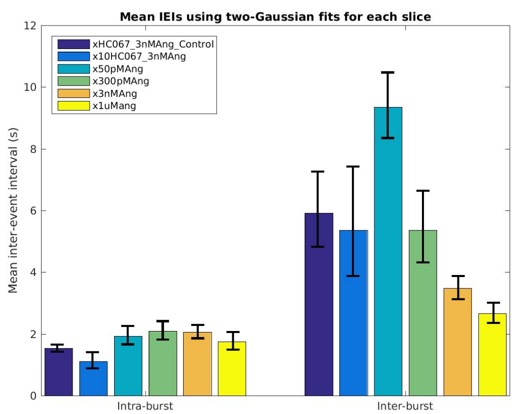


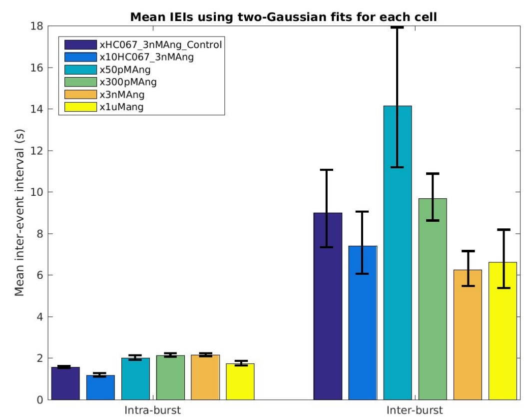


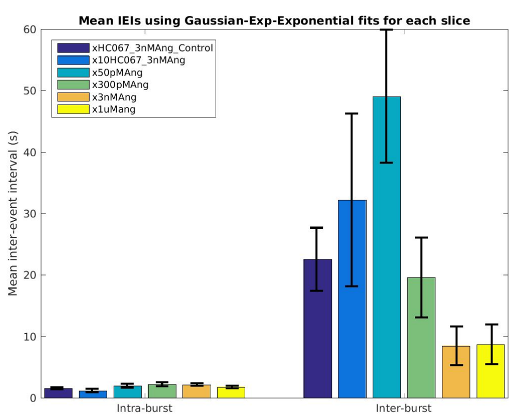


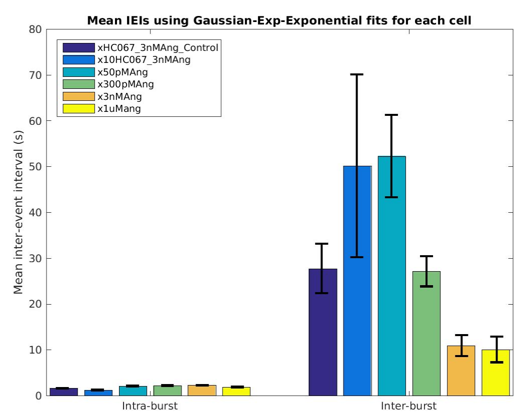

Mean IEIs using kernel distribution fits for each slice
xHC067_3nMAng_Control
x10HC067_3nMAng
x50pMAng
x300pMAng
x3nMAng
x1uMang
Mean inter-event interval (s)
0
50
100
150
200
250
300
Intra-burst
Inter-burst


Mean IEIs using kernel distributions for each cell
xHC067_3nMAng_Control
x10HC067_3nMAng
x50pMAng
x300pMAng
x3nMAng
x1uMang
Mean inter-event interval (s)
0
5
10
15
20
25
30
35
40
45
50
Intra-burst
Inter-burst

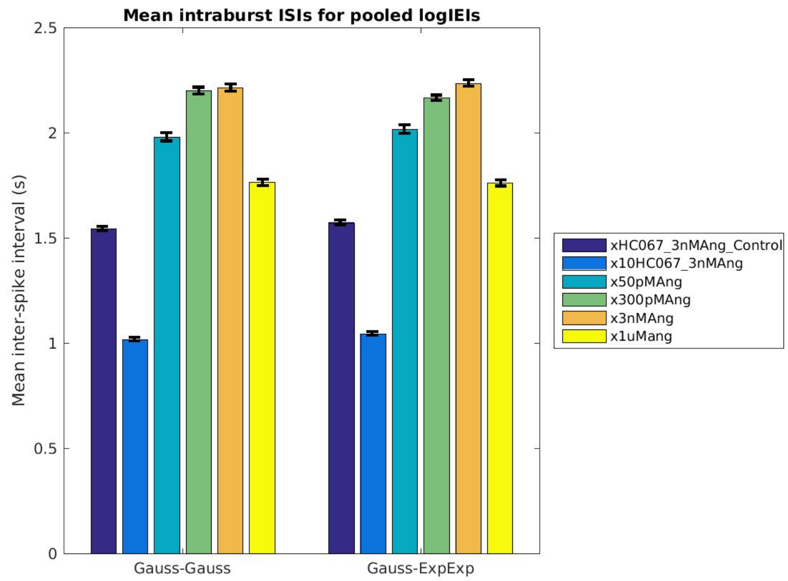

Mean IEIs using two-Gaussian fits for each slice
xHC067_3nMAng_Control
x10HC067_3nMAng
x50pMAng
x300pMAng
x3nMAng
x1uMang
Mean inter-event interval (s)
0
2
4
6
8
10
12
Intra-burst
Inter-burst

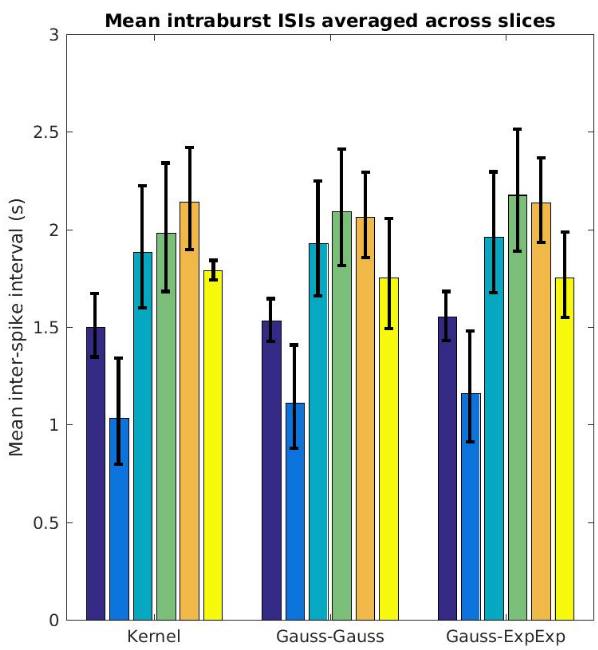

Mean IEIs using two-Gaussian fits for each cell
xHC067_3nMAng_Control
x10HC067_3nMAng
x50pMAng
x300pMAng
x3nMAng
x1uMang
Mean inter-event interval (s)
0
2
4
6
8
10
12
14
16
18
Intra-burst
Inter-burst

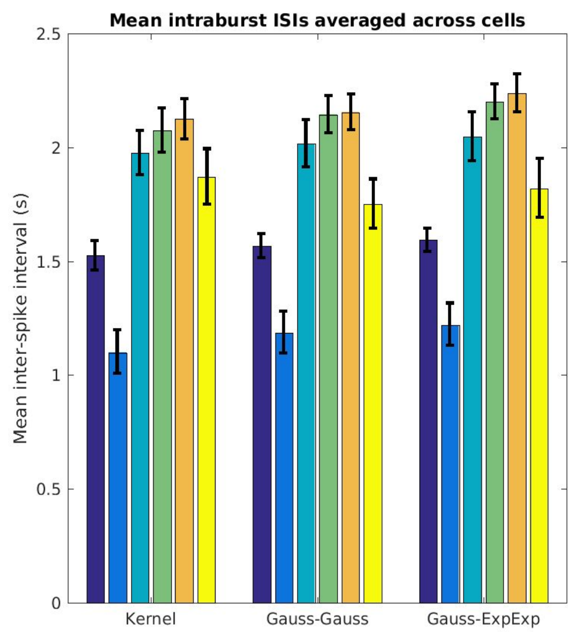

Mean IEIs using Gaussian-Exp-Exponential fits for each slice
xHC067_3nMAng_Control
x10HC067_3nMAng
x50pMAng
x300pMAng
x3nMAng
x1uMang
Mean inter-event interval (s)
0
10
20
30
40
50
60
Intra-burst
Inter-burst


Mean IEIs using Gaussian-Exp-Exponential fits for each cell
xHC067_3nMAng_Control
x10HC067_3nMAng
x50pMAng
x300pMAng
x3nMAng
x1uMang
Mean inter-event interval (s)
0
10
20
30
40
50
60
70
80
Intra-burst
Inter-burst

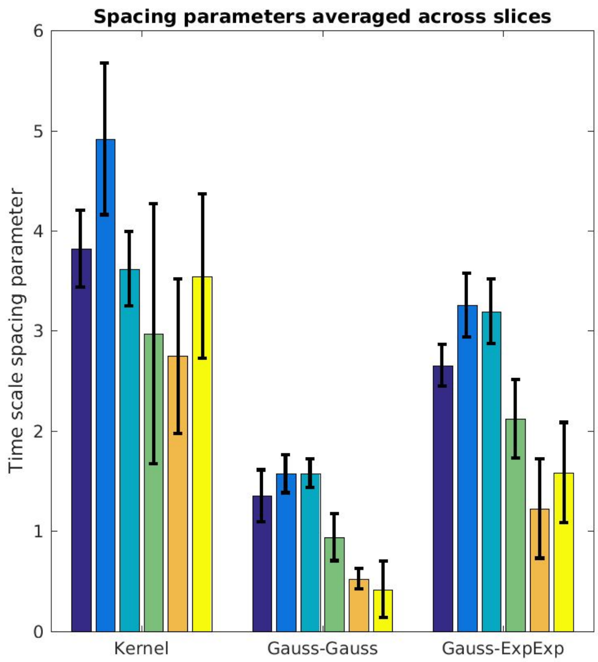
- Intra-burst means

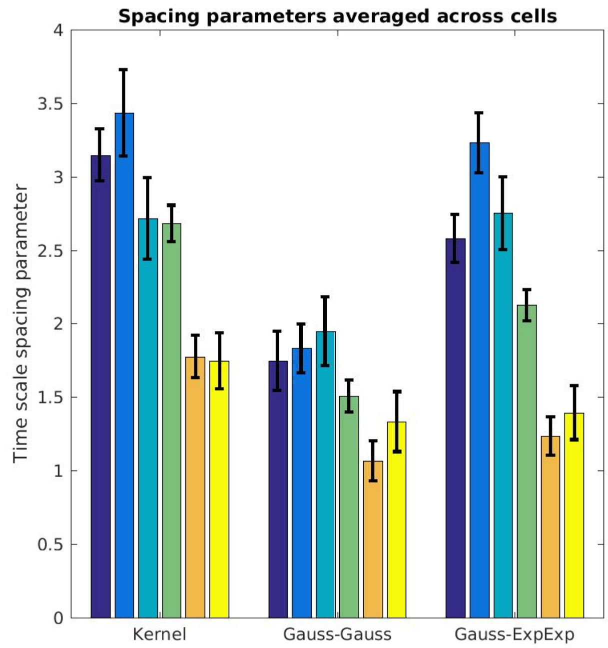




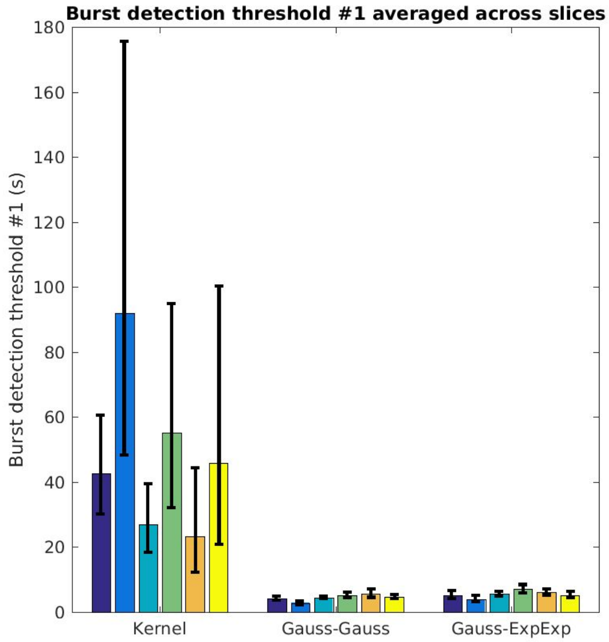


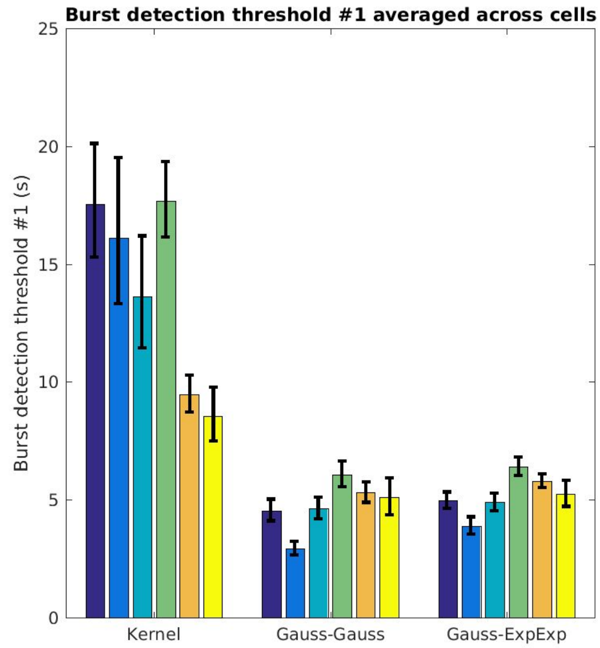
- Spacing parameters (Difference between intra-burst and inter-burst mean)



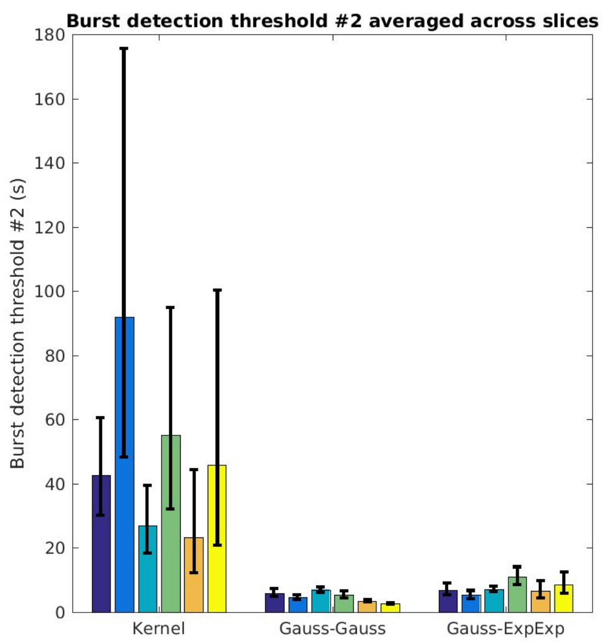


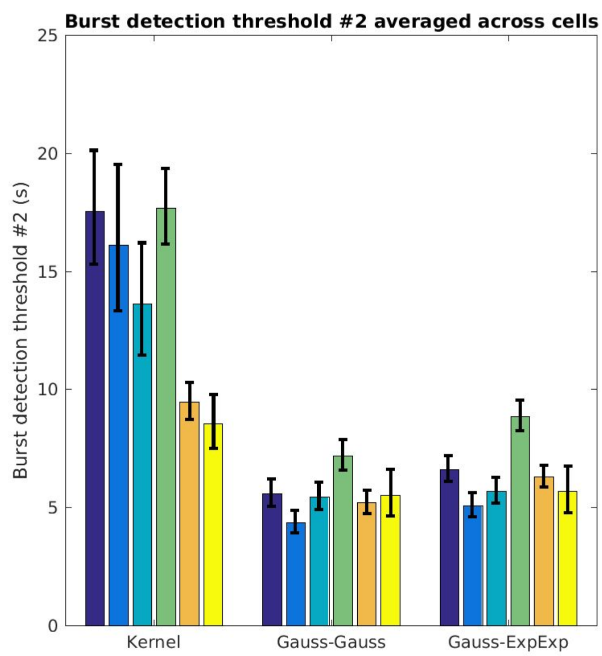
- Threshold #1s (intersections)



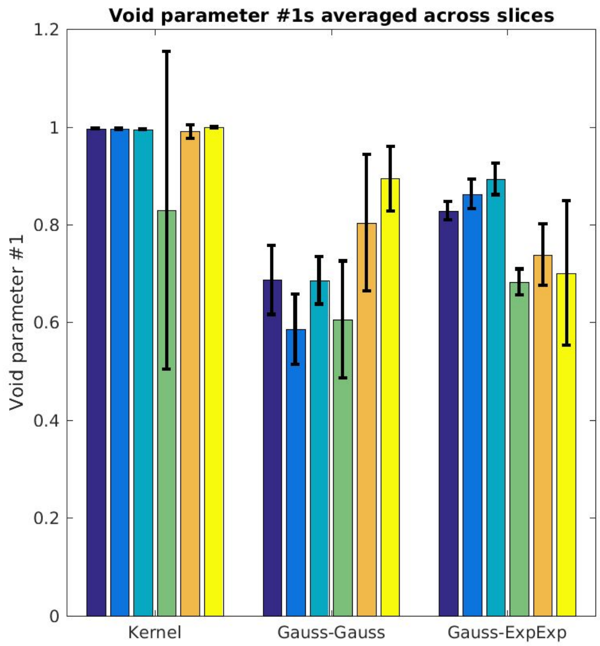


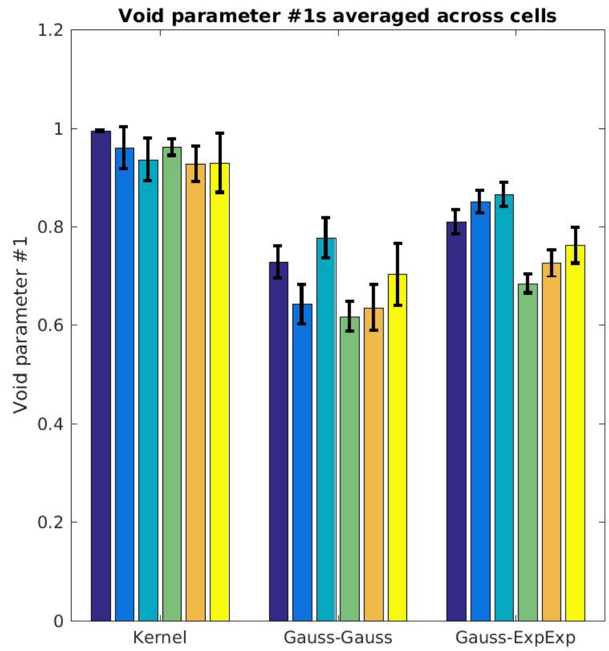
- Threshold #2s (minimums)



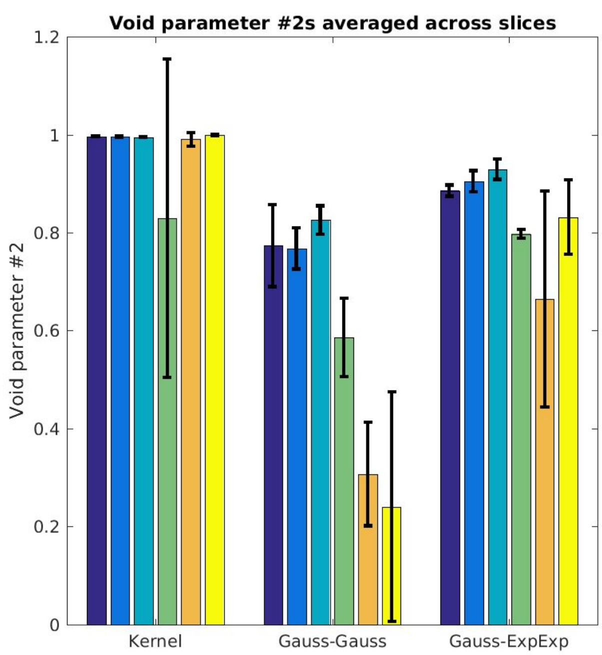


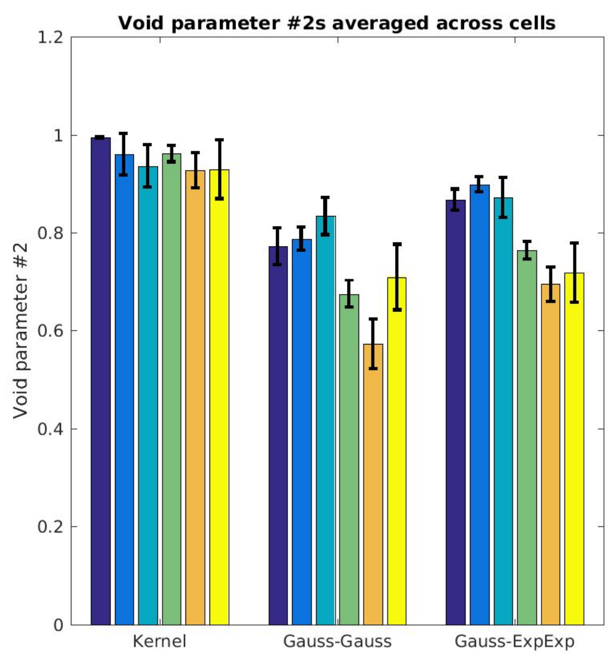
- Void parameter #1s (intersections)





- Void parameter #2s (minimums)





Plan for next week

- Paula’s IEIs
  - Overlay fits of **each slice** of the **same experimen**t on top of each other. Overlay fits of **each cell** of the **same slice** on top of each other
  - Plot **histograms** of interburst means, intra-burst means, spacing parameters, thresholds, void parameters **for each cell colored by slice**
  - Discuss with Paula
- Dynamic Clamp Data Analysis:
  - Extract **spike threshold** & **maximum slope time**
  - Plot correlation diagrams both ways and perform regression analyses
- Single Neuron Fitting
  - Figure out problem running **NEURON** on Rivanna (with ACRS staff)
  - Adapt code so that **parallel MATLAB toolbox** could be called **without using a license**
  - Fit 12 traces (1 trace per condition) for each cell on Rivanna, **20 initial conditions**
  - Fit **all traces (5~15 traces per condition)** for each cell on Rivanna, 20 initial conditions
- Network
  - Implement **network simulations without HH currents** by predicting **burst onset time**, **spikes per burst** & **spike frequency** based on **maximum LTS slope time** and **value**.
  - Plot **autocorrelograms** and compute **oscillatory index**, **oscillation period**.
- Oscillation experiments
  - **Move** Paula’s rig?
  - Learn how to perform **oscillation experiments**.

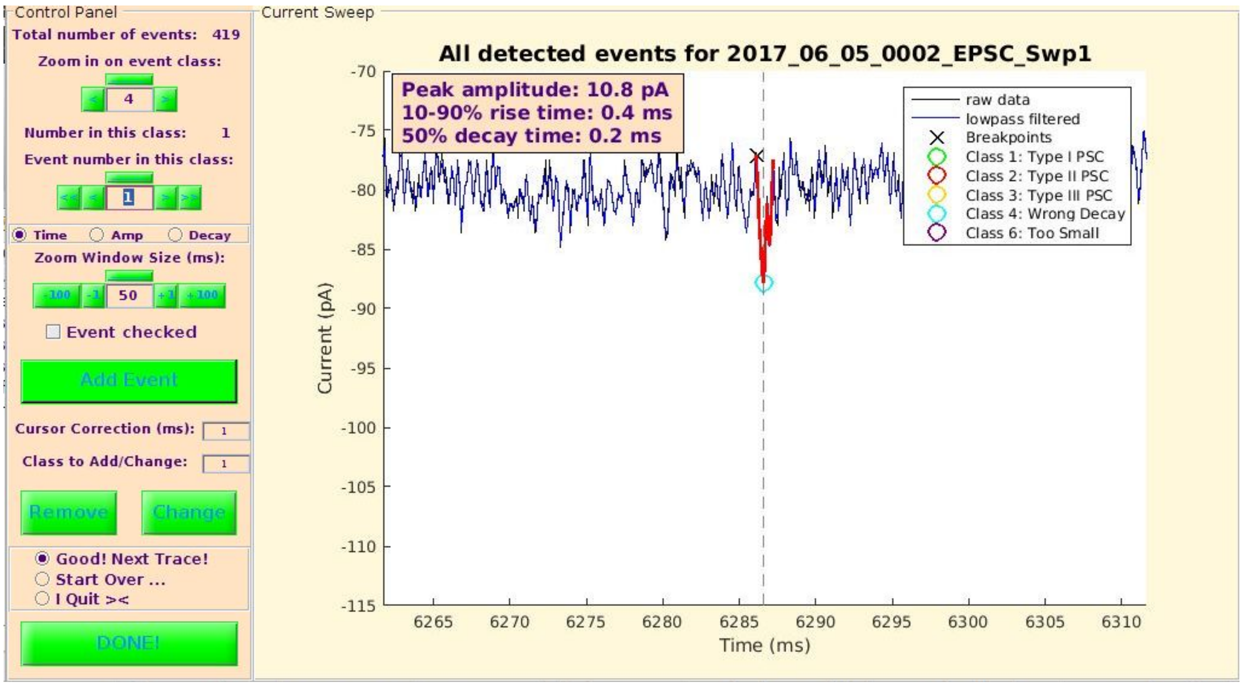
10/16/2017~10/18/2017

Updates to minEASE

- Now creates **empty output files** if no events are detected, so that events are combined whenever all sweeps are passed at least once.

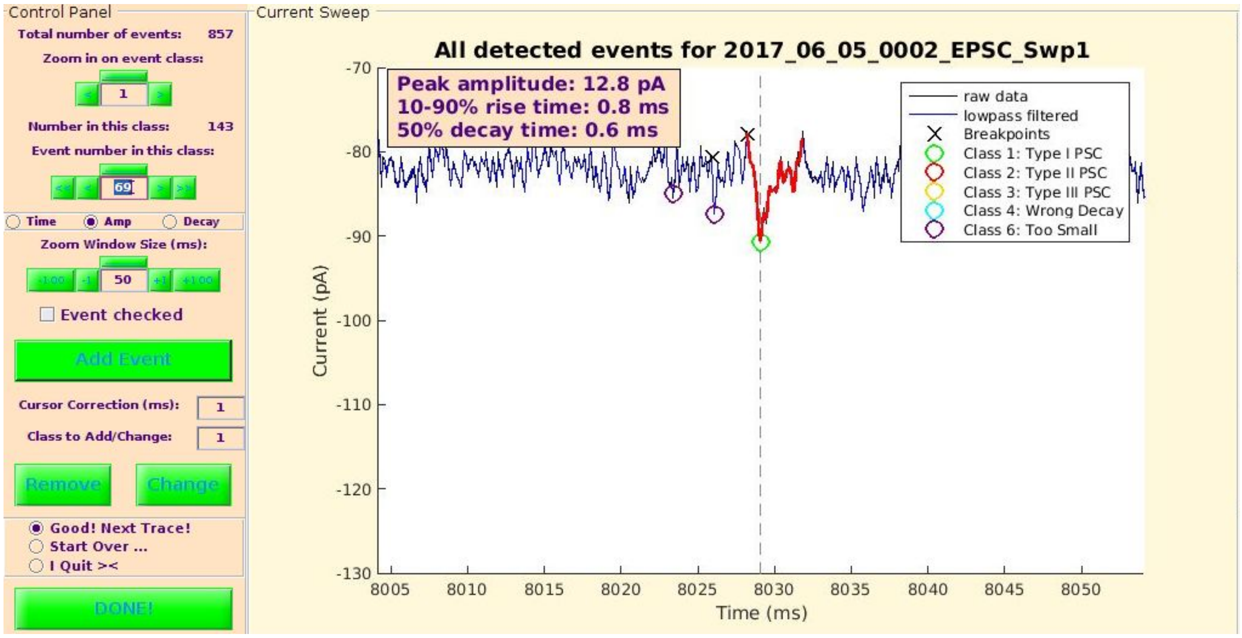
- Now allows the manual mode to be skipped
    - Usage: **minEASE('miniTest_Peter.xlsx', 'SkipManual', true);**

- Added a parameter to **exclude too short events** (minimum decay time)
    - Add a column to the input Excel file called "**Minimum PSC 50% Decay Time (ms)**"; if no such column is present, the default is **0.3 ms**
    - **Class 4** events are now called "**Wrong decay**" events
    - An example of a class 4 event:

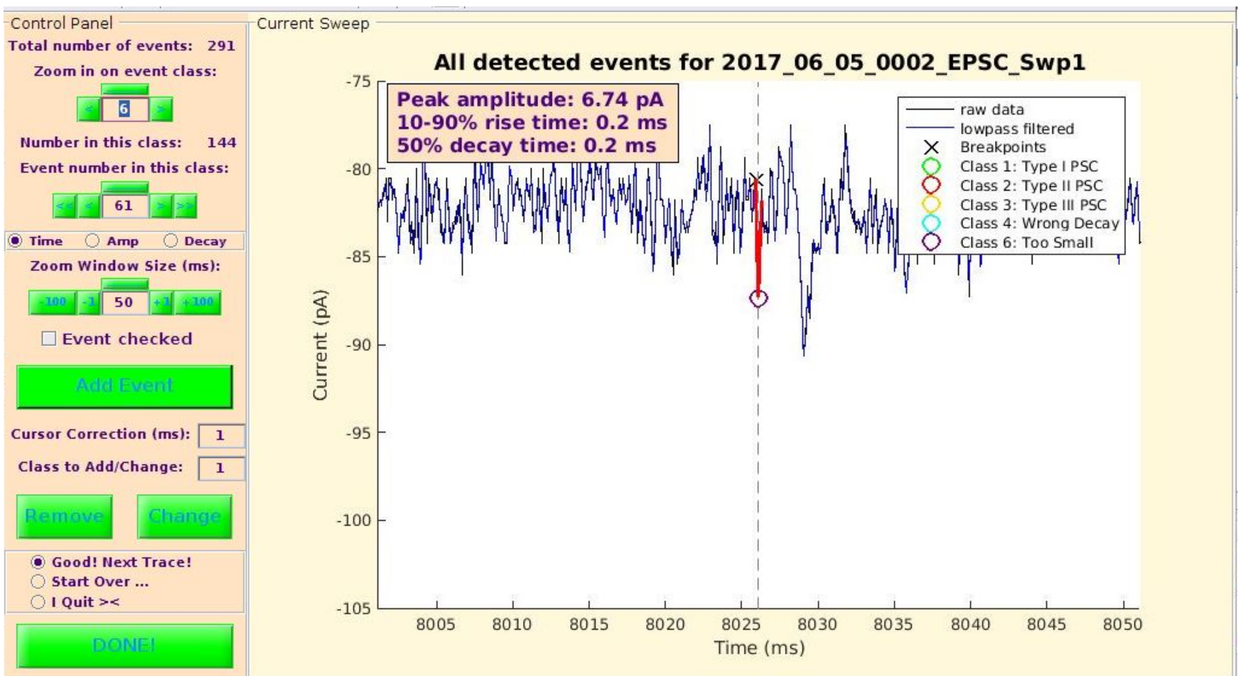


- Added parameters to allow a **directional event** to have a breakpoint below baseline only up to a certain percentage of the peak amplitude
    - Add a column to the input Excel file called "**Baseline Window Size (ms)**"; if no such column is present, the default is **5 ms**
    - Add a column called "**Maximum Below Baseline Percentage (%)**"; if no such column is present, the default is **100 %**
    - Direction Factor * (Baseline value - Breakpoint value)/Peak Amplitude x 100% < Maximum Below Baseline Percentage

- An example of an event **present at 100%**:



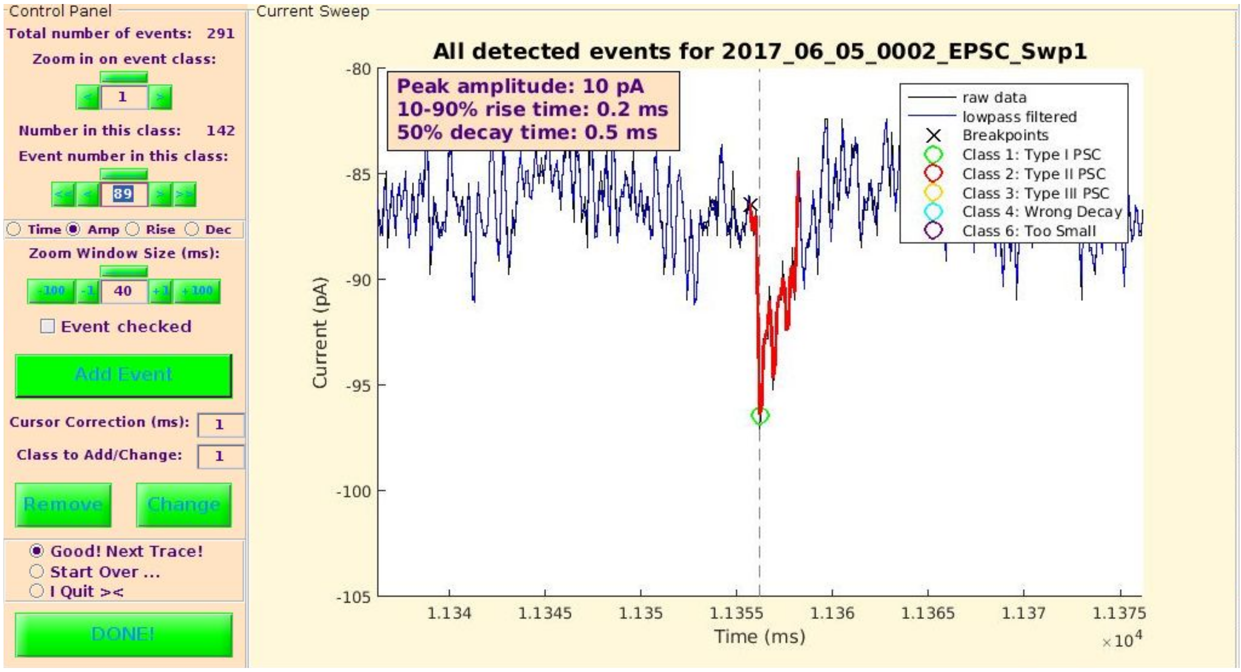
- The same event is **not present at 30%**:



Note that the number of events for class 1 is now **142** (not much changed)

20171022

- Events are now ranked internally to allow for different modes of **incrementing/decrementing event numbers**
    - By **time (default)**
    - By **amplitude**
    - By **10-90% rise time**
    - By **50% decay time**

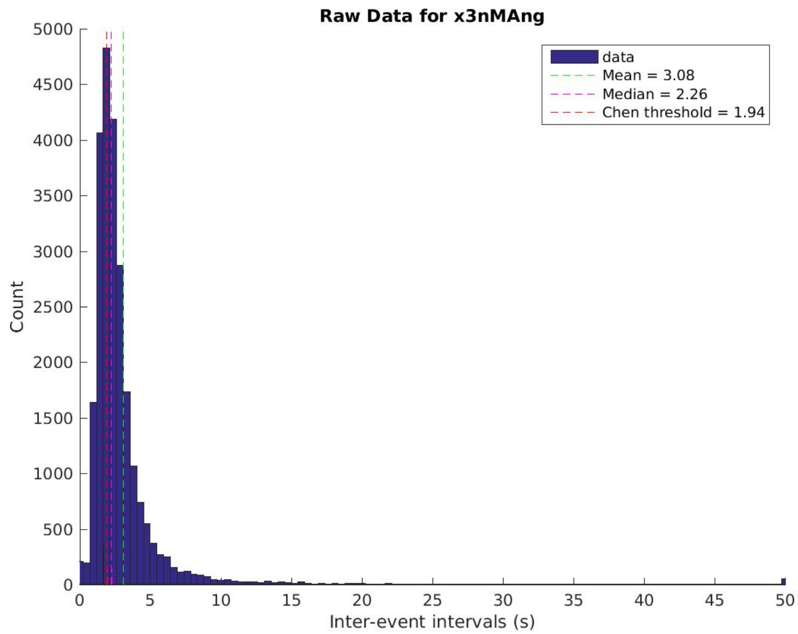


- Fixed **bug**: Wrong prompt occurred when changing from class 8
    - Moved **verify_classNoNew()** into **change_class()** so that it is executed after computing next-event-dependent statistics in case an event is added

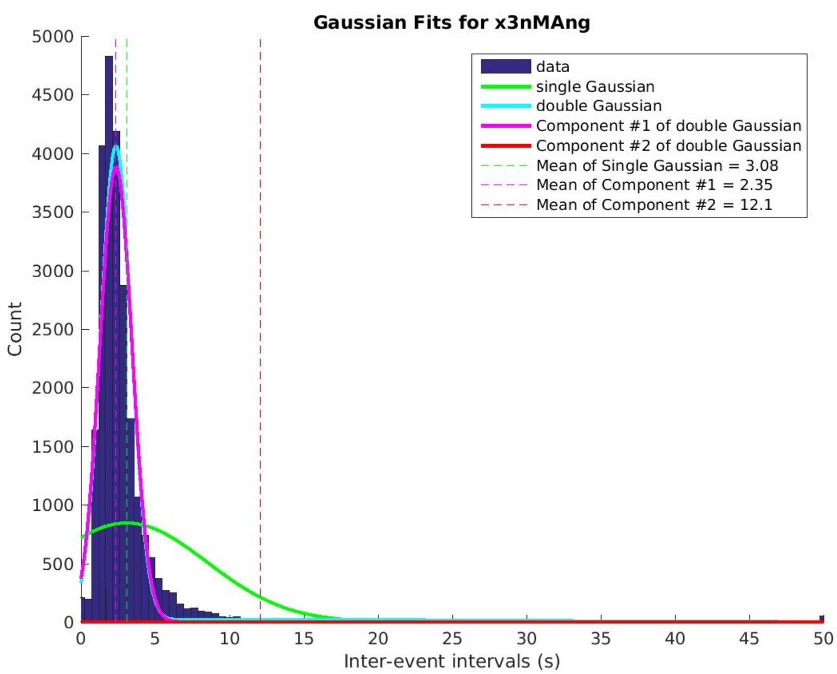
10/19/2017

Fitting of Paula's IEI histograms

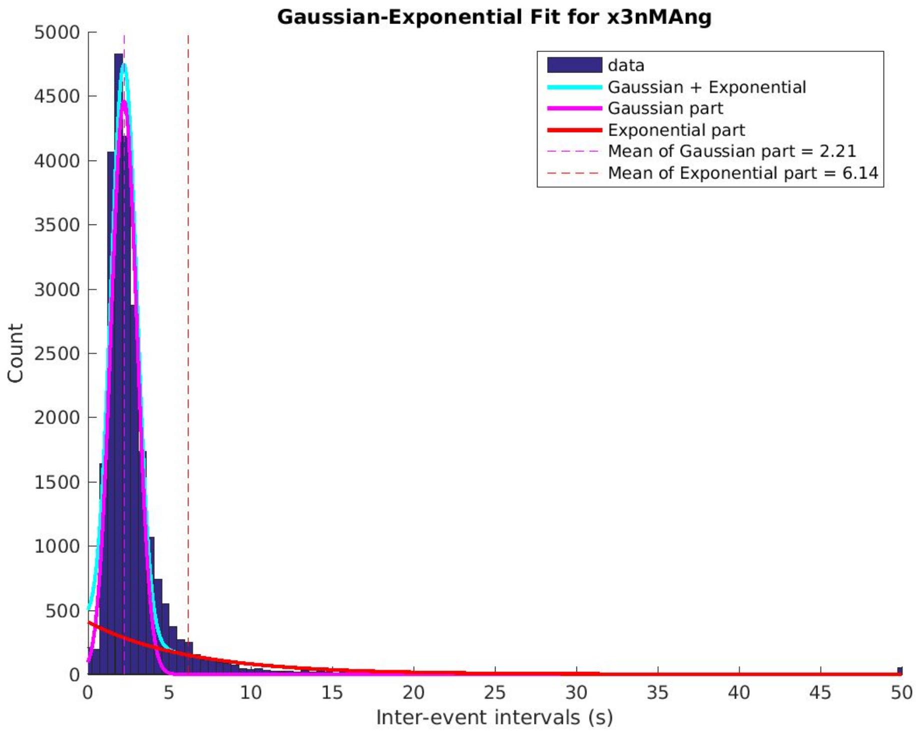
- Separation of intra-burst and inter-burst ISIs in literature
  - Chen et al., 2009 ("Detection of bursts in neuronal spike trains by the mean inter-spike interval method")

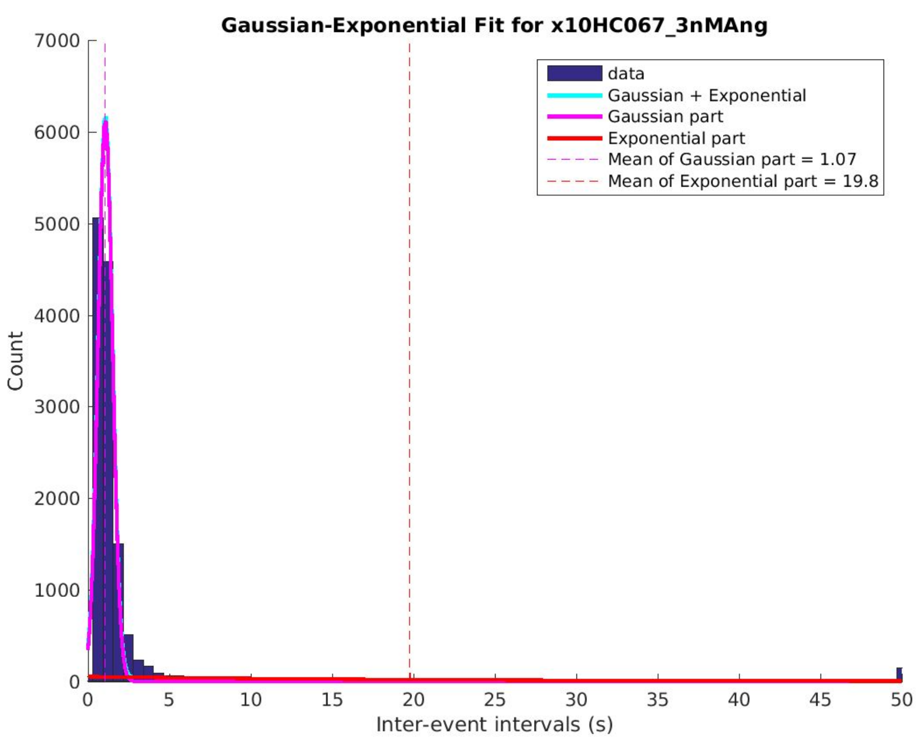


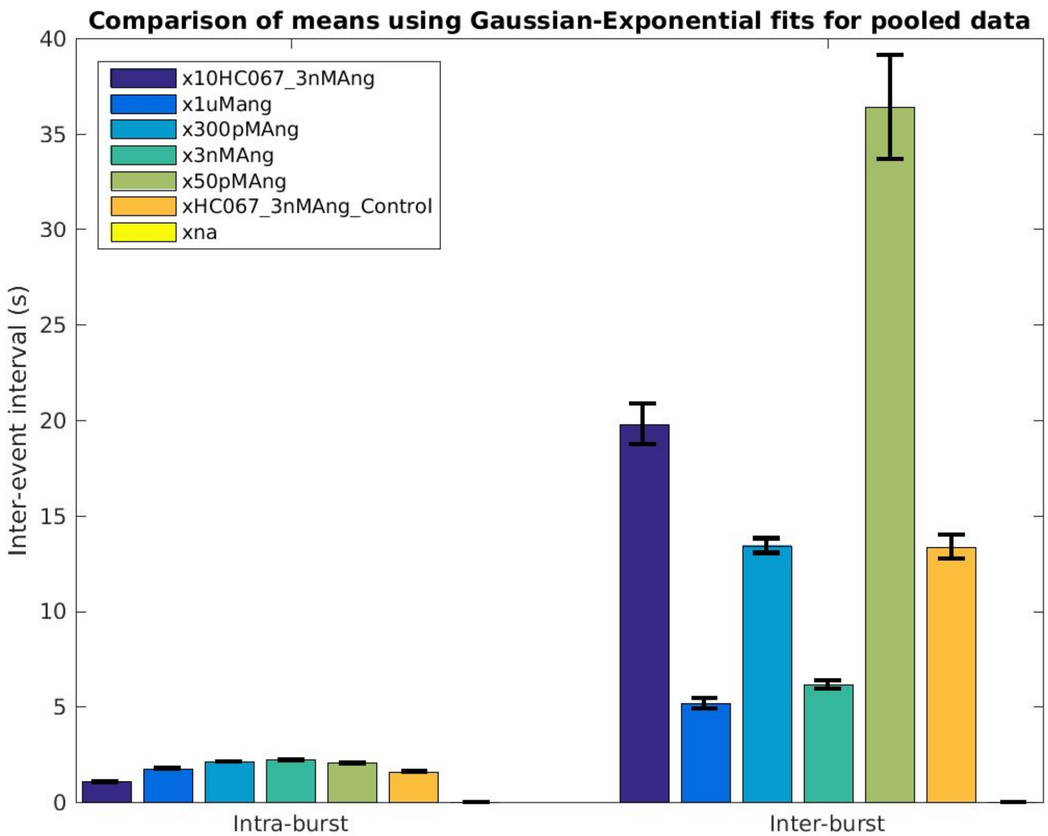
- Separation of intra-burst and inter-burst ISIs using a **Gaussian-mixture model**

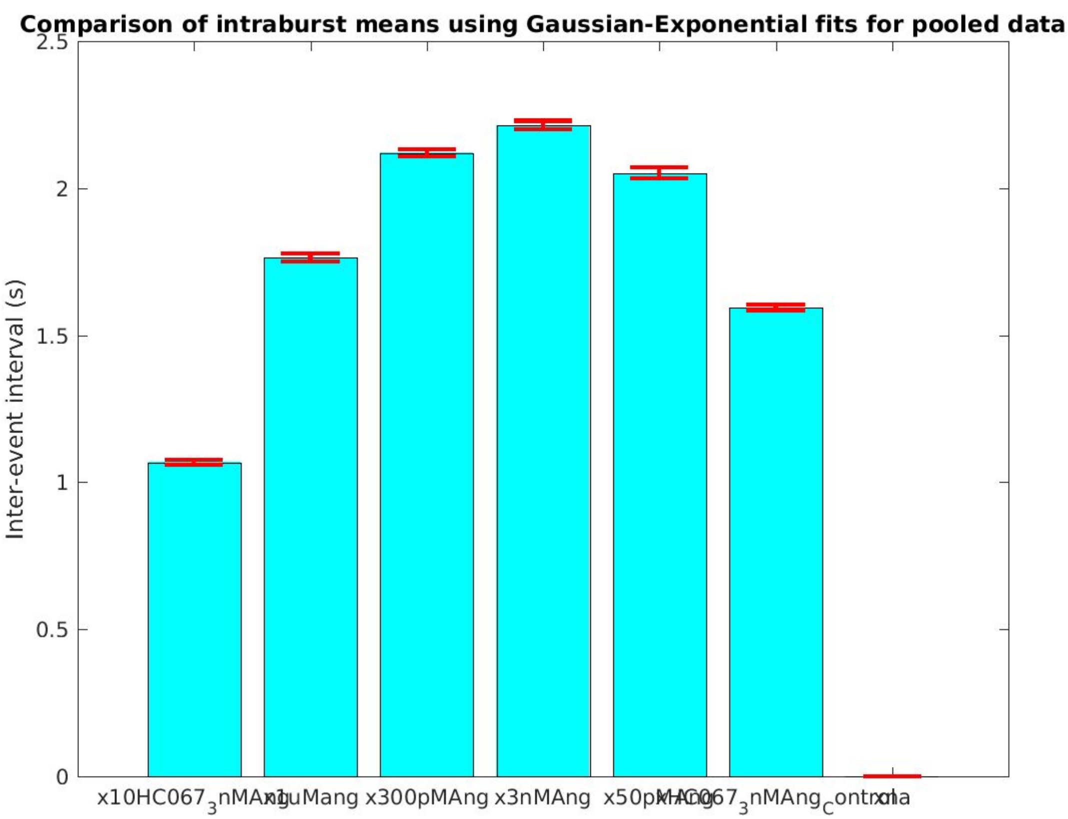


- Separation of intra-burst and inter-burst ISIs using a **Gaussian-Exponential mixture model**

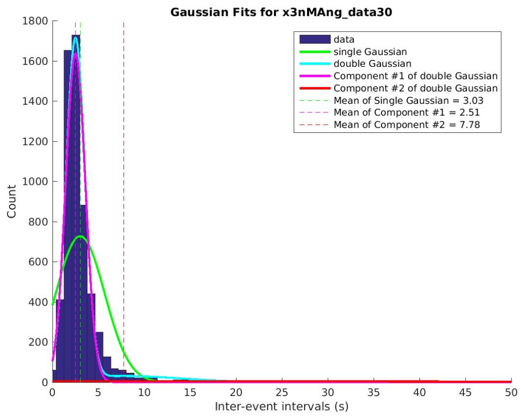


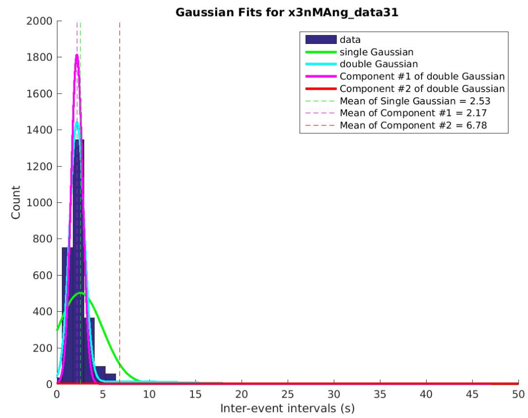


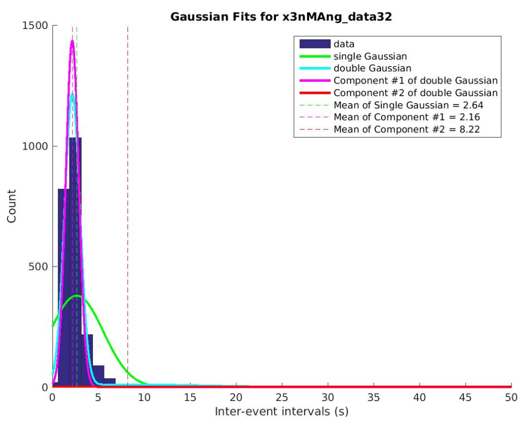

Comparison of means using Gaussian-Exponential fits for pooled data
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna
Inter-event interval (s)
0
5
10
15
20
25
30
35
40
Intra-burst
Inter-burst

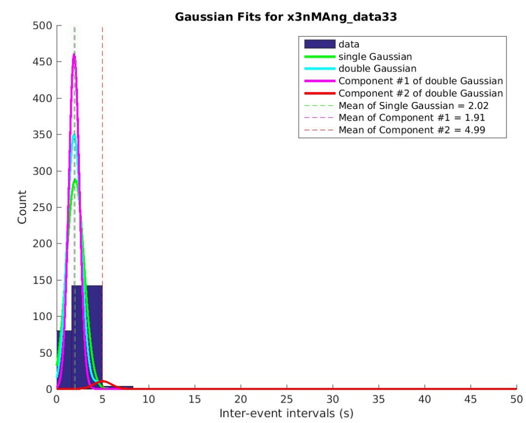

Comparison of intraburst means using Gaussian-Exponential fits for pooled data
Inter-event interval (s)
0
0.5
1
1.5
2
2.5
x300pMAng
x3nMAng

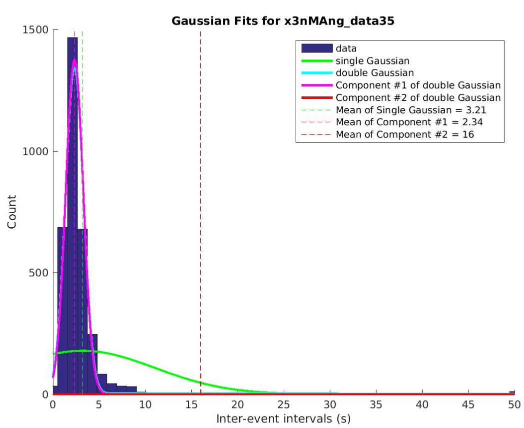
- Separate intra-burst and inter-burst ISIs using a two **Gaussians model** for **each slice**, then compute the average and standard deviations of the means obtained from the fits for each slice

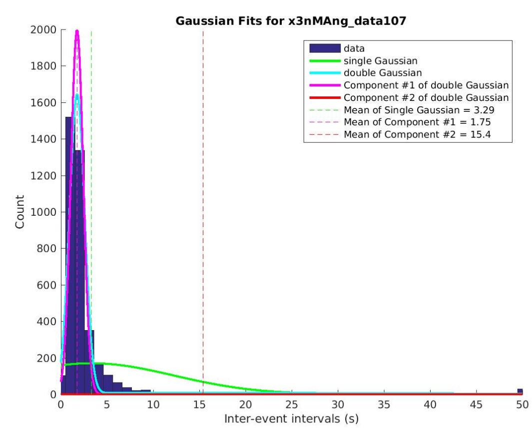


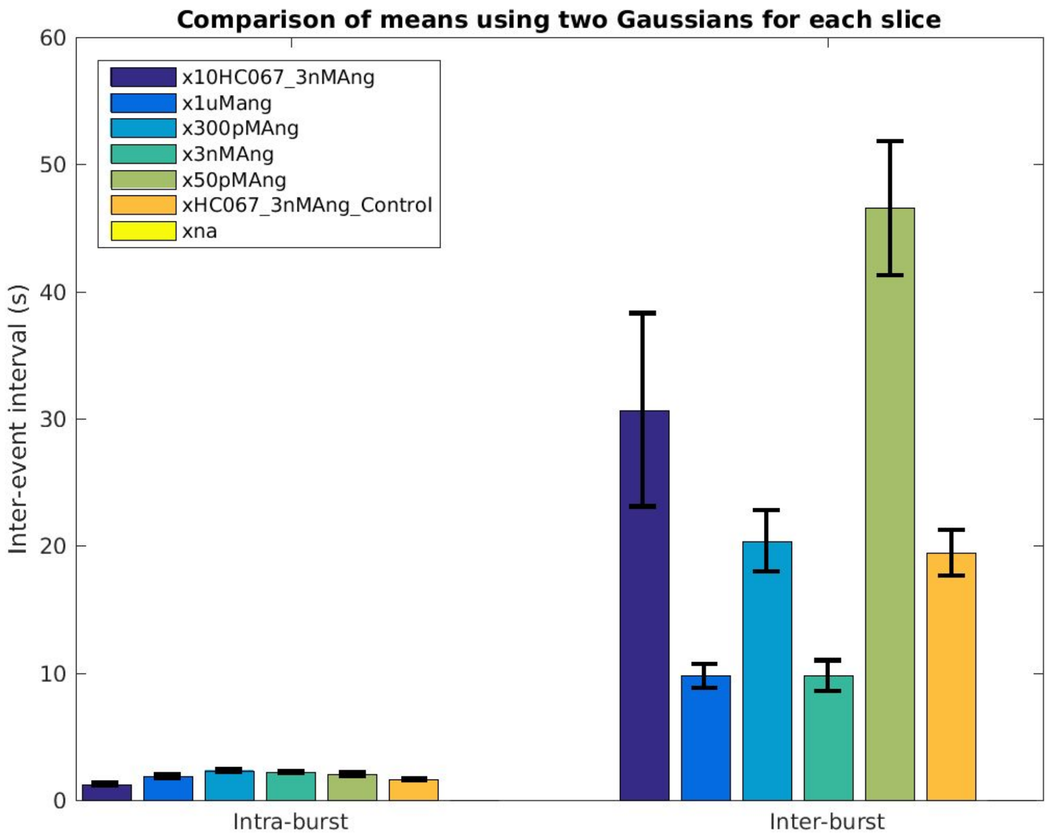




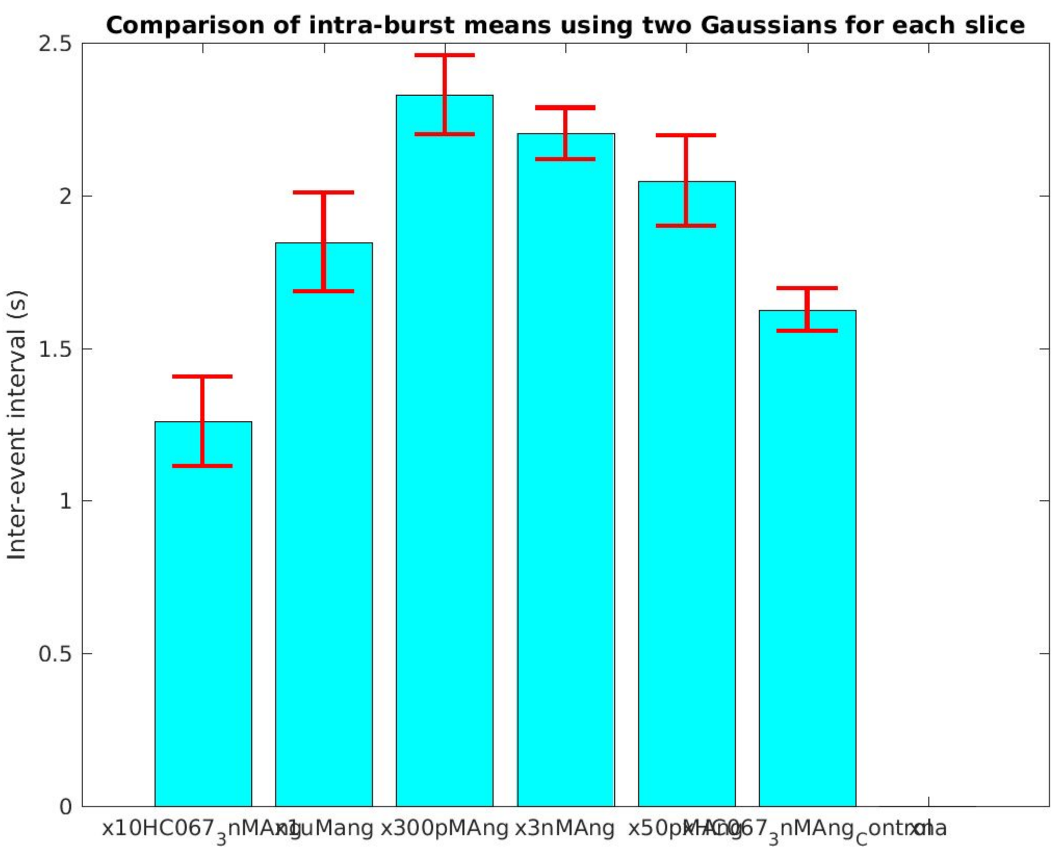






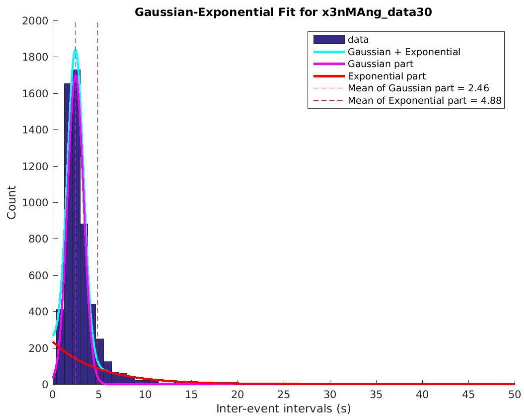


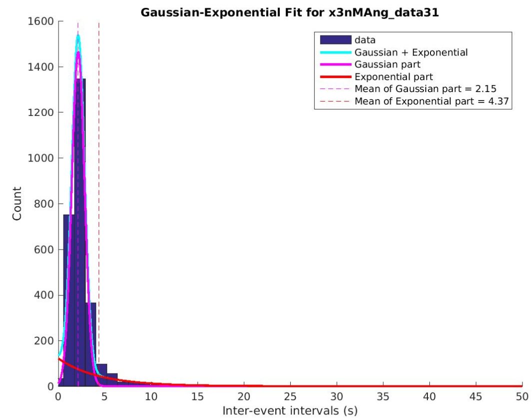
Comparison of means using two Gaussians for each slice
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna
Inter-event interval (s)
60
50
40
30
20
10
0
Intra-burst
Inter-burst

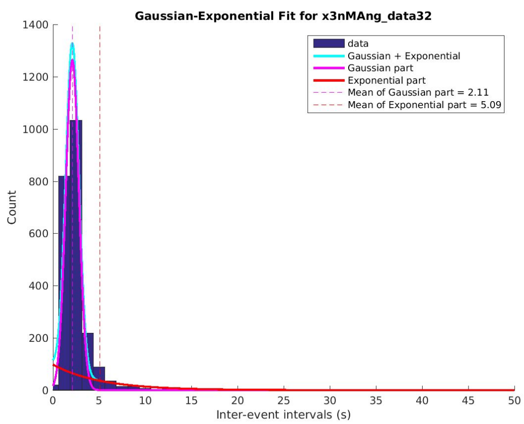


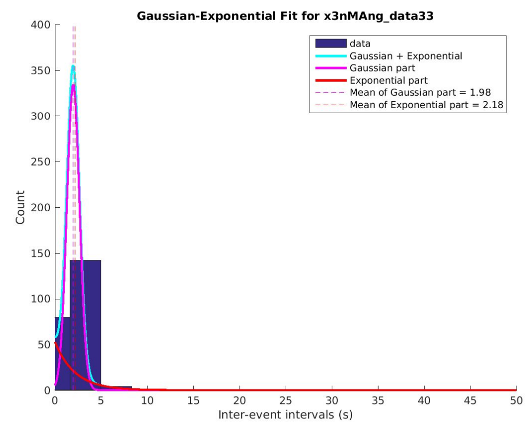
Comparison of intra-burst means using two Gaussians for each slice
Inter-event interval (s)
2.5
2
1.5
1
0.5
0
x300pMAng
x3nMAng

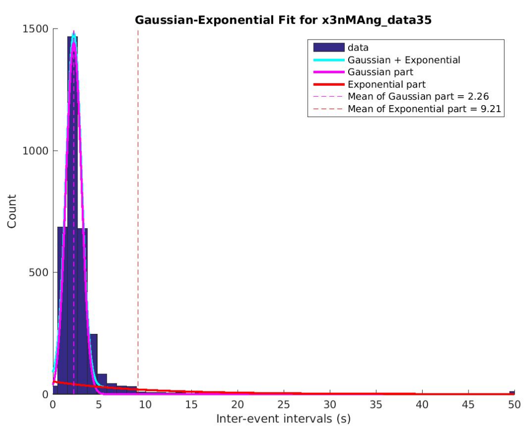
- Separate intra-burst and inter-burst ISIs using a **Gaussian-Exponential mixture model** for **each slice**, then compute the average and standard deviations of the means obtained from the fits for each slice

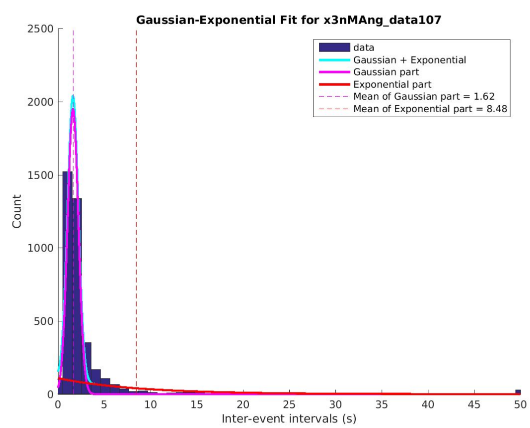


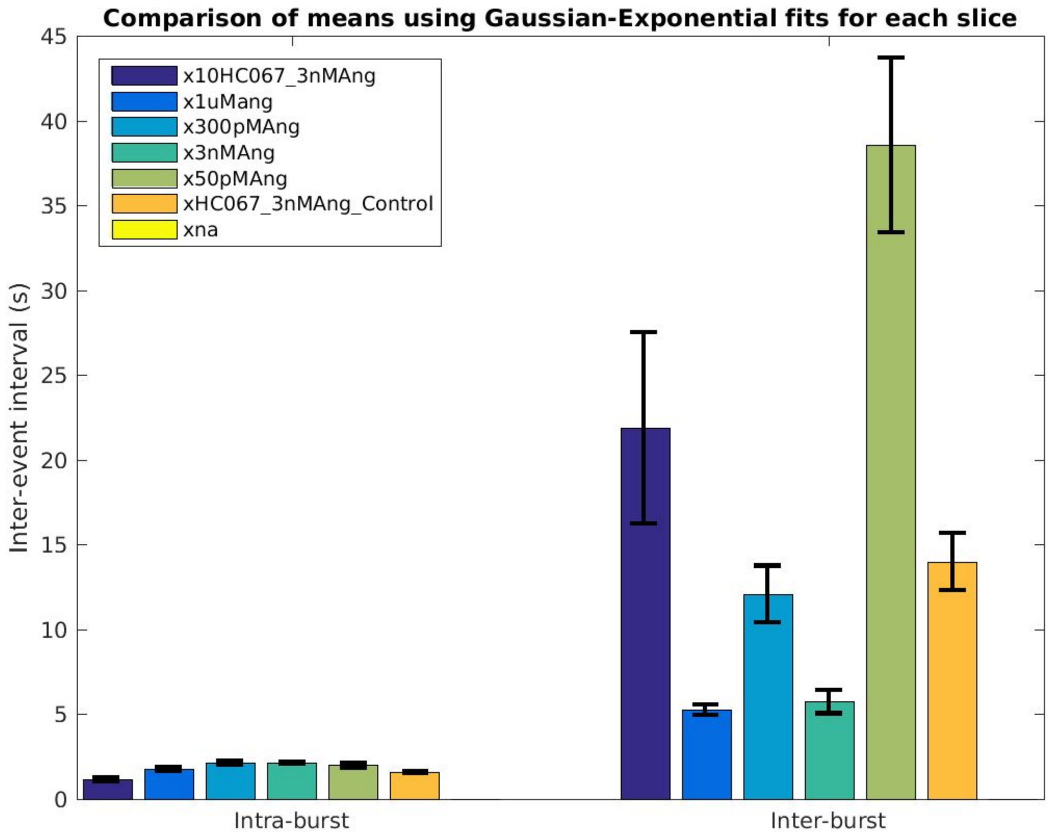








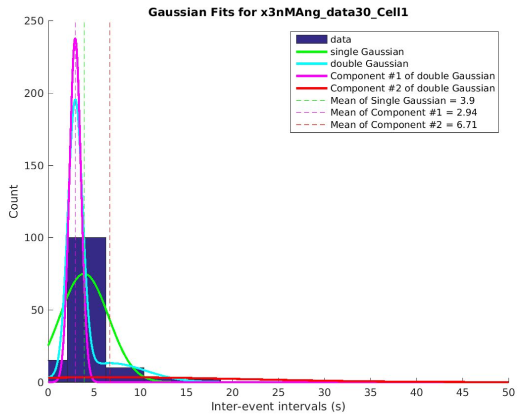


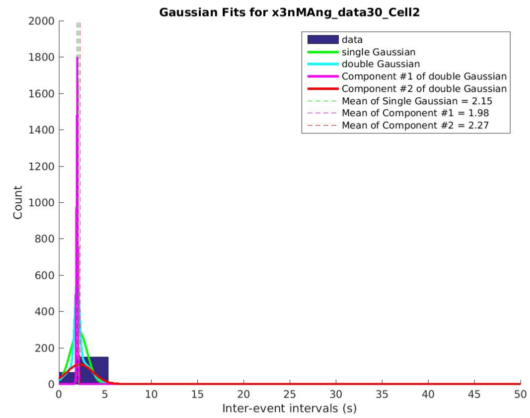


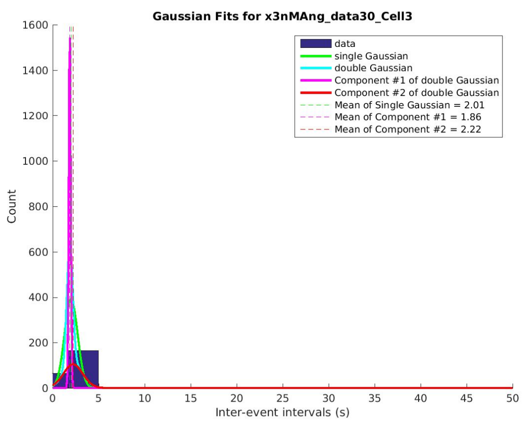
Comparison of means using Gaussian-Exponential fits for each slice
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna
Inter-event interval (s)
Intra-burst
Inter-burst

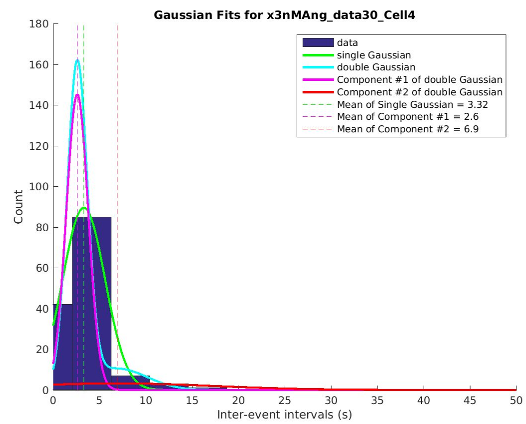
Comparison of intra-burst means using Gaussian-Exponential fits for each slice
Inter-event interval (s)
x300pMAng
x3nMAng

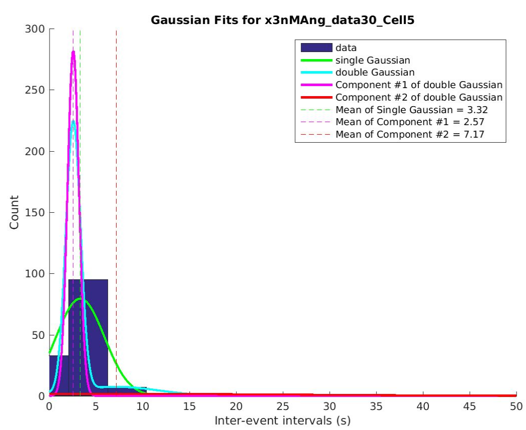
- Separate intra-burst and inter-burst ISIs using **two Gaussians** for **each cell**, then compute the average and standard deviations of the means obtained from the fits for each cell, ignoring those that don't fit

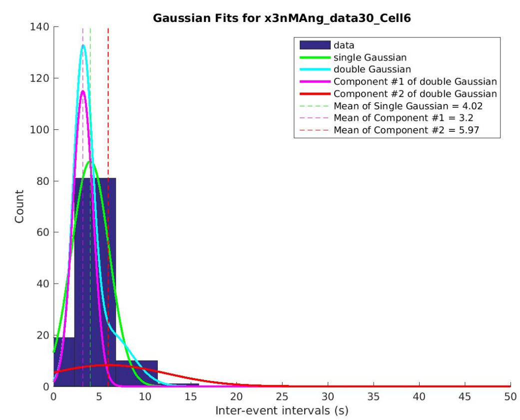


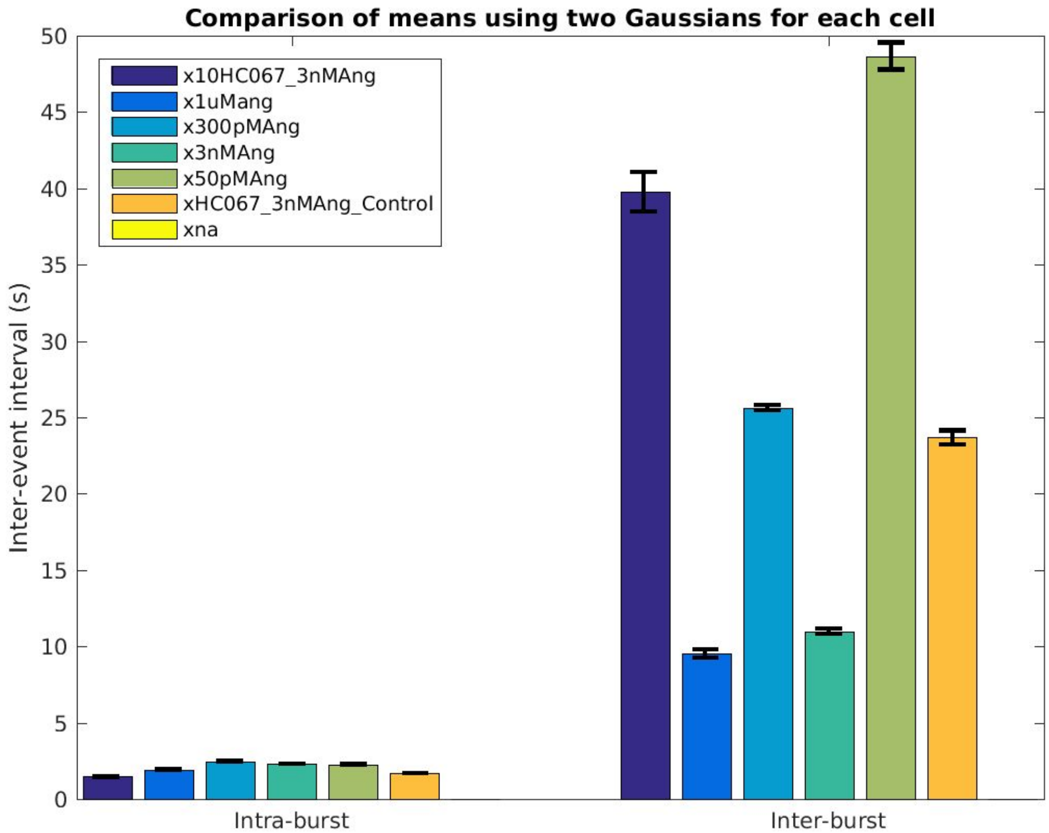


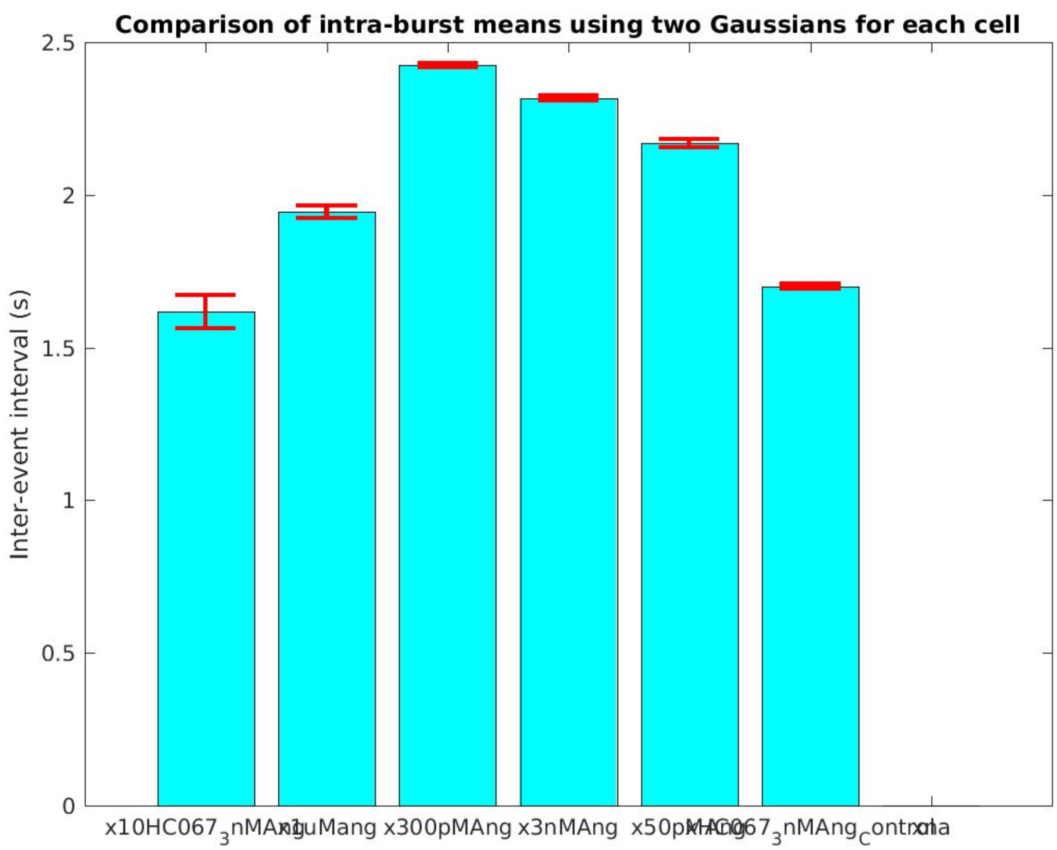




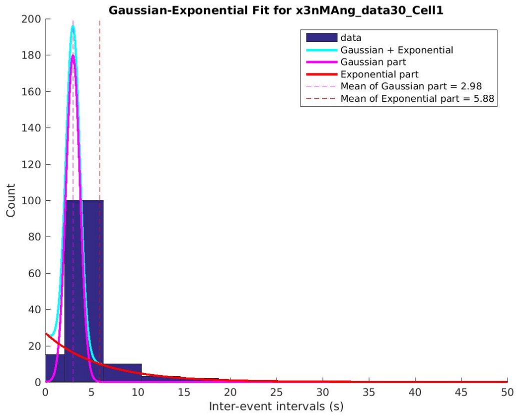


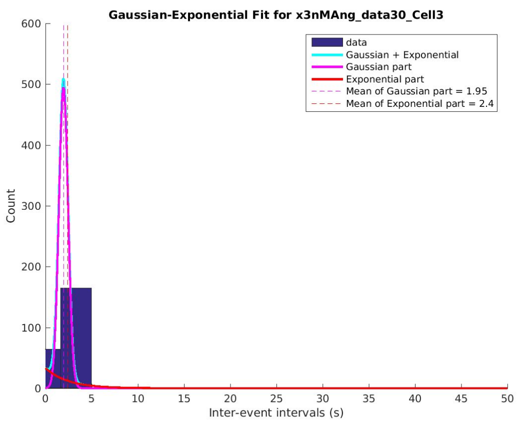


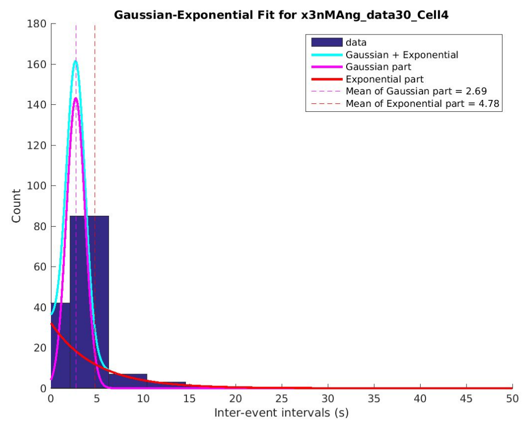

Comparison of means using two Gaussians for each cell
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna
Inter-event interval (s)
0
5
10
15
20
25
30
35
40
45
50
Intra-burst
Inter-burst

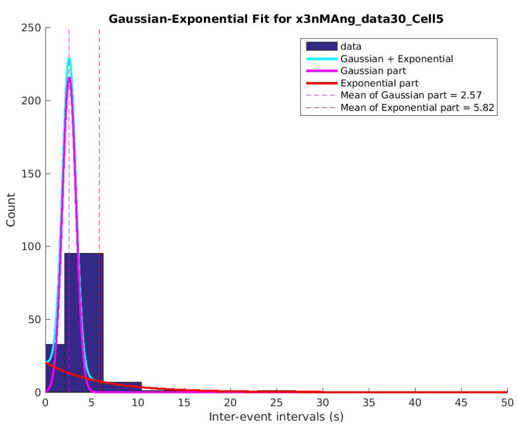

Comparison of intra-burst means using two Gaussians for each cell
Inter-event interval (s)
0
0.5
1
1.5
2
2.5
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna

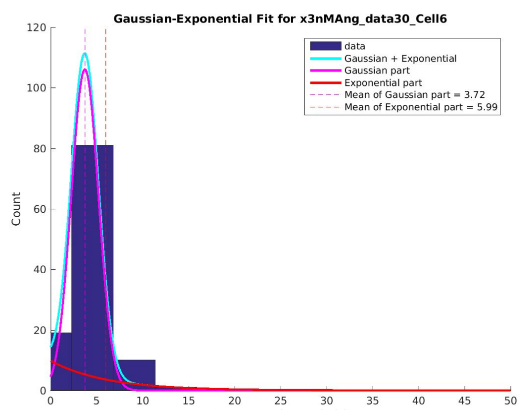
- Separate intra-burst and inter-burst ISIs using a **Gaussian-Exponential mixture model** for **each cell**, then compute the average and standard deviations of the means obtained from the fits for each cell, ignoring those that don't fit

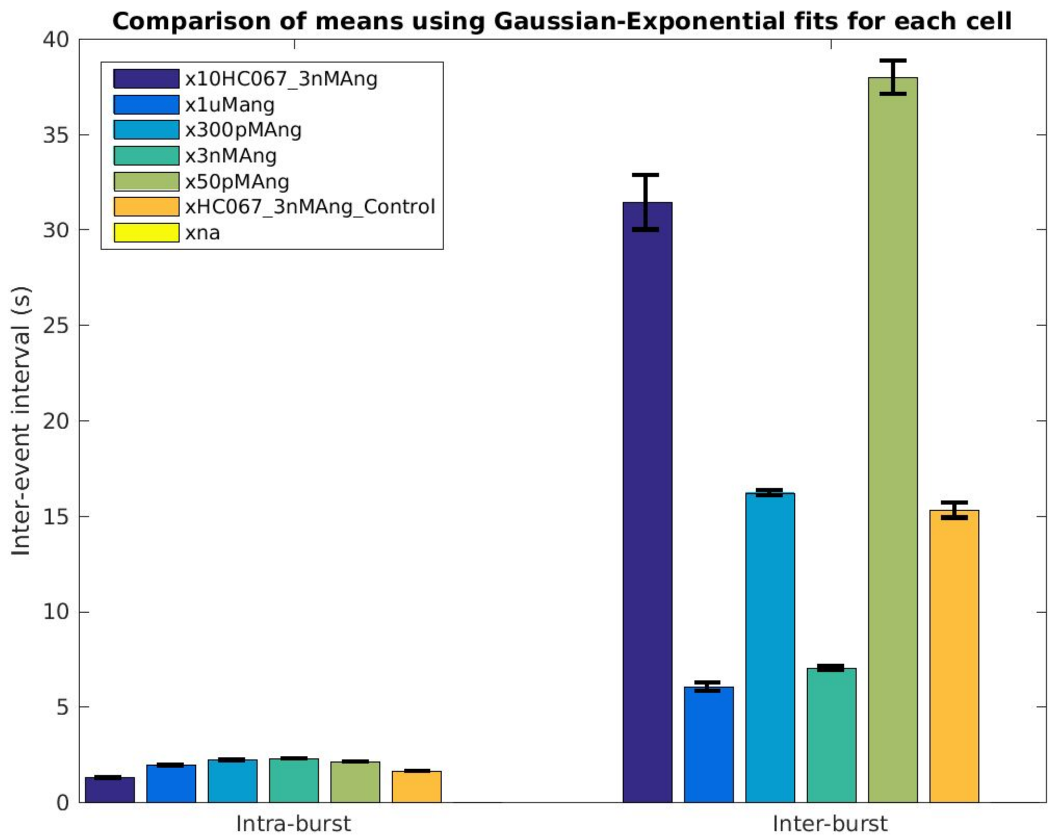




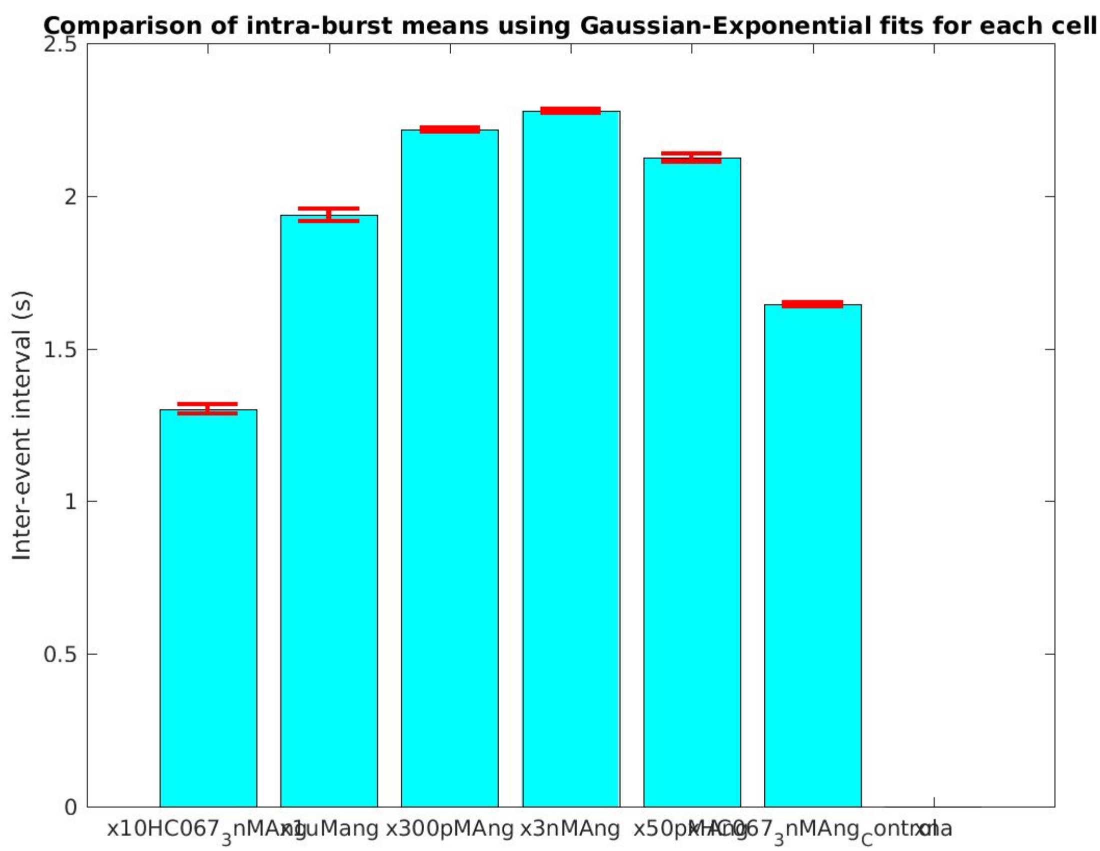








Comparison of means using Gaussian-Exponential fits for each cell
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna
Inter-event interval (s)
Intra-burst
Inter-burst

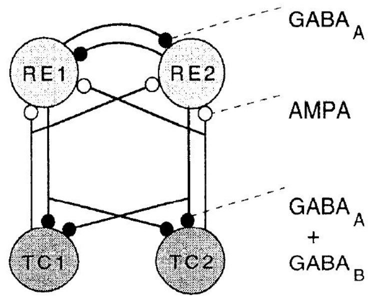


Comparison of intra-burst means using Gaussian-Exponential fits for each cell
Inter-event interval (s)
x10HC067_3nMAng
x1uMang
x300pMAng
x3nMAng
x50pMAng
xHC067_3nMAng_Control
xna

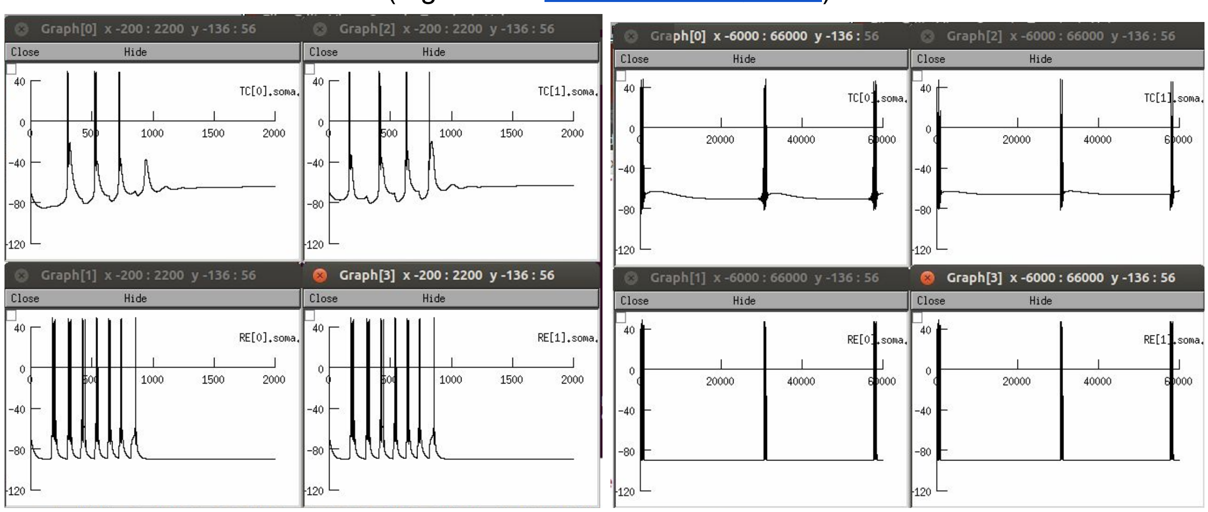
10/18/2017~

Investigation of the Destexhe 1996 Model

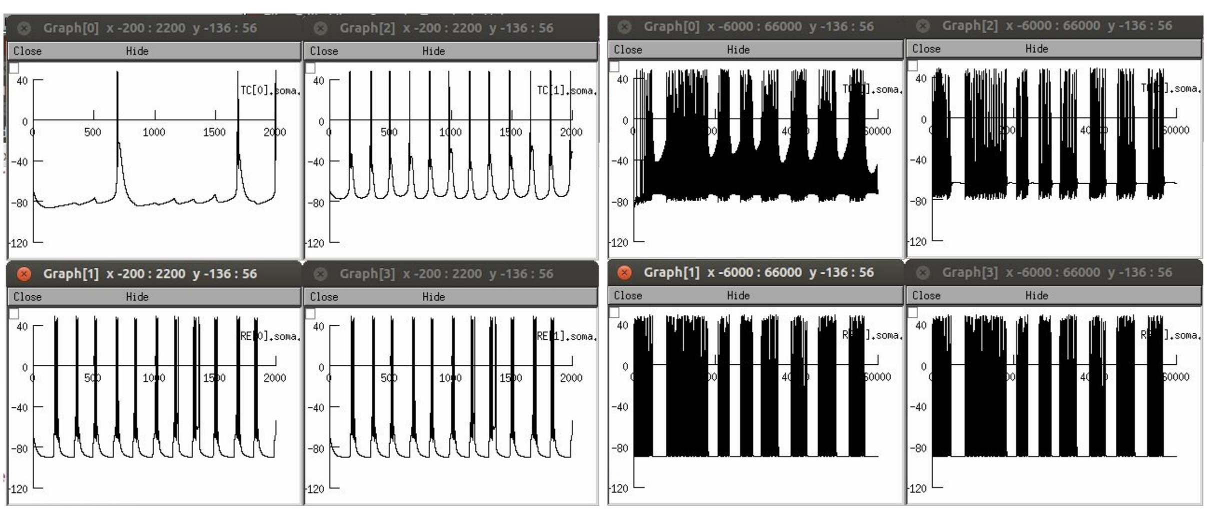
- Network structure:
    - **2 RT** neurons & **2 TC** neurons
    - RT-RT inhibition present
    - RT-TC and TC-RT are both **all-to-all**
- **Spindle oscillations**



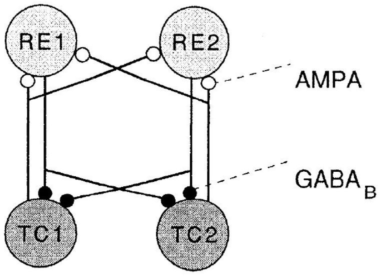
(Figure 7 of Destexhe et al., 1996)



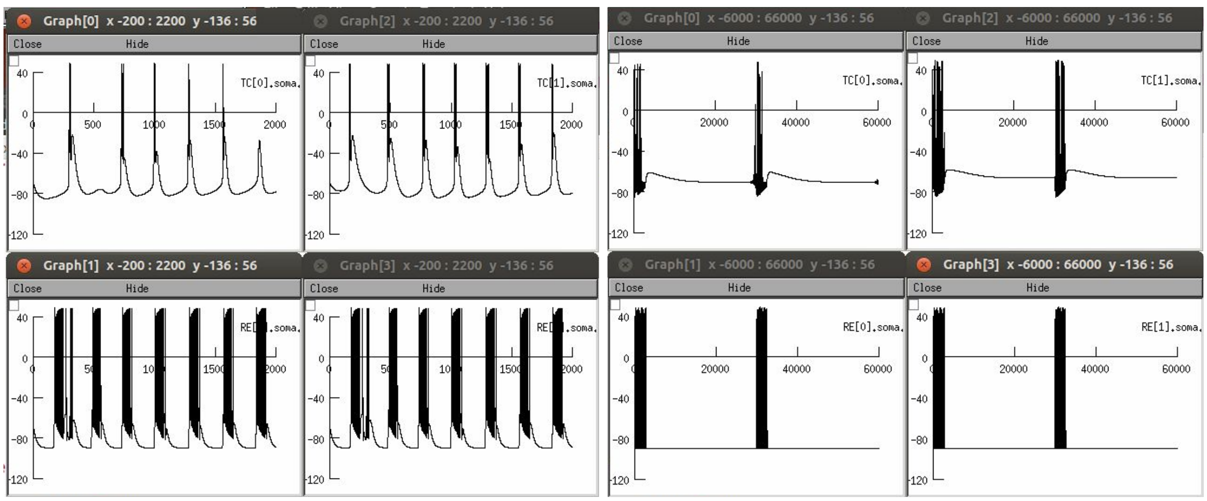
- **Delta oscillations**



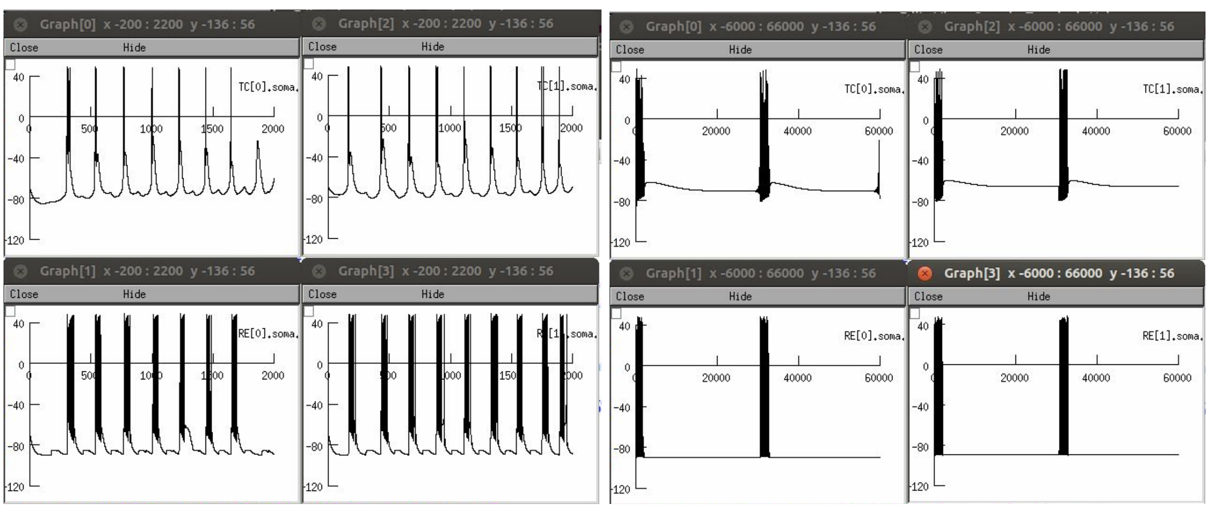
- **Bicuculline-induced paroxysmal oscillations**



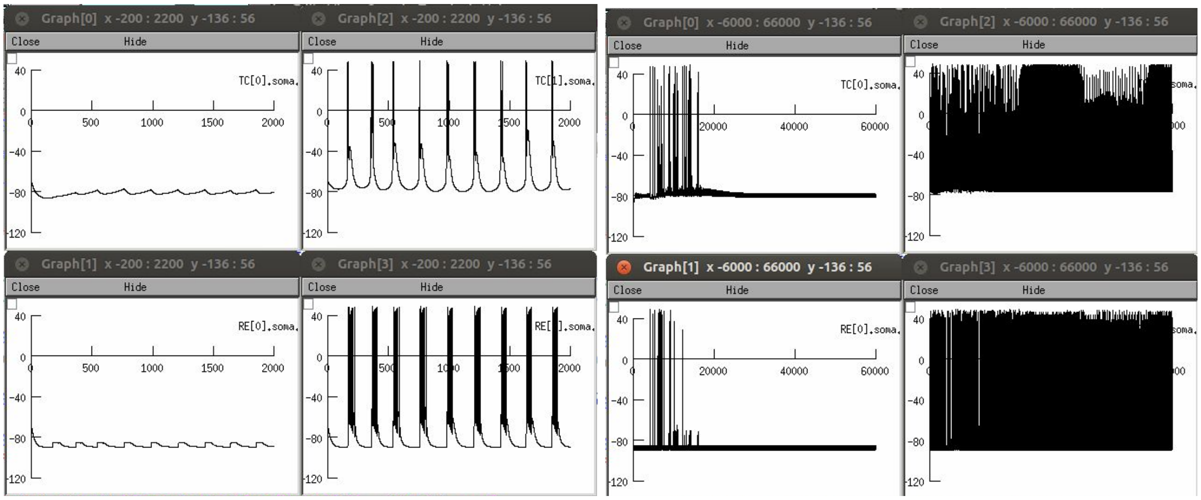
(Figure 8 of [Destexhe et al., 1996])



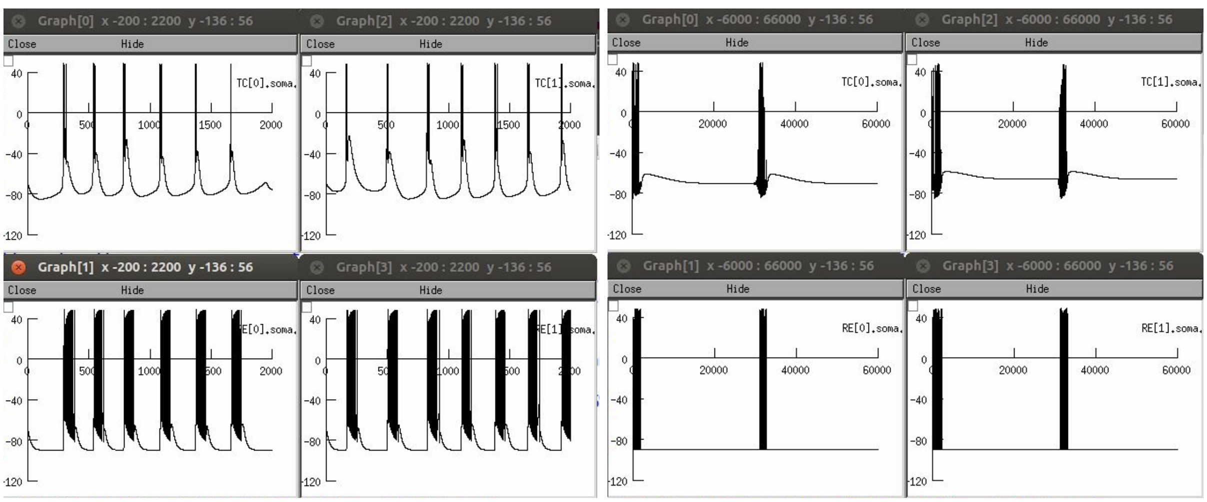
- Remove divergence of TC-RT connections:
    - TC1->RT1, TC2->RT2 (now with double the strength as before)
    - Spindle oscillations have **longer duration**



- Delta oscillations are now **localized**



- Bicuculline-induced paroxysmal oscillations have **shorter duration**



-

Plan for next week

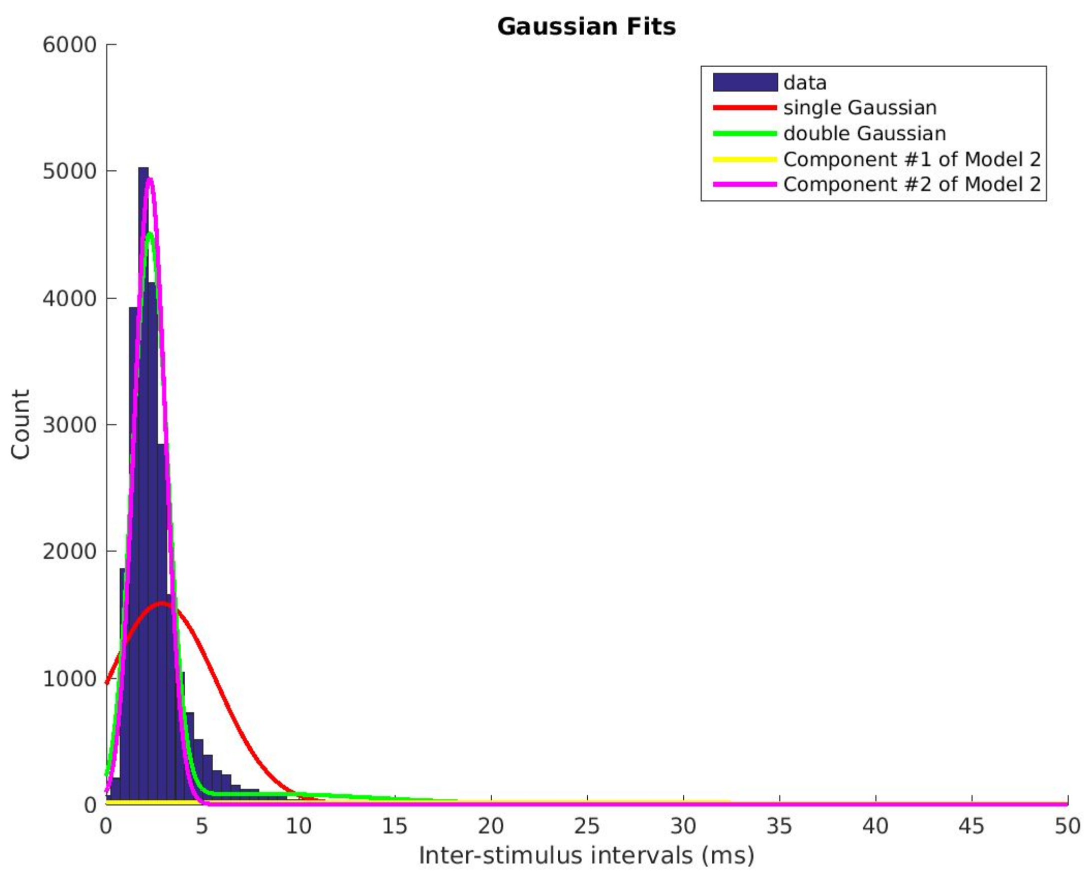
- Single Neuron Model:
    - Make histograms of errors across cells (using output files from the respective output directories)
        - Format: error_histogram(expDate)
    - Summary I-V curve of **all ionic currents**
    - Start with default parameters for those to be fitted across trials, and best parameters for those that were fitted across cells, fit across trials using the "**most representative trace**" (Of all trials of the same condition, see if most have bursts or LTS or neither. If neither, choose one without LTS with minimum noise. If most have LTSs but not bursts, choose one with LTS but not bursts with minimum noise. If most have bursts, choose one with bursts with minimum noise)
    - Compare plots of the **geometry** before and after fitting
    - Compare **I-V curves** before and after fitting
    - Write out the voltage relationships between compartments. Is the **cable equation** used by NEURON? No. Are the diameters tapered? No.
    - Try ball-and-stick model with 2 nodes for the stick instead? Use theory to estimate build parameters (lengths and diameters) and fit only epas & gpas? If doesn't work, use 3/2 diameter rule?
    - What is the appropriate **post-stimulus start point** for passive fitting? Apply the procedure in Major et al., 1994?
    - Should we account for series resistance and capacitive transients?
    - Try writing out an **explicit objective function**
    - Investigate where **shiftm, shifth, slopem, slopeh** should be placed. Should we make T_1/2 and k parameters instead? (Perhaps no, because taum and minf should vary together, see Pinsky-Rinzel model.)
    - Make g's and p's linearly vary from soma->dend1->dend2?
    - Explore Ed's way of **parallelizing Matlab without using a toolbox license**.

- Knowledge buildup:
    - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)
    - Cohen (*Analyzing Neural Time Series Data*)

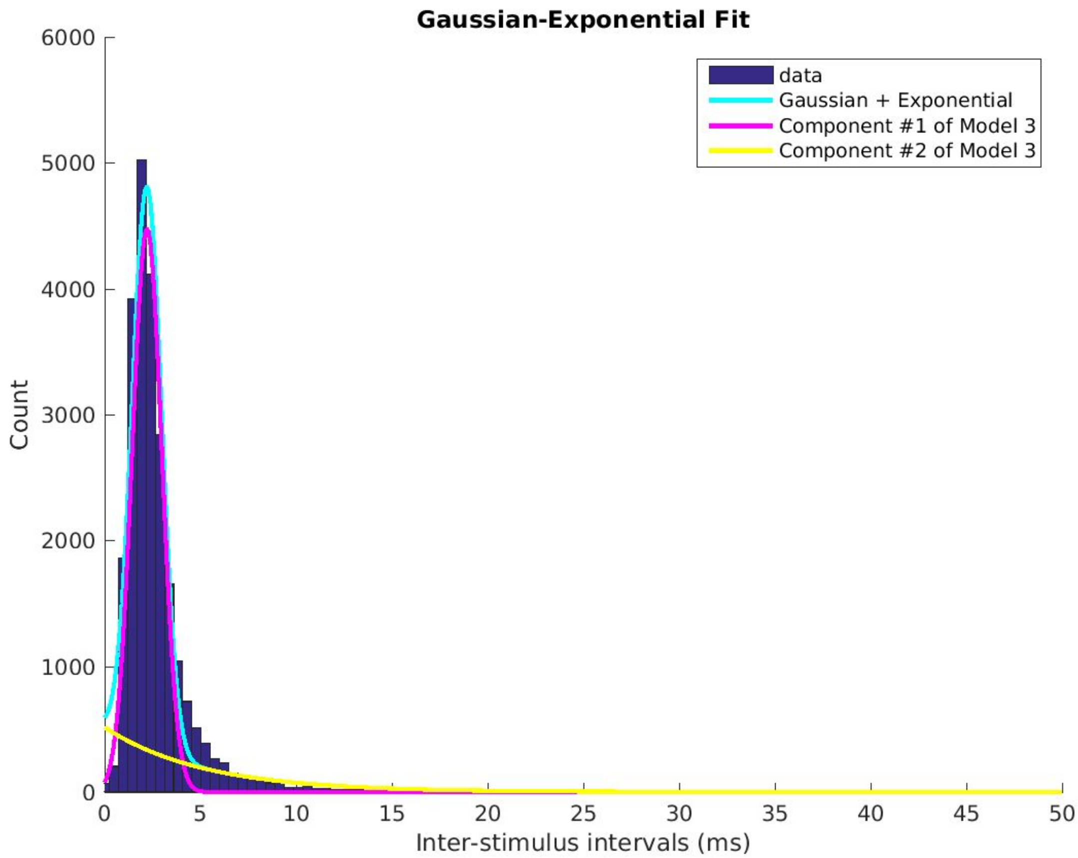
10/12/2017~10/13/2017

Fitting of Paula's ISI histogram

- Separation of intra-burst and inter-burst ISIs in literature
  - Cocatre & Zilgien, 1992 ("Identification of bursts in spike trains")
    1. Use **sqrt(N)** or **1.87*(N-1)^0.4** for the number of bins in the ISI histogram
    2. Smooth the histogram by a **moving average filter of 3 bins**
    3. Locate the first mode, then locate the **first local minimum** or the **first inflection point** right of the first mode as the upper limit of intra-burst ISIs.
  - Chen et al., 2009 ("Detection of bursts in neuronal spike trains by the mean inter-spike interval method")
    1. Compute the **mean of all ISIs**
    2. Eliminate ISIs greater than the mean
    3. Compute a **new mean for the remaining ISIs** and make it the upper limit of intra-burst ISIs.
- Separation of intra-burst and inter-burst ISIs using a **Gaussian-mixture model**



- Separation of intra-burst and inter-burst ISIs using a **Gaussian-Exponential mixture model**
    - *Rationale:* If bursts occur randomly and follows a Poisson process, the **inter-burst ISIs** should approximate an exponential distribution. On the other hand, **intra-burst ISIs** are dependent upon the intrinsic oscillatory rhythm so should more approximate a Gaussian distribution. These can therefore



10/13/2017~

Updates to minEASE

- These **bugs** were fixed:
    - First or last event not updated when removed
- Keystroke for **removing events**: Use the **Delete** key.
    - This performs the same action as **clicking the Remove button**, which would look for the nearest event of the selected class after removing the event.
    - The difference is, events will continue to be incremented until an event that **has not been marked** is found.

<u>Plan for next week</u>

- Single Neuron Model:
    - Make histograms of errors across cells (using output files from the respective output directories)
        - Format: error_histogram(expDate)
    - Summary I-V curve of **all ionic currents**
    - Start with default parameters for those to be fitted across trials, and best parameters for those that were fitted across cells, fit across trials using the "**most representative trace**" (Of all trials of the same condition, see if most have bursts or LTS or neither. If neither, choose one without LTS with minimum noise. If most have LTSs but not bursts, choose one with LTS but not bursts with minimum noise. If most have bursts, choose one with bursts with minimum noise)
    - Compare plots of the **geometry** before and after fitting
    - Compare **I-V curves** before and after fitting
    - Write out the voltage relationships between compartments. Is the **cable equation** used by NEURON? No. Are the diameters tapered? No.
    - Try ball-and-stick model with 2 nodes for the stick instead? Use theory to estimate build parameters (lengths and diameters) and fit only epas & gpas? If doesn't work, use 3/2 diameter rule?
    - What is the appropriate **post-stimulus start point** for passive fitting? Apply the procedure in [Major et al., 1994]?
    - Should we account for series resistance and capacitive transients?
    - Try writing out an **explicit objective function**
    - Investigate where **shiftm, shifth, slopem, slopeh** should be placed. Should we make T_1/2 and k parameters instead? (Perhaps no, because taum and minf should vary together, see Pinsky-Rinzel model.)
    - Make g's and p's linearly vary from soma->dend1->dend2?
    - Explore Ed's way of **parallelizing Matlab without using a toolbox license**.

- minEASE:
    - Fix bug: Cannot add an event if it overlaps with removed events
    - Fix bug: Changing class 8 to class 1
    - Ability to preliminarily analyze a set of files without clicking through
    - Add parameter to exclude too short events (minimum decay time)
    - Add parameter to only begin an event from a point a set number of SDs above baseline
    - Rank quality of peaks
    - Tune auto-detect parameters. Deal with **EPSCs mixed in with IPSCs**
    - Implement **online detection**

- Knowledge buildup:
    - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)
    - Cohen (*Analyzing Neural Time Series Data*)

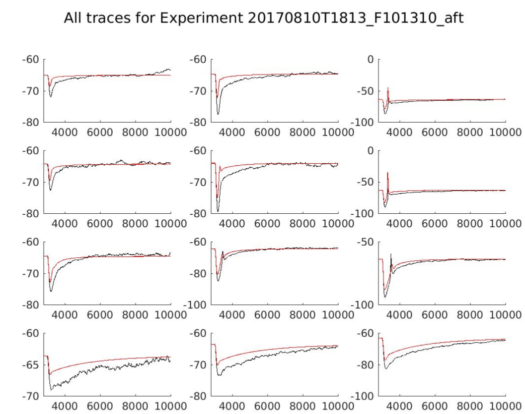
8/13/2017~8/20/2017

<u>Single Neuron Fitting (continued)</u>

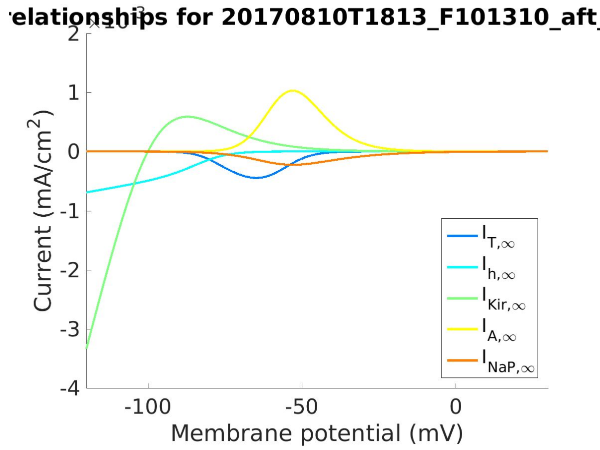
- **singleneuronfitting11.m (continued)**

F101310

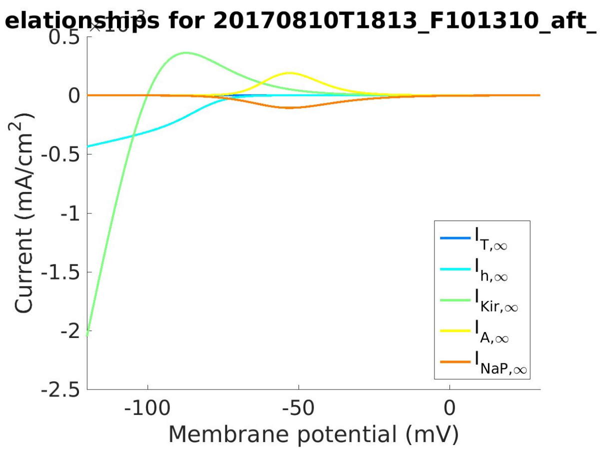
All traces:



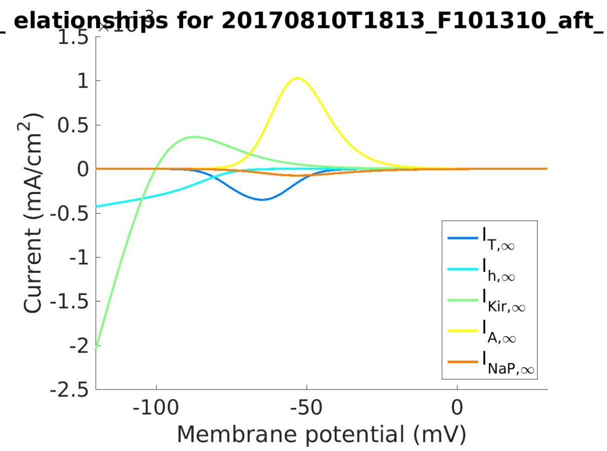
Steady-state I-V curves for **soma, dend0**:



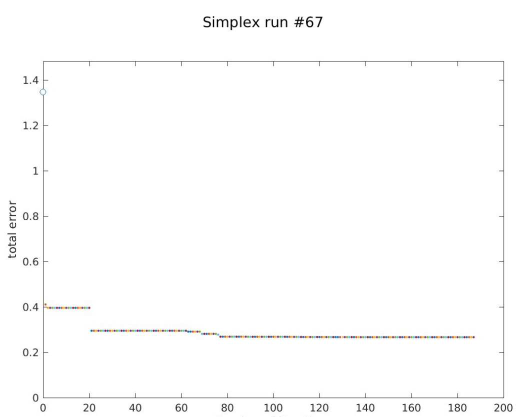
Steady-state I-V curves for **dend1**:



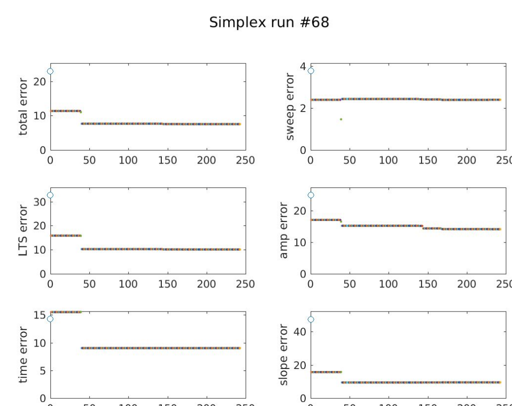
Steady-state I-V curves for **dend2**:



Passive fitting history:

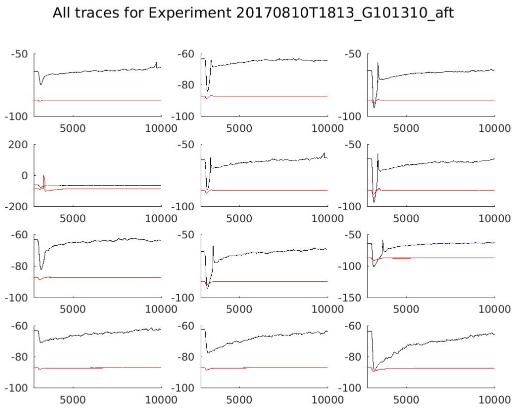


Active fitting history:

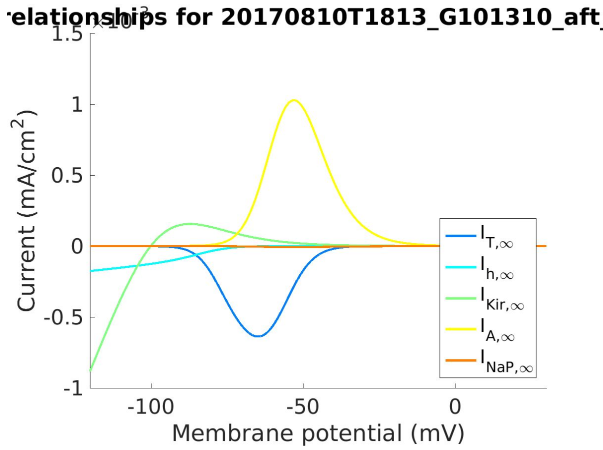


G101310

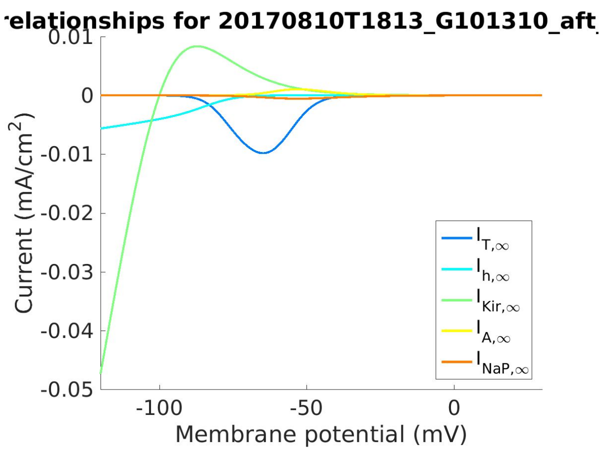
All traces:



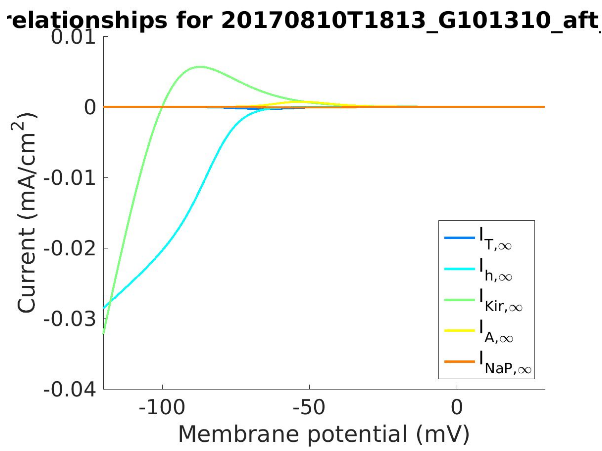
Steady-state I-V curves for **soma, dend0**:



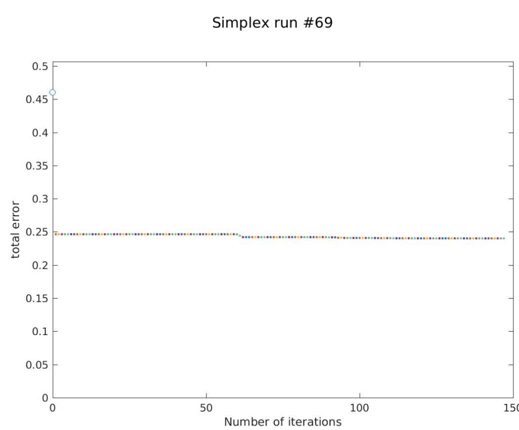
Steady-state I-V curves for **dend1**:



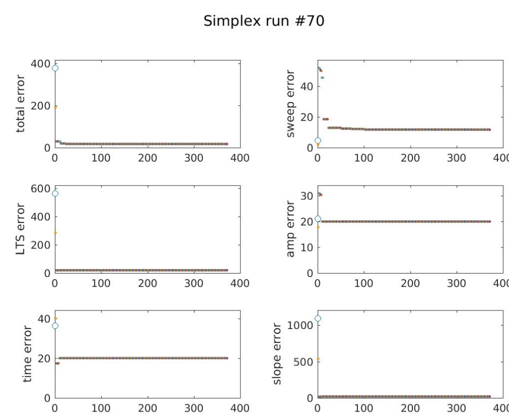
Steady-state I-V curves for **dend2**:



Passive fitting history:



Active fitting history:



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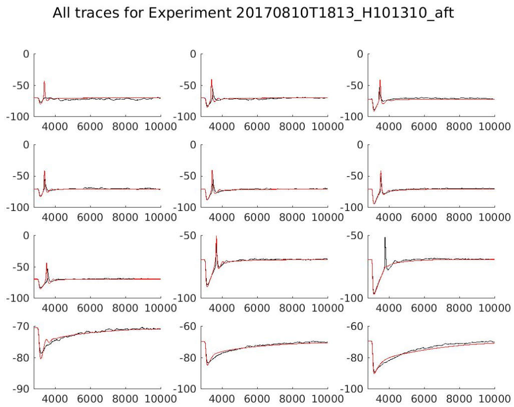
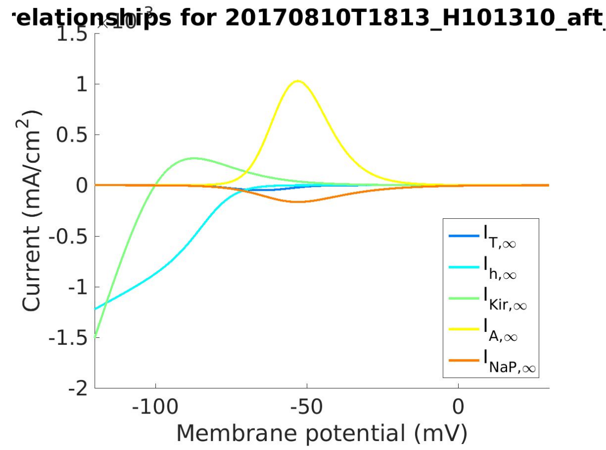
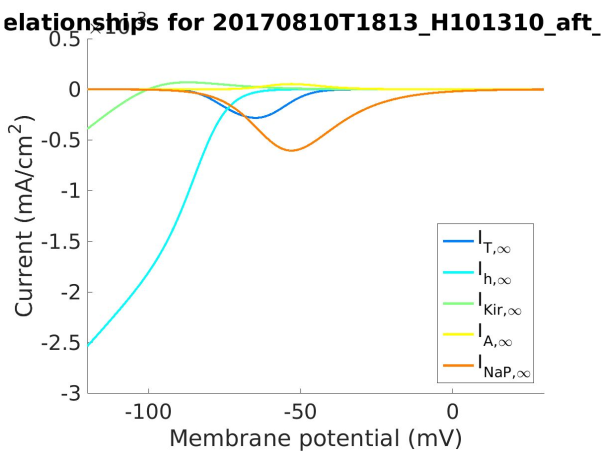
All traces:



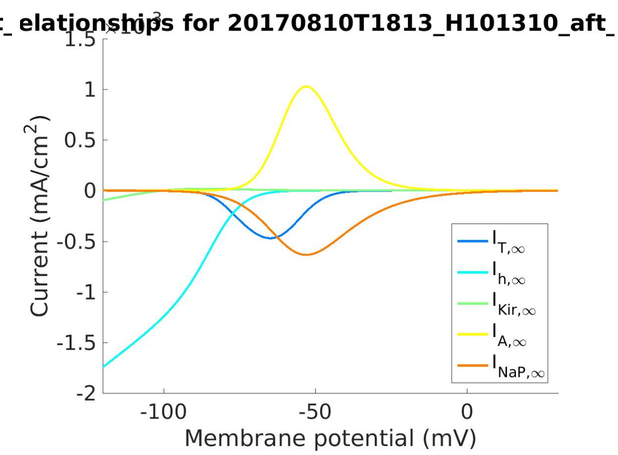
Steady-state I-V curves for **soma, dend0**:



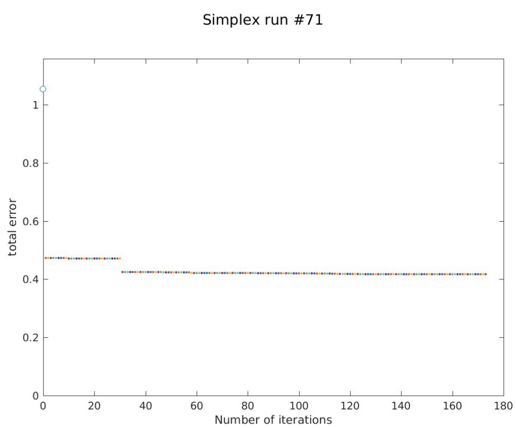
Steady-state I-V curves for **dend1**:



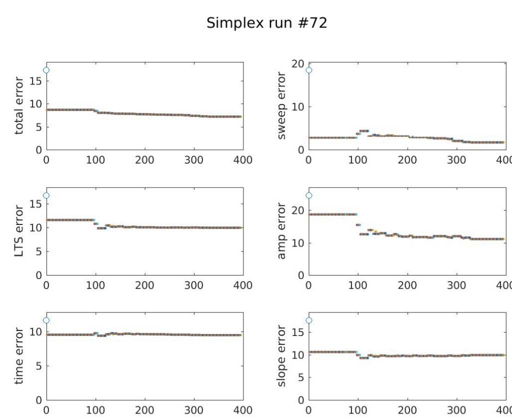
Steady-state I-V curves for **dend2**:



Passive fitting history:

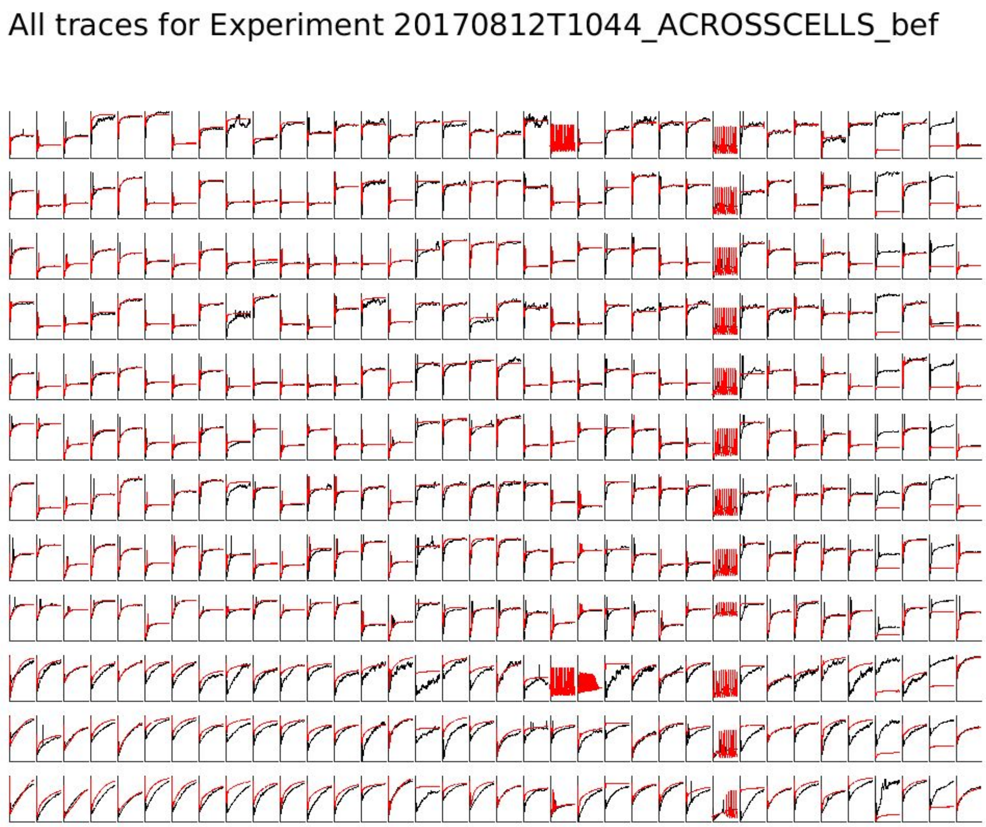


Active fitting history:

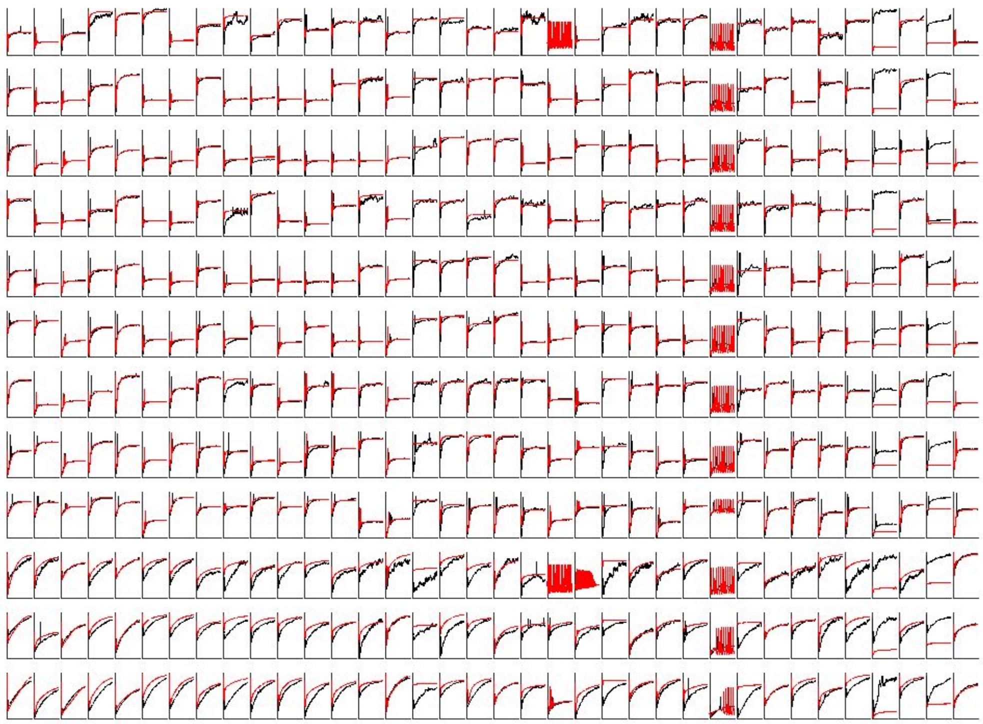


- Wrote code for **fitting across cells**:
    - Picks **a trace** from all trials for each cell for each input GABAB IPSC waveform (each pharm x g incr condition pair), with priority given to a trace with bursts, then to a trace with LTSs
    - Best parameters for each cell are used for the NEURON parameters that were fitted across trials.

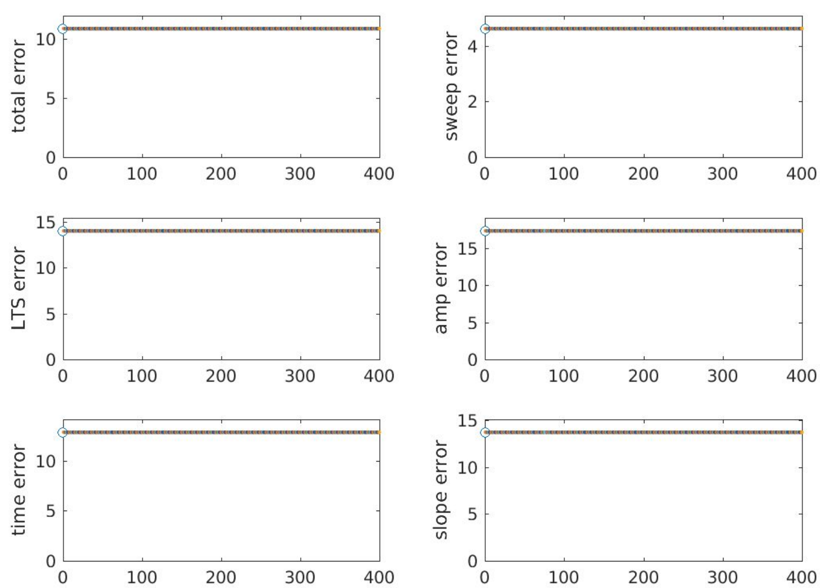
- **singleneuronfitting12.m**: Fitted across cells using the best parameters from **singleneuronfitting11**
    - The best-fit parameters did not change at all...



All traces for Experiment 20170812T1044_ACROSSCELLS_aft



Simplex run #1



- **singleneuronfitting12.m**: Tried again with **12 initial conditions**
  - The best-fit parameters still **did not change**, although they did change for the other 11 initial conditions

Iteration #	Final tota	Initial tot	shiftmIT	shifthIT	slopemIT	slopehIT	ehIh	shiftmIh
1	10.9079	10.9079	1	1	1	1	-28	0
2	14.3939	21.0342	30	-30	3.85764	2.70372	-24	22.5184
3	14.5761	15.2728	6.49096	4.75192	0.236758	1.3489	-31.9719	23.891
4	14.9019	80.3407	-12.2345	-29.5255	10	5.71387	-24	-25.0119
5	14.4978	99.6839	30	-30	7.93893	10	-27.3981	1.17606
6	14.5038	27.1863	30	-30	10	1.72402	-32	30
7	15.1559	83.0137	-30	-30	0.3013	10	-32	-24.0413
8	14.7474	71.2523	13.0706	-30	10	10	-24	-5.57825
9	14.5694	22.2247	-30	-28.7818	10	1.54045	-24	30
10	14.4095	29.0781	30	-30	10	1.90753	-29.9668	-1.277
11	14.3637	20.1286	24.6568	-29.4215	5.68088	2.11613	-27.9906	-0.10537
12	13.9354	69.5339	-22.1687	-18.4358	0.224145	1.01127	-31.7432	30

shiftmIT_0	shifthIT_0	slopemIT_0	slopehIT_0	ehIh_0	shiftmIh_0	Final error change	Error tole
1	1	1	1	-28	0	0.0660672	0.01
-3.84031	-28.4444	1.25697	0.742412	-28.6371	-10.1799	0.00581717	0.01
3.04787	12.4889	0.381777	1.05113	-24.8564	23.7776	1.87E-05	0.01
28.0218	2.83393	8.81797	2.68926	-26.4182	-17.0346	8.18E-05	0.01
-16.6804	22.2439	0.259083	6.87419	-28.0927	6.70463	0.00579174	0.01
23.5716	-10.0812	4.38994	0.121169	-31.1387	5.70312	0.00906033	0.01
-25.4215	16.7951	0.753041	2.79853	-24.1761	2.30975	1.08E-05	0.01
22.4058	28.1124	5.47506	1.15269	-30.1382	-29.3161	0.000210587	0.01
-29.3776	0.112476	0.980724	0.185208	-30.8631	-16.8865	0.00572856	0.01
16.2792	-28.7549	1.85053	3.14491	-28.0119	-16.5122	0.00175137	0.01
-19.1838	-28.8315	0.844184	2.81753	-28.6384	-0.874374	0.00225614	0.01
-20.7502	14.403	0.336225	1.1681	-31.8834	25.1248	0.00935629	0.01

Plan for next week

- Will be in Maryland Thursday, 8/24 to help my sister move in
- Will be in New York this weekend to meet high school friends and coming back next Monday
- Area paper:
    - Talk to Dr. Greg Gerling. Finalize committee members and defense date
    - Work on **Area Paper outline**
    - Start writing the **Background** section
    - Continue to edit PPT slides for qualifying exam
- Single Neuron Model:
    - Make histograms of errors across cells (using output files from the respective output directories)
        - Format: error_histogram(expDate)
    - **Transient** I-V curve for **Ih**
    - Summary I-V curve of **all ionic currents**
    - Make plots of the **geometry** before and after fitting
    - Start with default parameters for those to be fitted across trials, and best parameters for those that were fitted across cells, fit across trials using the "**most representative trace**" (Of all trials of the same condition, see if most have bursts or LTS or neither. If neither, choose one without LTS with minimum noise. If most have LTSs but not bursts, choose one with LTS but not bursts with minimum noise. If most have bursts, choose one with bursts with minimum noise)
    - Write out the voltage relationships between compartments. Is the **cable equation** used by NEURON? No. Are the diameters tapered? No.
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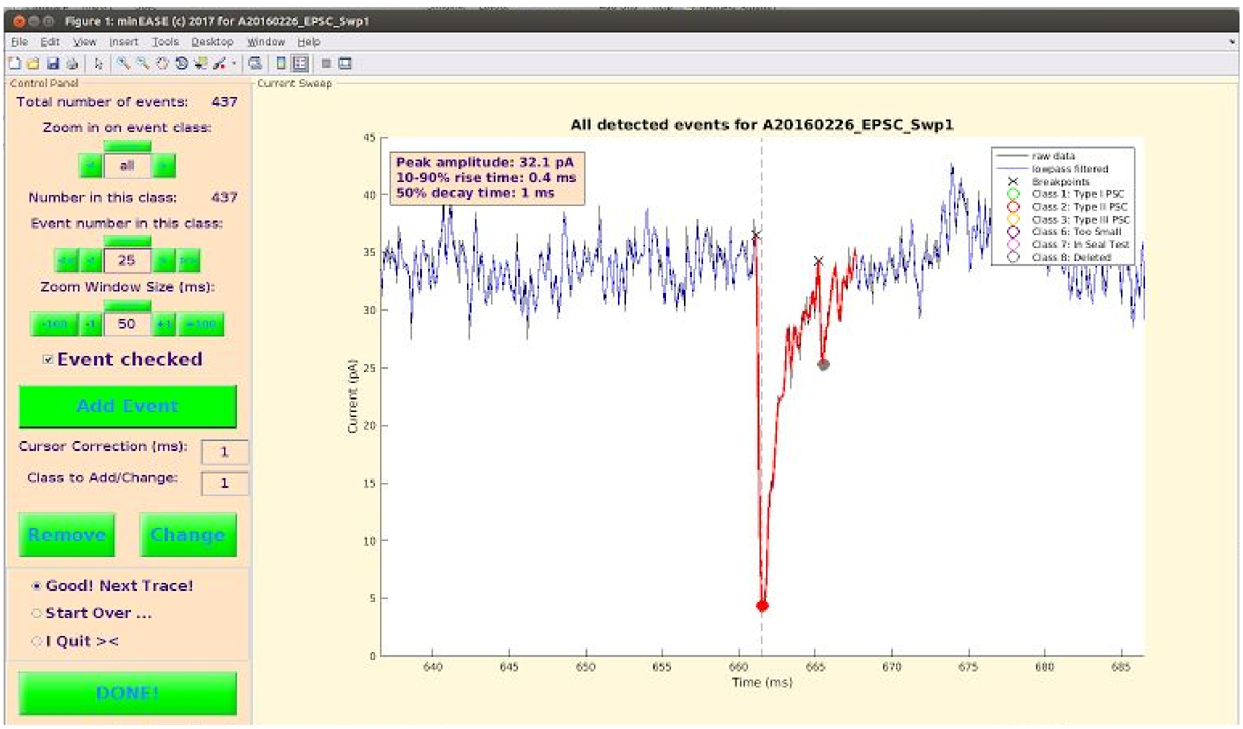
    - Make g's and p's linearly vary from soma->dend1->dend2?
    - Explore Ed's way of **parallelizing Matlab without using a toolbox license**.
- Knowledge buildup:
    - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)

8/7/2017~8/8/2017

<u>minEASE (updates)</u>

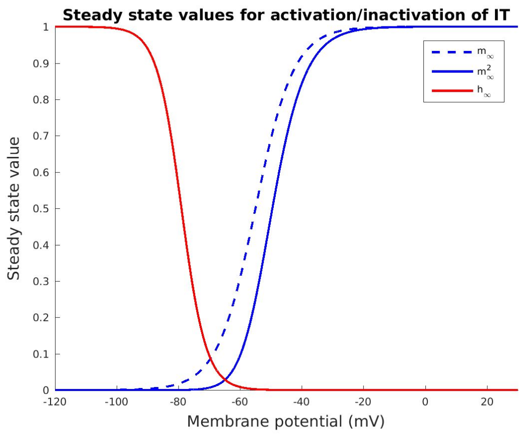
- **Event removal** is implemented as changing to class 8 (deleted).
- **Event addition** is now implemented in two steps:
    1. Add an event of class 8 (deleted)
    2. Change the event from class 8 to class to add
- **Removed events (class 8)** now have **NaNs** for IEIs, ISIs and decay times. And computations of IEIs, ISIs for other events now **skips events of class 8** when looking for the next event.
- Now recomputes IEIs, ISIs and decay times, both for the event in question and for the **previous event**, after an event is added (changed from class 8) or removed (changed to class 8).

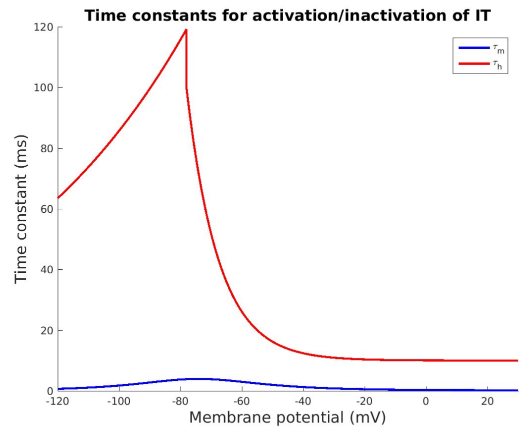


8/7/2017~8/13/2017

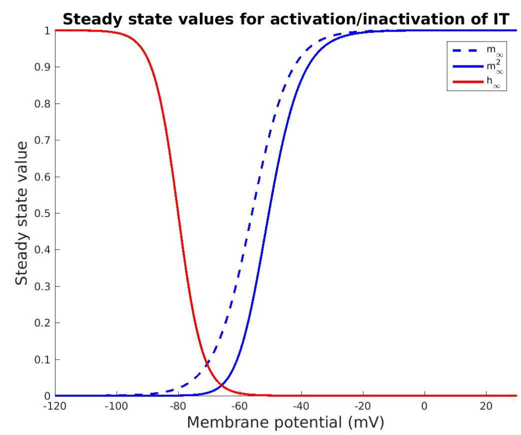
Single Neuron Fitting (continued)

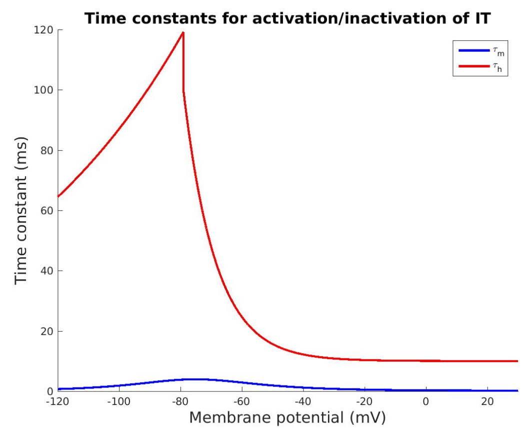
- Activation/inactivation curves of **IT**
  - Destexhe old: shiftmIT = **2**, shifthIT = **0**, slopemIT = **1**, slopehIT = **1**



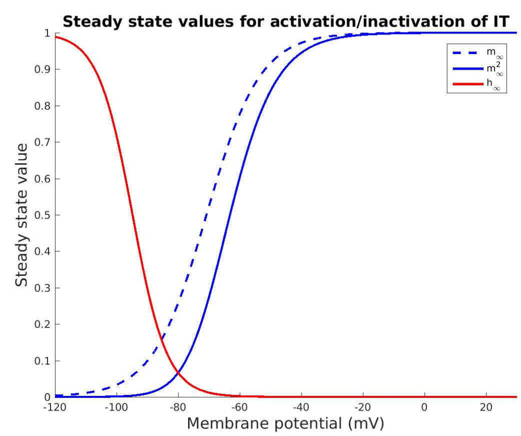


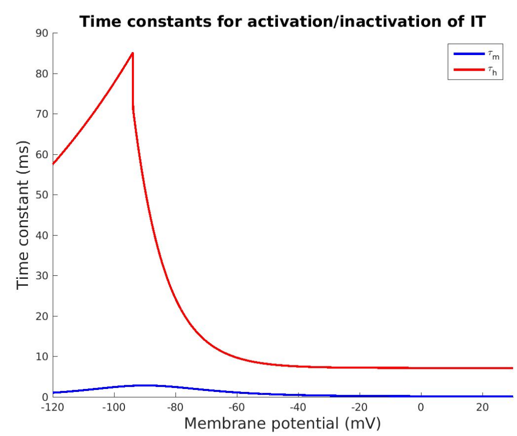
  - Destexhe 1998: shiftmIT = **1**, shifthIT = **1**, slopemIT = **1**, slopehIT = **1**



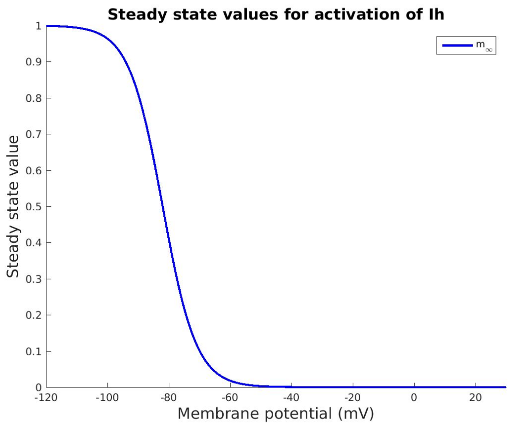


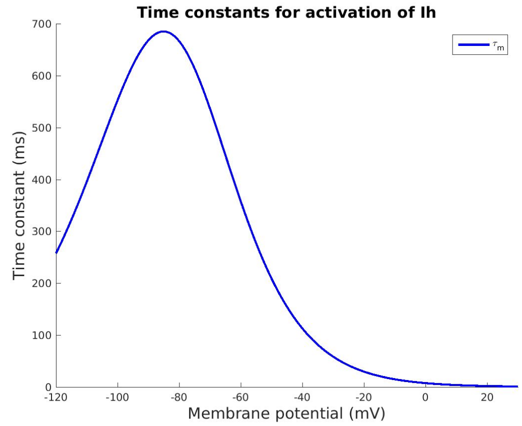
  - Christine/SingleNeuronFitting5:
    shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**



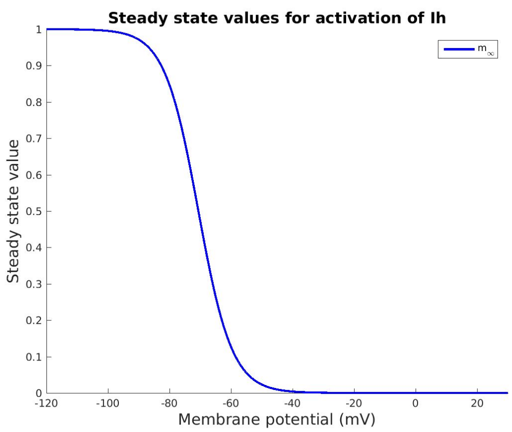


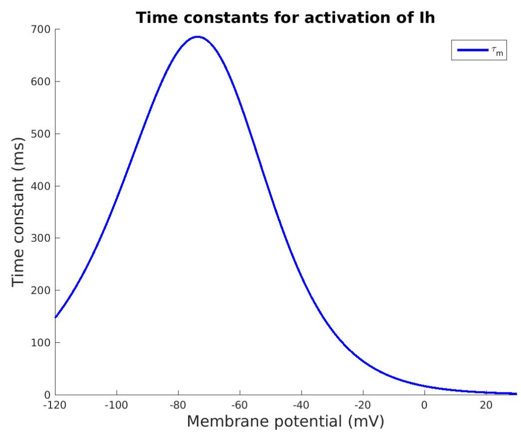
- Activation/inactivation curves of **Ih**
  - Destexhe 1998: shiftmIh = **0**



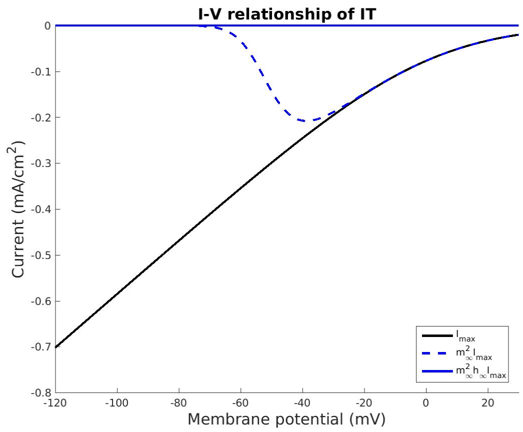


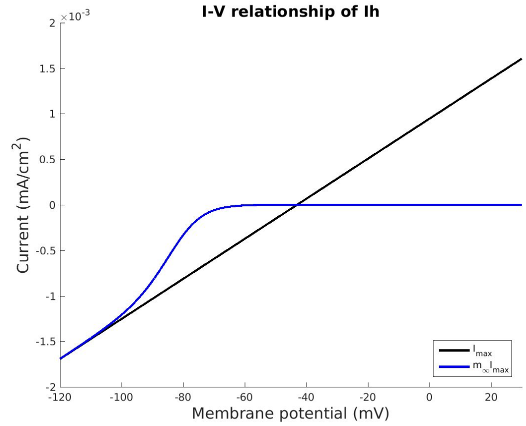
  - Christine/SingleNeuronFitting5: shiftmIh = **11.4**



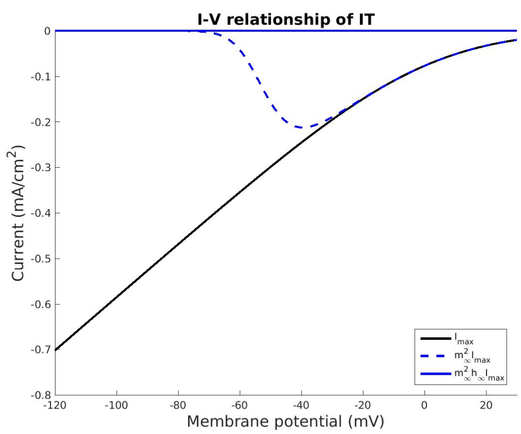


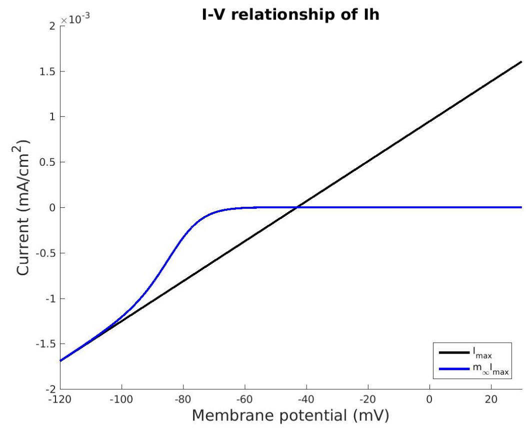
- I-V curves for IT & Ih
  - Destexhe old: pcabarIT = **.2e-3**, shiftmIT = **2**, shifthIT = **0**, slopemIT = **1,** slopehIT = **1,** ghbarIh = **2.2e-5**, shiftmIh = **0**



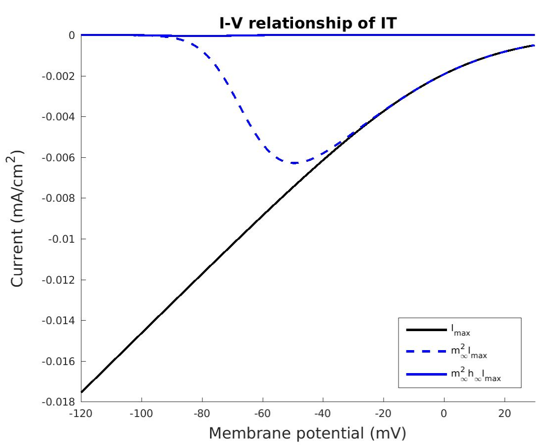


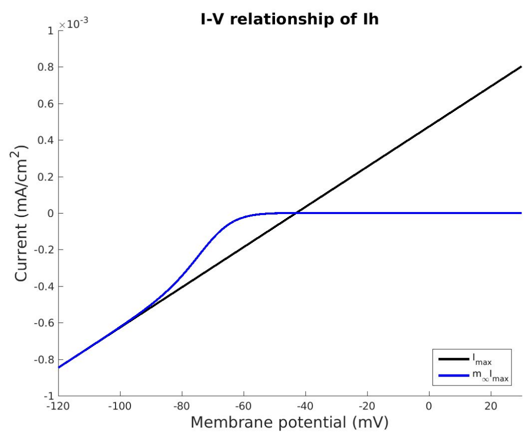
  - Destexhe 1998: pcabarIT = **.2e-3**, shiftmIT = **1**, shifthIT = **1**, slopemIT = **1**, slopehIT = **1**, ghbarIh = **2.2e-5**, shiftmIh = **0**



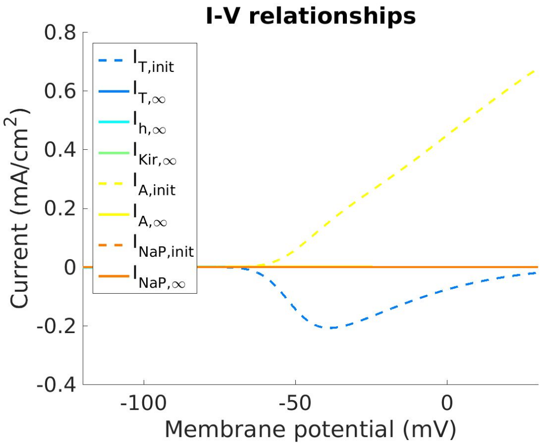


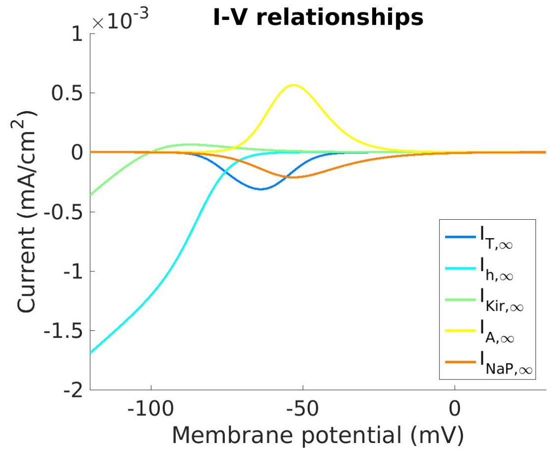
  - Christine_soma: pcabarIT = **5e-6**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarIh = **1.1e-5**, shiftmIh = **11.4**



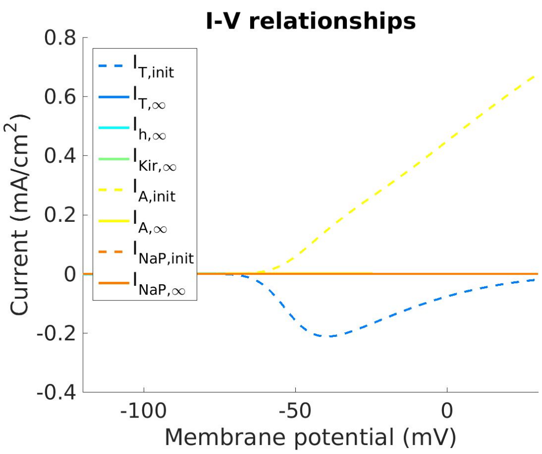


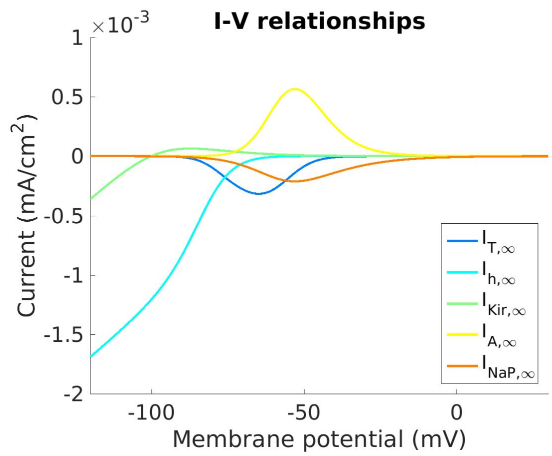
- All I-V curves
  - Destexhe old: pcabarIT = **.2e-3**, shiftmIT = **2**, shifthIT = **0**, slopemIT = **1,** slopehIT = **1,** ghbarIh = **2.2e-5**, shiftmIh = **0**



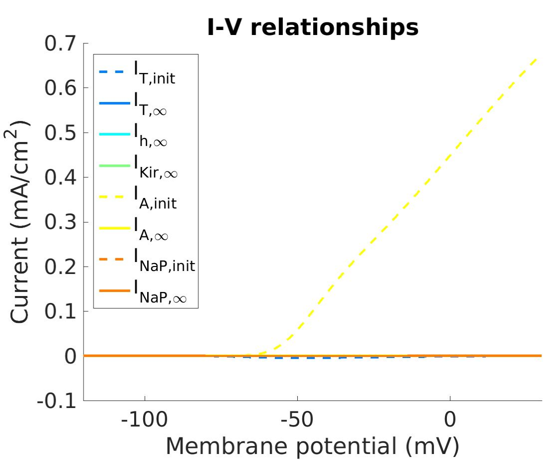


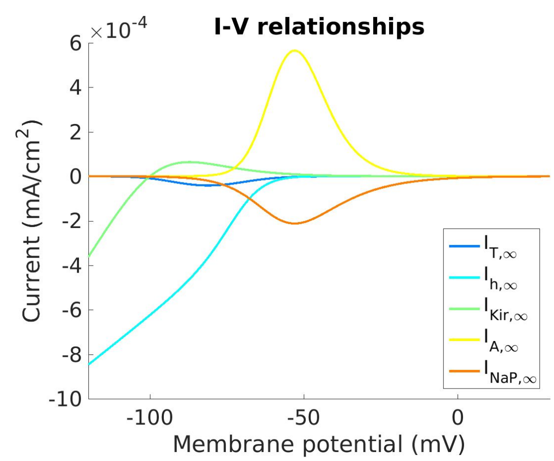
  - Destexhe 1998: pcabarIT = **.2e-3**, shiftmIT = **1**, shifthIT = **1**, slopemIT = **1**, slopehIT = **1**, ghbarIh = **2.2e-5**, shiftmIh = **0**



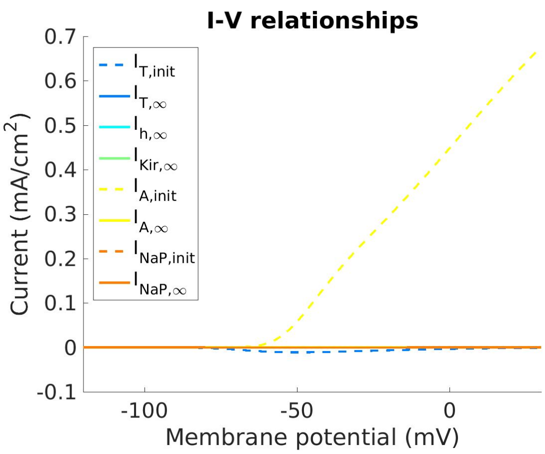


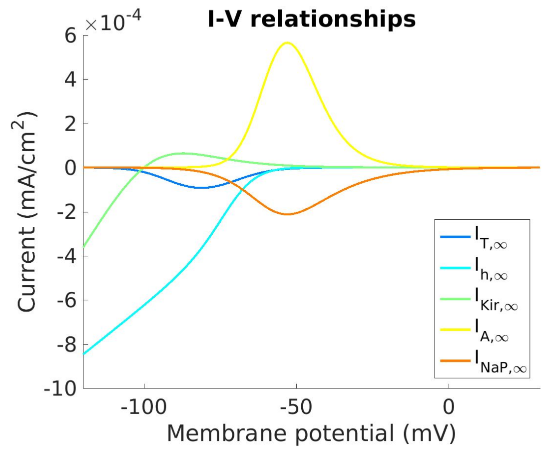
  - Christine_soma: pcabarIT = **5e-6**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarIh = **1.1e-5**, shiftmIh = **11.4**



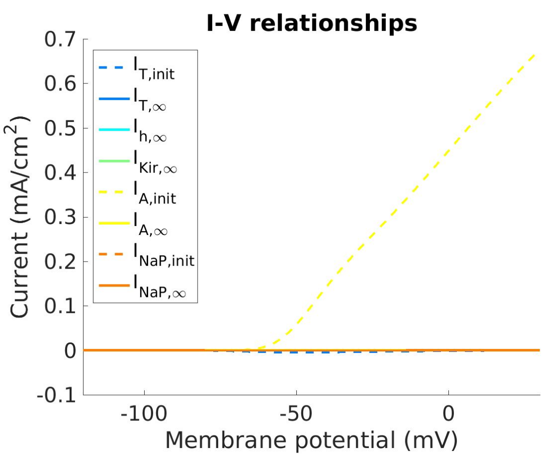


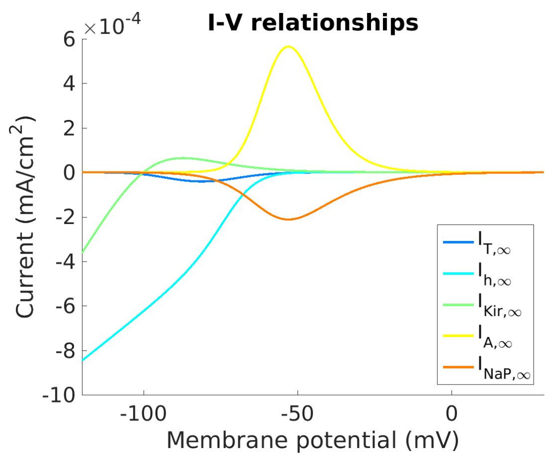
- Christine_dend1: pcabarIT = **8.91e-6**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarlh = **1.1e-5**, shiftmlh = **11.4**



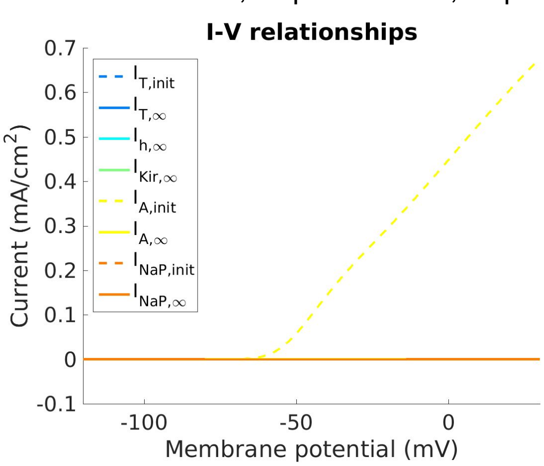


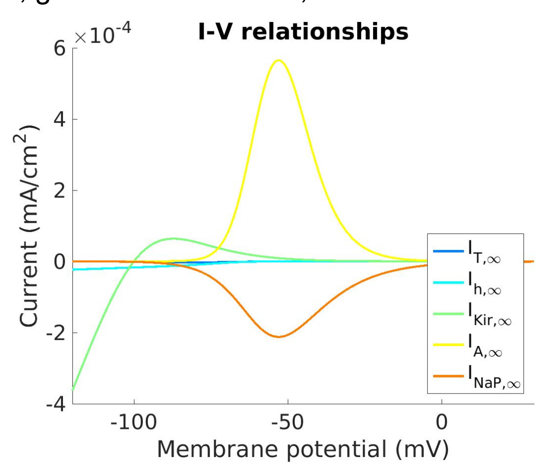
- Christine_dend2: pcabarIT = **3.98e-6**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarlh = **1.1e-5**, shiftmlh = **11.4**



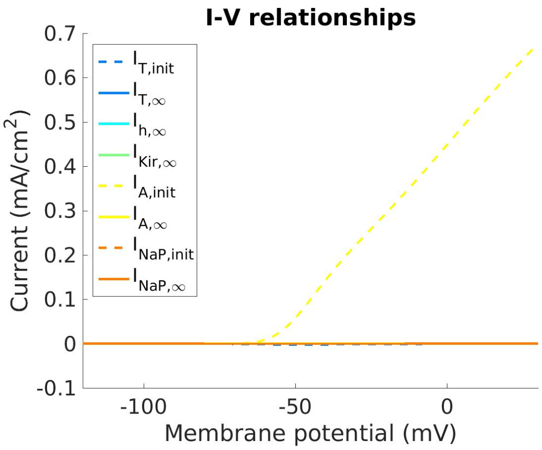


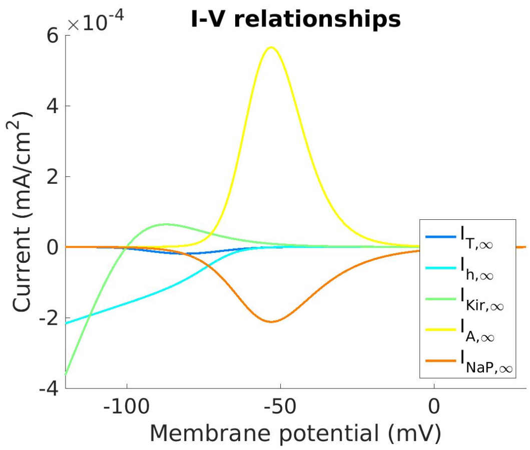
- SingleNeuronFitting5_soma: pcabarIT = **2.8216e-7**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarlh = **3.0206e-7**, shiftmlh = **11.4**



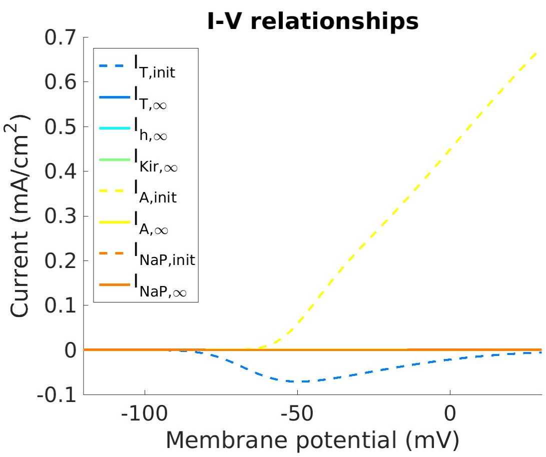


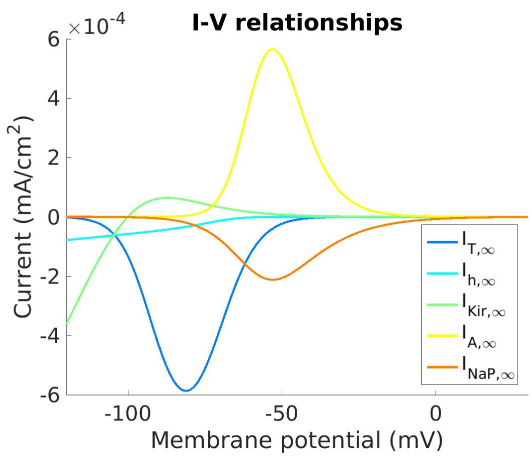
- SingleNeuronFitting5_dend1: pcabarIT = **1.8440e-6**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarIh = **1.0226e-6**, shiftmIh = **11.4**





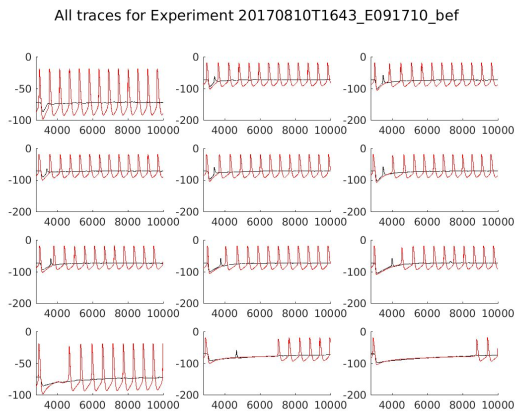
- SingleNeuronFitting5_dend2: pcabarIT = **5.6634e-5**, shiftmIT = **-13.8**, shifthIT = **-4.8**, slopemIT = **1.4**, slopehIT = **1**, ghbarIh = **1.0226e-6**, shiftmIh = **11.4**

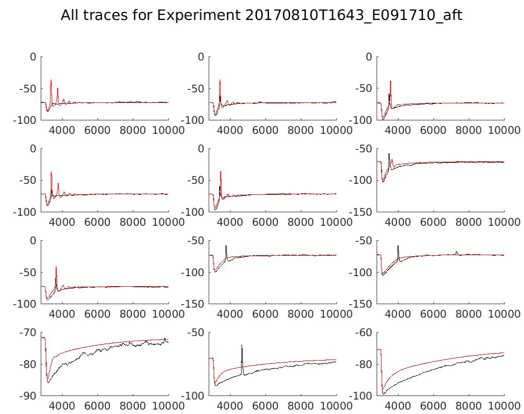




- Created **compare_and_plot_across_IC.m** and **compare_and_plot_across_IC2.m** for compare across different initial sets of NEURON parameters
- Created **compare_neuronparams.m** for comparing sets of parameters that:
  - Determine which parameters were changed
  - Plot graphs according to what parameters were changed
  - Usage: **compare_neuronparams(paramNames, paramValues, suffices)**
- **optimizer_4compgabab.m** now plots **activation/inactivation, I-V curves** for initial and final sets of NEURON parameters after optimization
- Reran **singleneuronfitting10.m** for Destexhe default after the following changes:
  - **ek**: -97 -> **-100 mV**
  - **shiftmIT**: -2 -> **1 mV**
  - **shiftmIh**: 0 -> **1 mV**

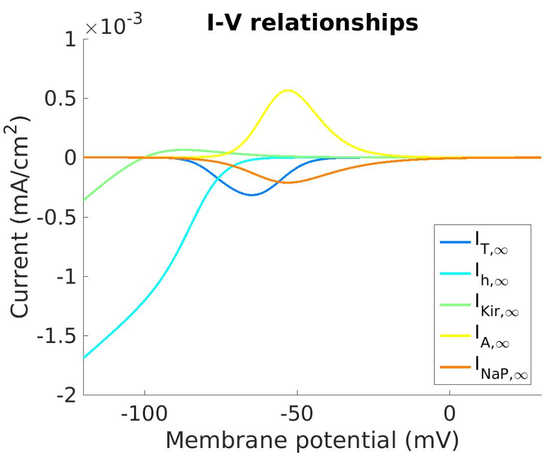
- Before and after optimization:



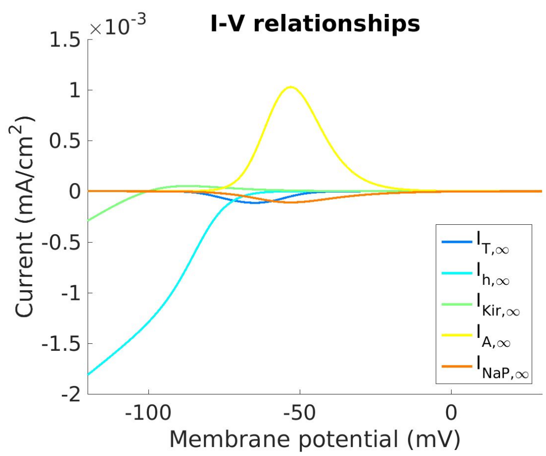


- Steady-state I-V curves for **soma**:

Before:

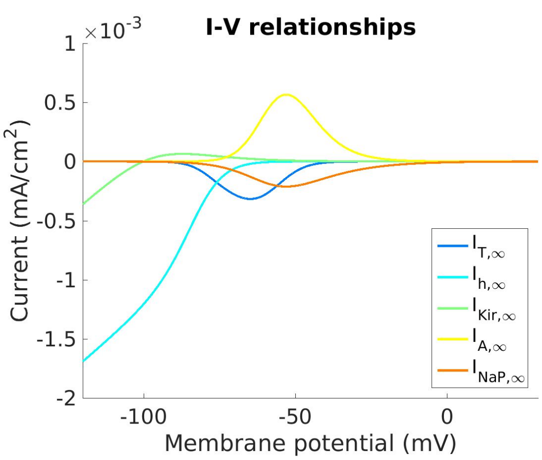


After:

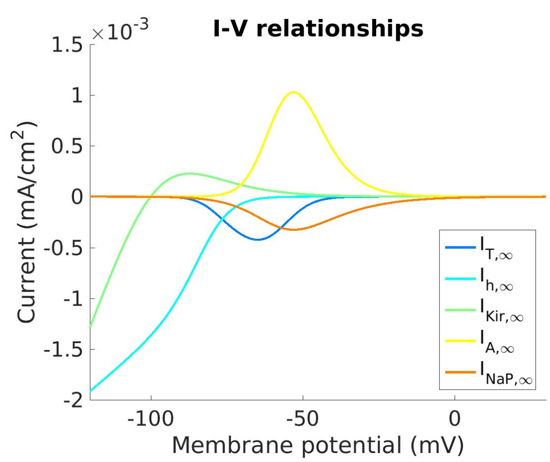


- Steady-state I-V curves for **dend1**:

Before:

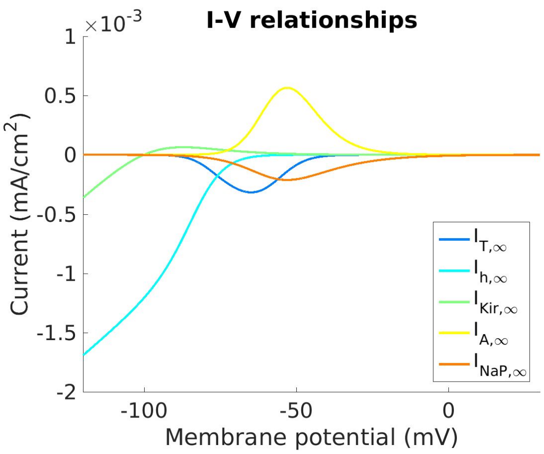


After:

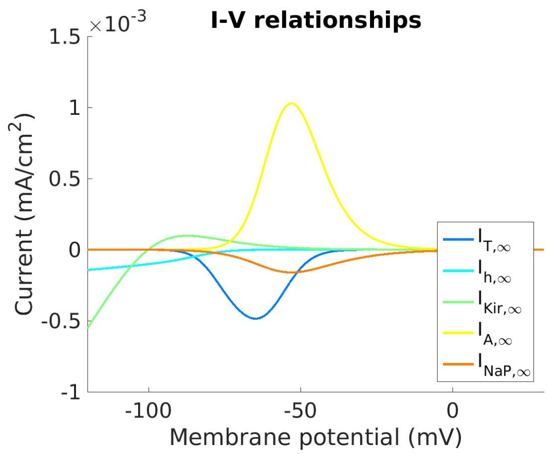


- Steady-state I-V curves for **dend2**:

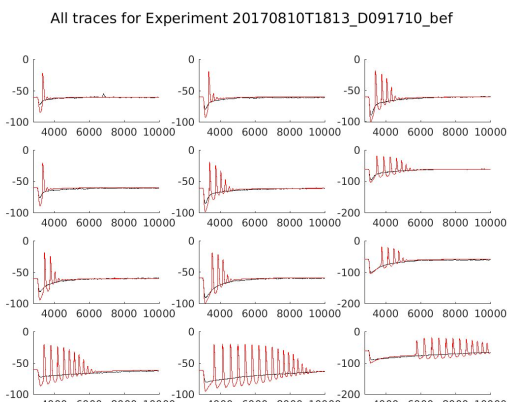
Before:

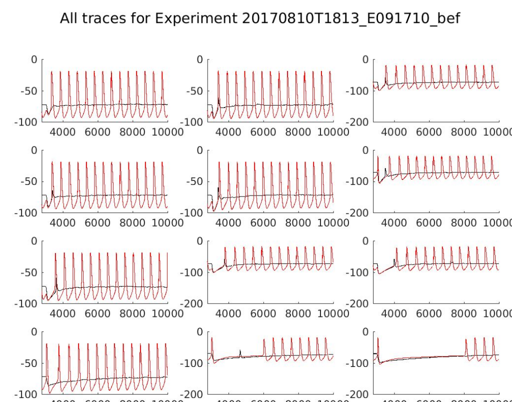


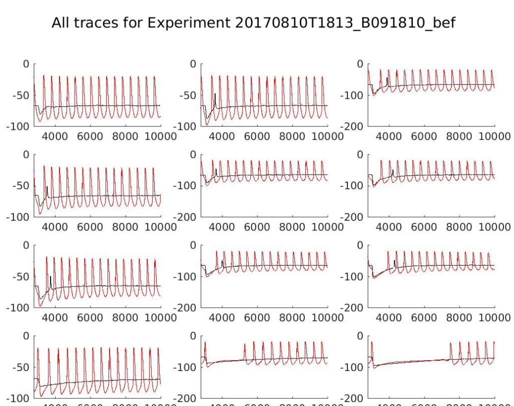
After:

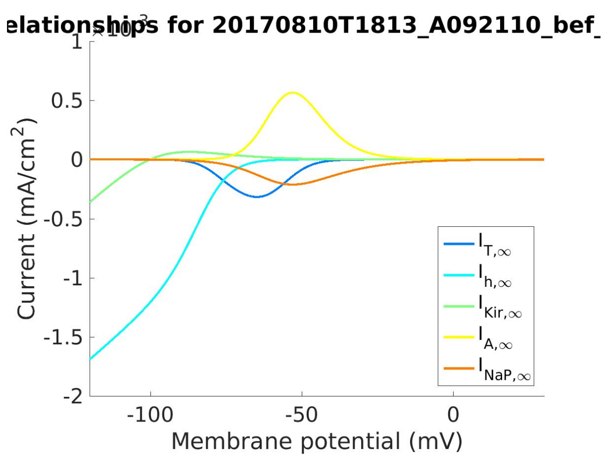


- **singleneuronfitting11.m**: Changed **eh** from -43 mV to **-28 mV** and bound it by **-24~-32 mV**. (Based on [Na+]out = 127.25 mM, [Na+]in = 4.5 mM, [K+]out = 2.5 mM, [K+]in = 113 mM & celsius = 33 degC, the GHK voltage equation yields -24 ~ -32 mV)
- Fitted **all 36 cells** on fishfish, using **one arbitrary trace** per input condition
    - **Before** optimization (starting with the same default parameters):





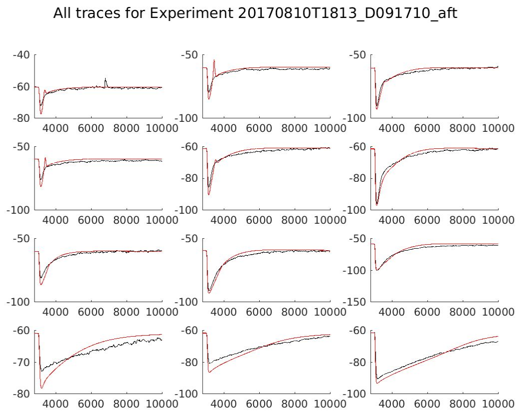




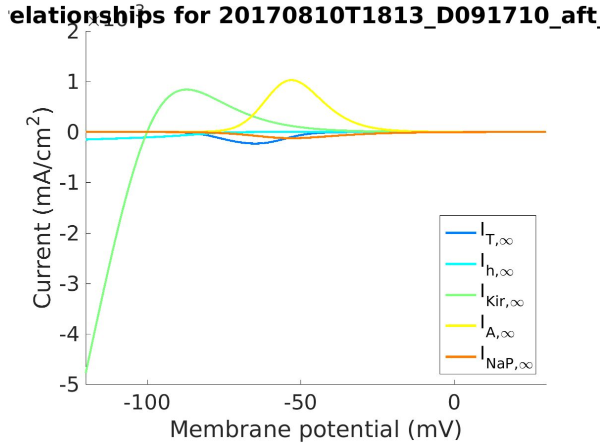
- **After** optimization:

D091710

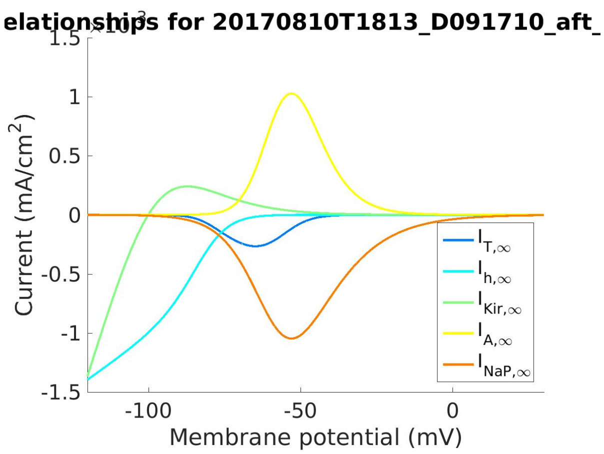
All traces:



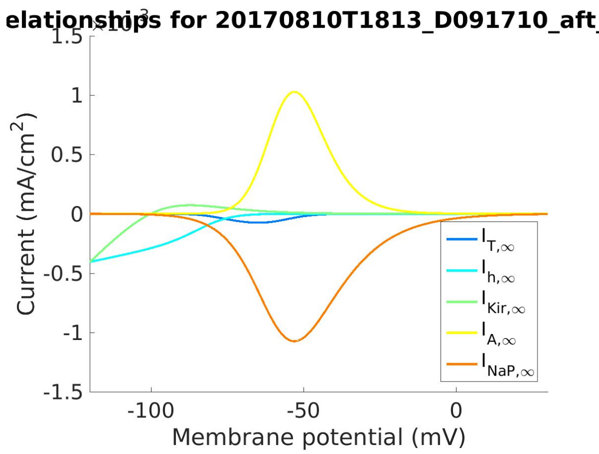
Steady-state I-V curves for **soma, dend0**:



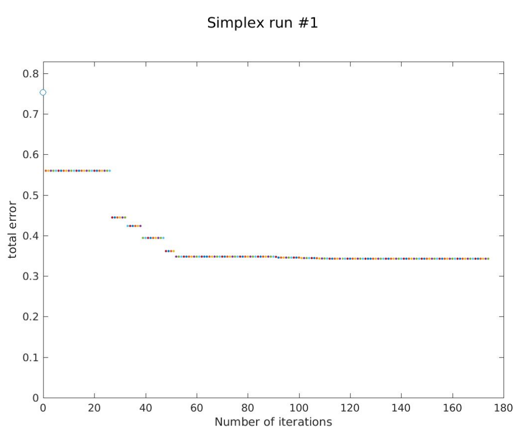
Steady-state I-V curves for **dend1**:



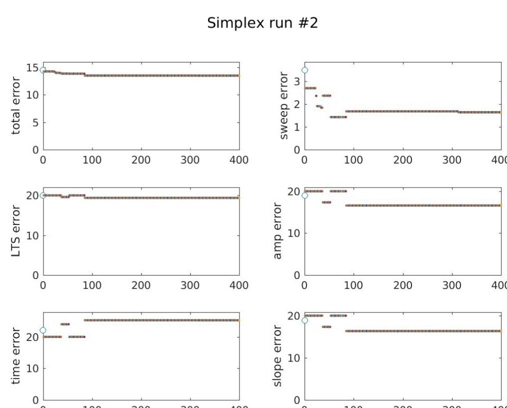
Steady-state I-V curves for **dend2**:



Passive fitting history:

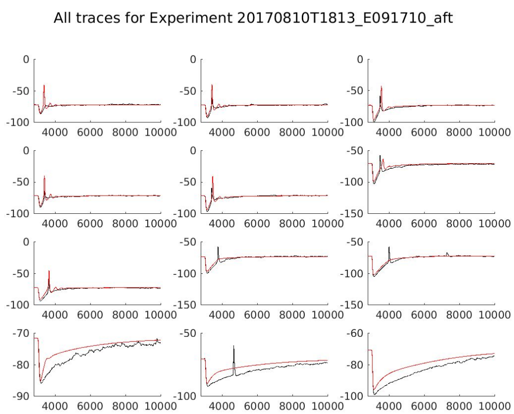


Active fitting history:

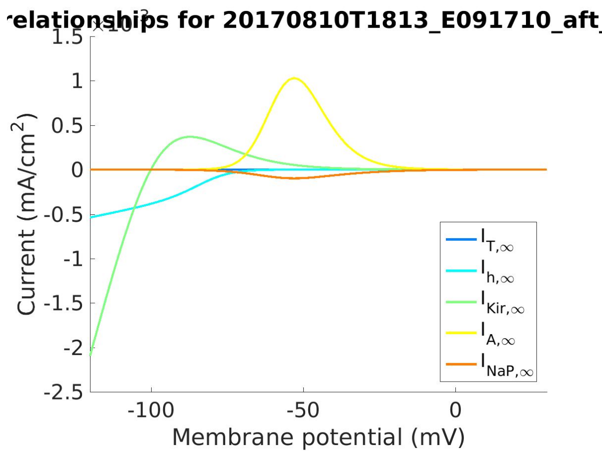


E091710

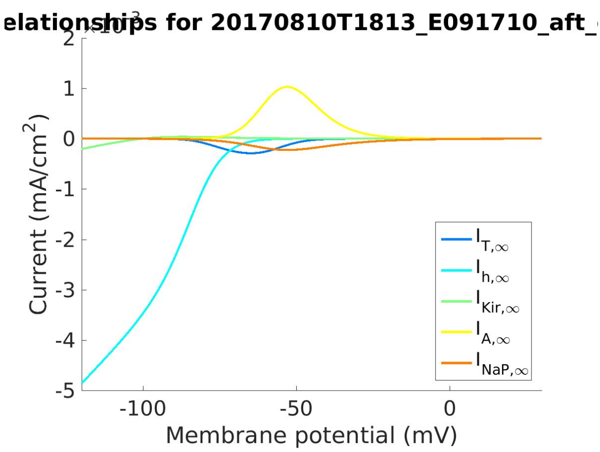
All traces:



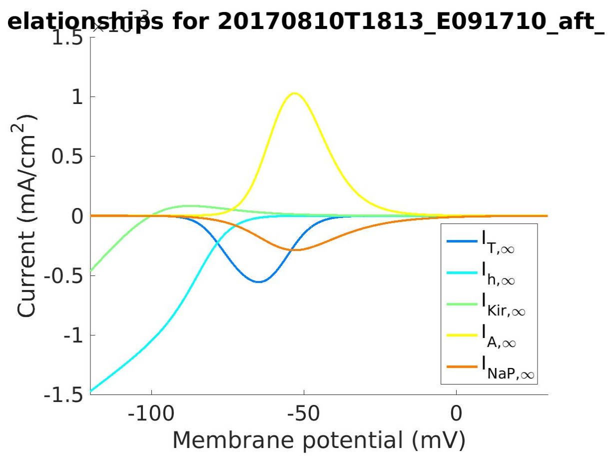
Steady-state I-V curves for **soma, dend0**:



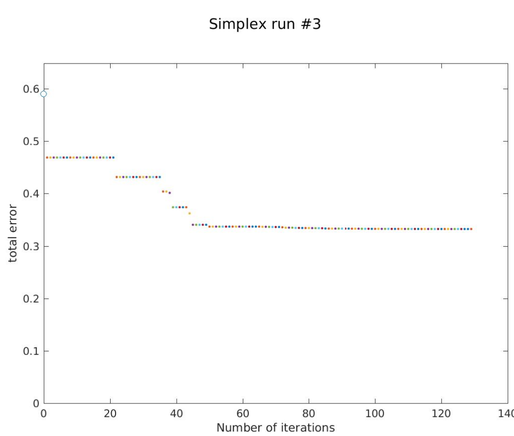
Steady-state I-V curves for **dend1**:



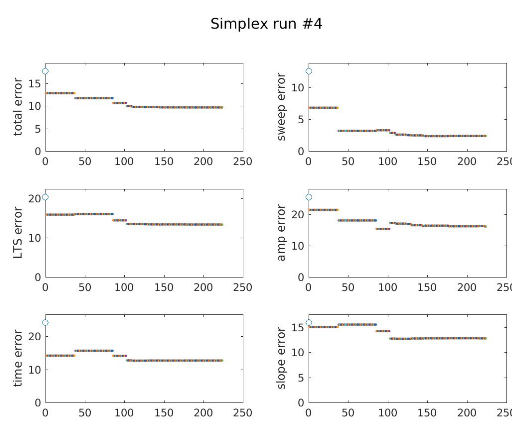
Steady-state I-V curves for **dend2**:



Passive fitting history:

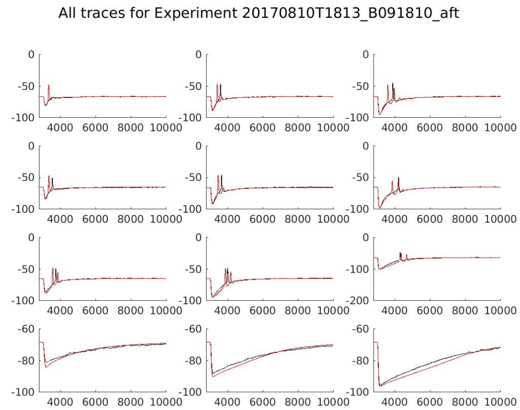


Active fitting history:

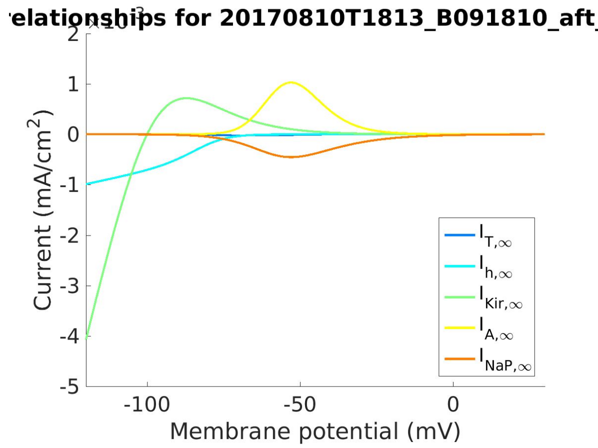


B091810

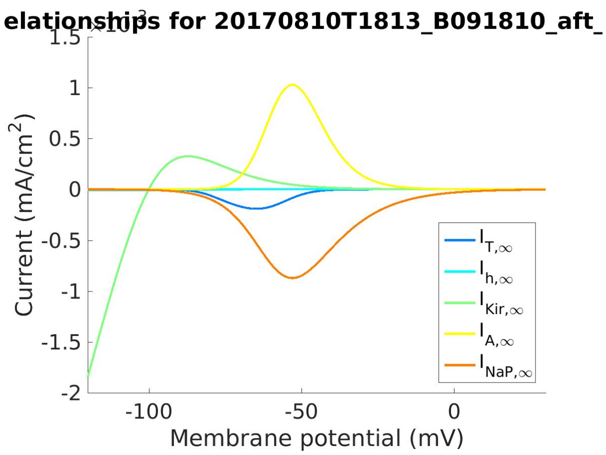
All traces:



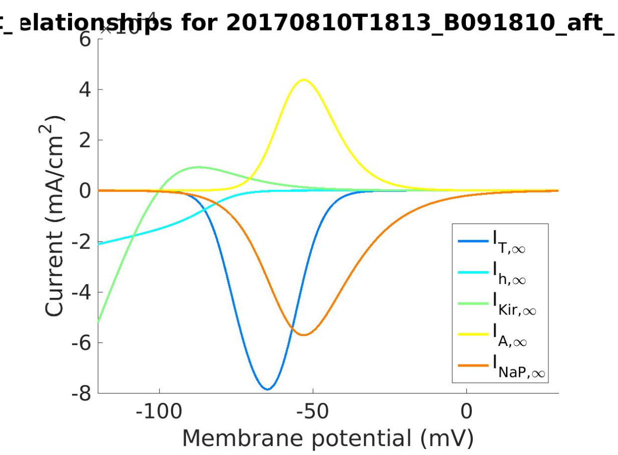
Steady-state I-V curves for **soma, dend0**:



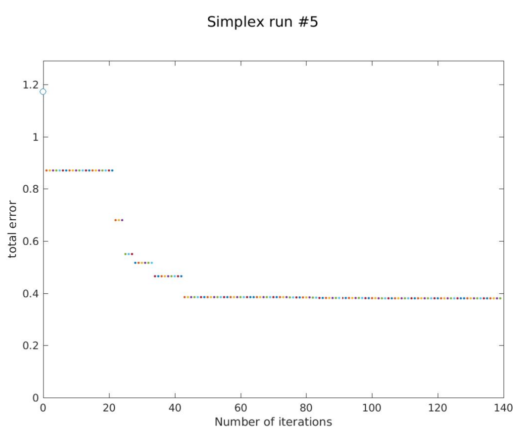
Steady-state I-V curves for **dend1**:



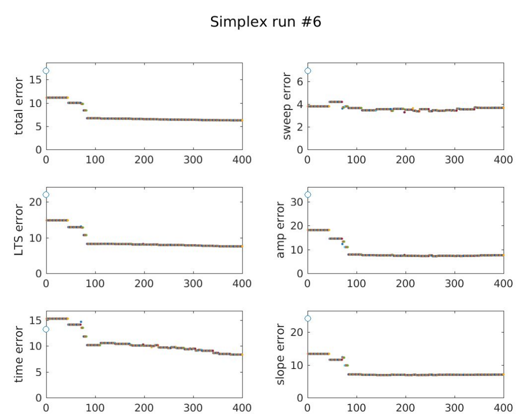
Steady-state I-V curves for **dend2**:



Passive fitting history:

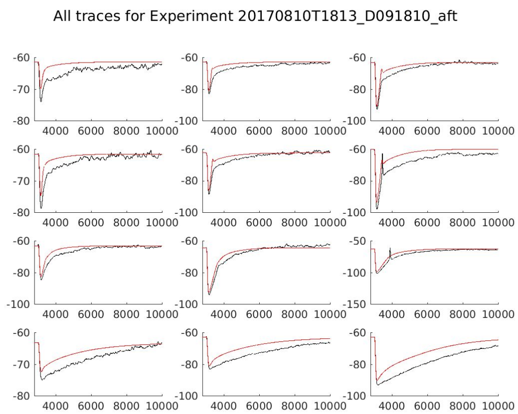


Active fitting history:

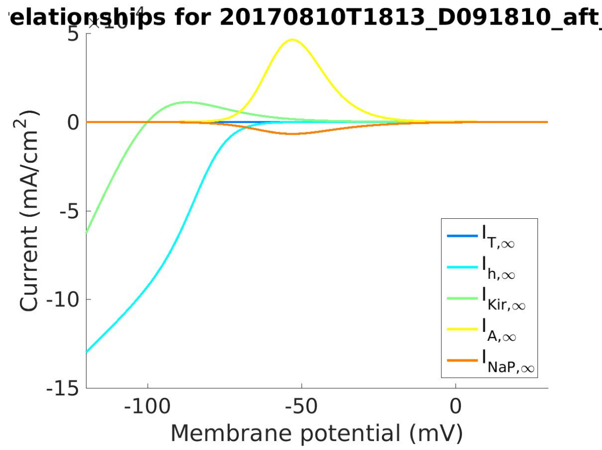


D091810

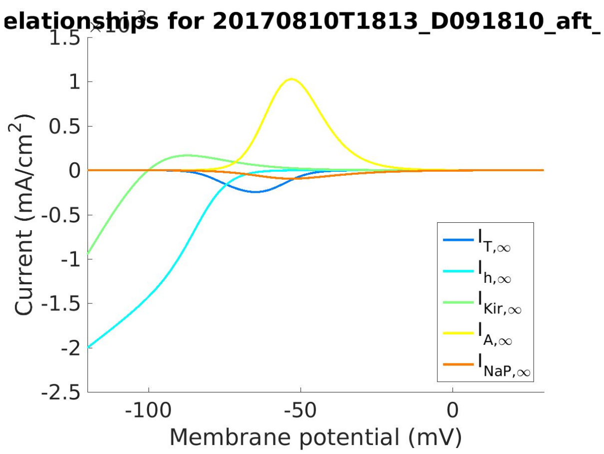
All traces:



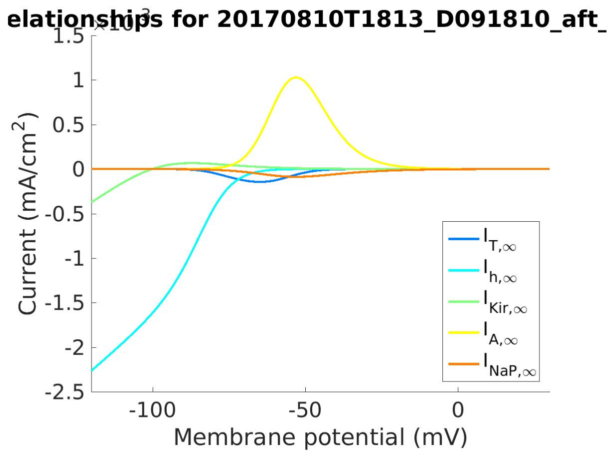
Steady-state I-V curves for **soma, dend0**:



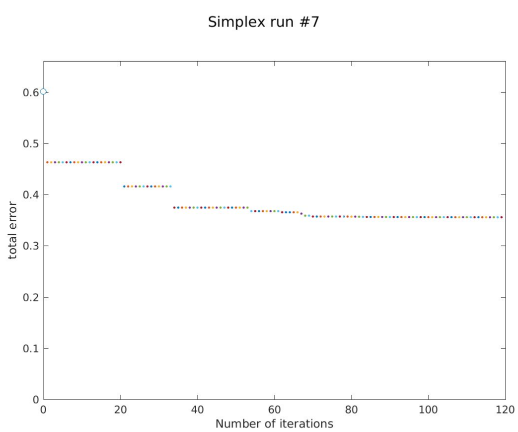
Steady-state I-V curves for **dend1**:



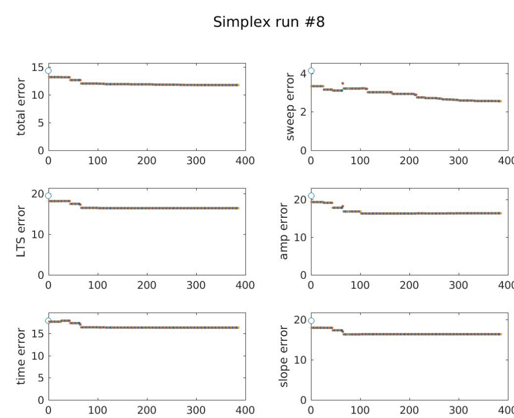
Steady-state I-V curves for **dend2**:



Passive fitting history:

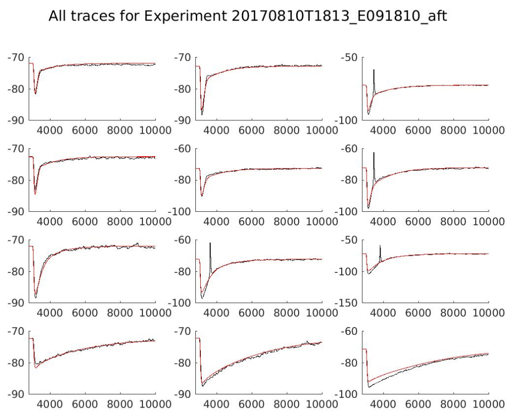


Active fitting history:

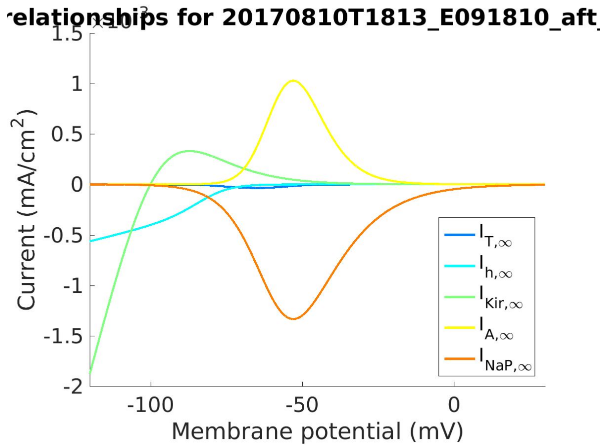


E091810

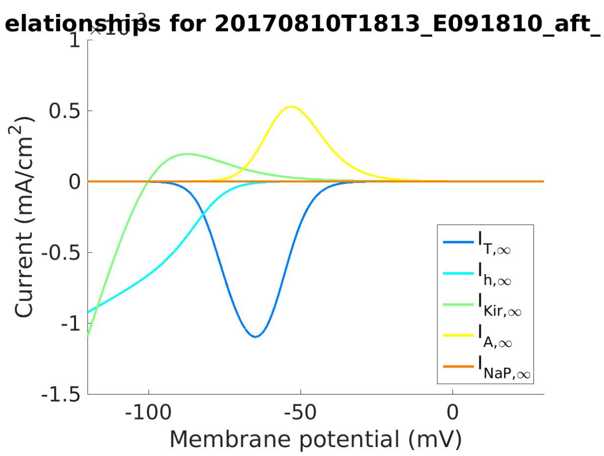
All traces:



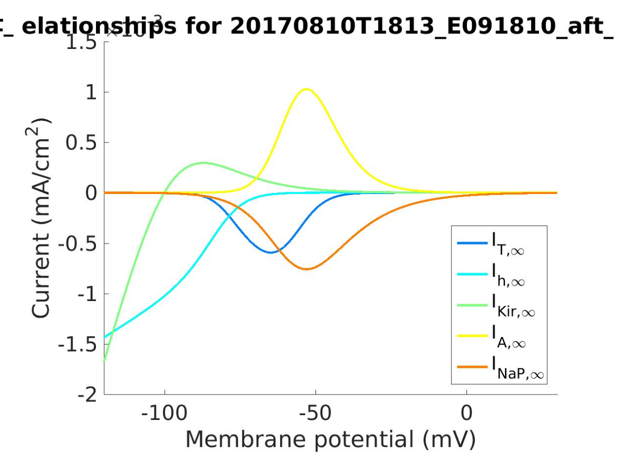
Steady-state I-V curves for **soma, dend0**:



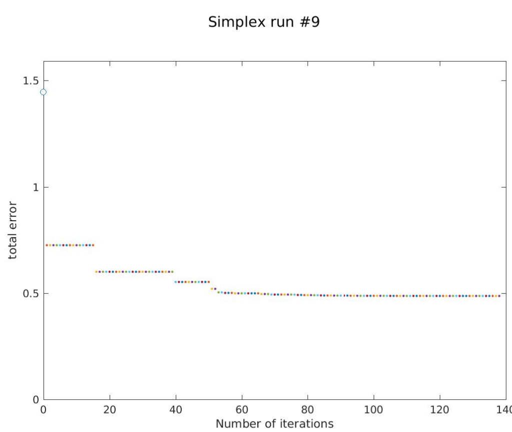
Steady-state I-V curves for **dend1**:



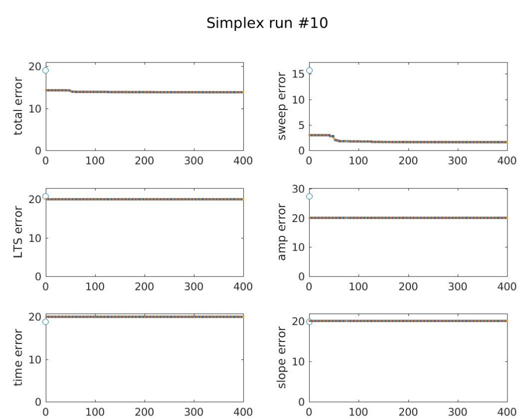
Steady-state I-V curves for **dend2**:



Passive fitting history:

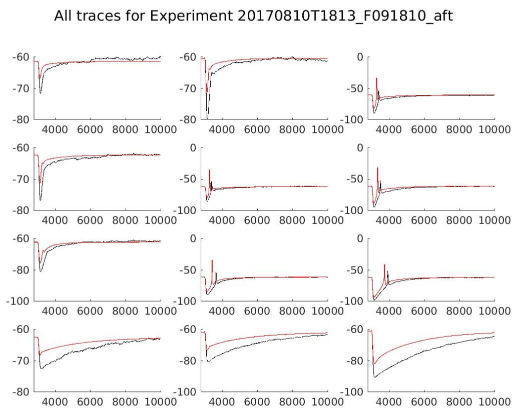


Active fitting history:

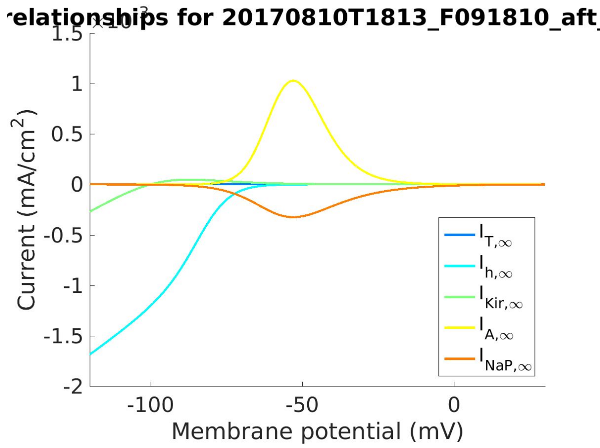


F091810

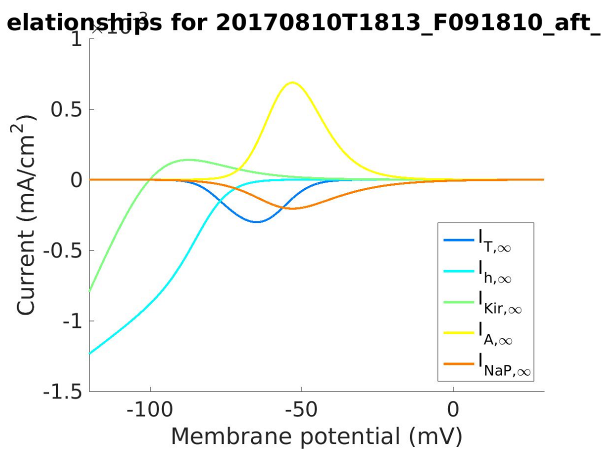
All traces:



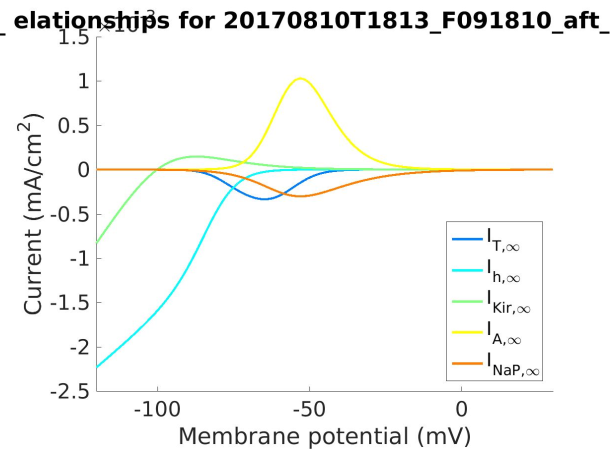
Steady-state I-V curves for **soma, dend0**:



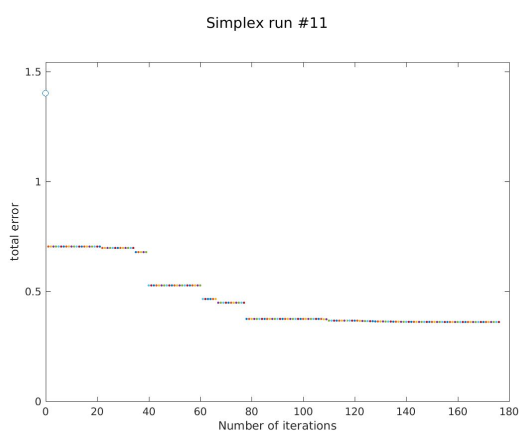
Steady-state I-V curves for **dend1**:



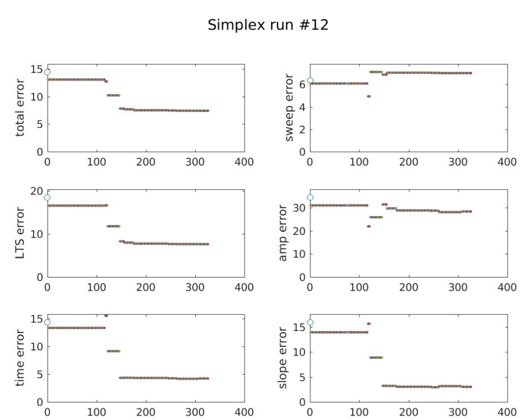
Steady-state I-V curves for **dend2**:



Passive fitting history:

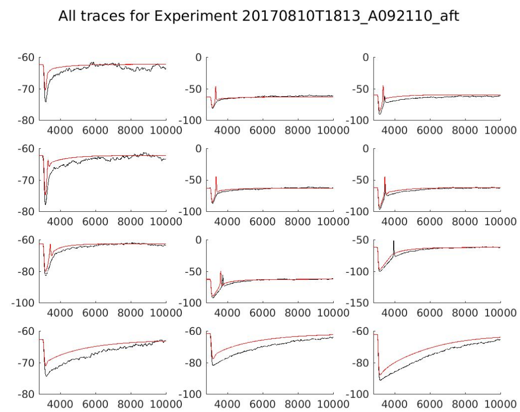


Active fitting history:

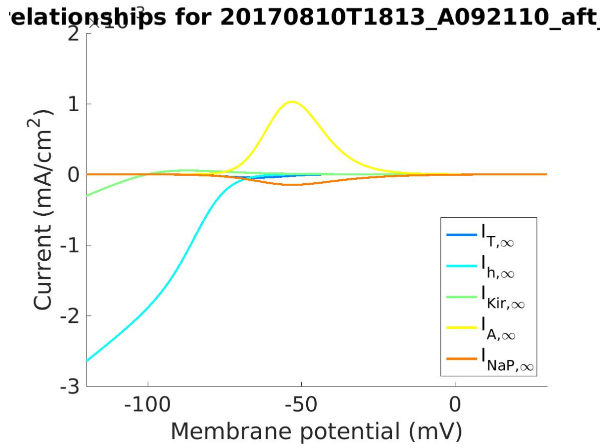


A092110

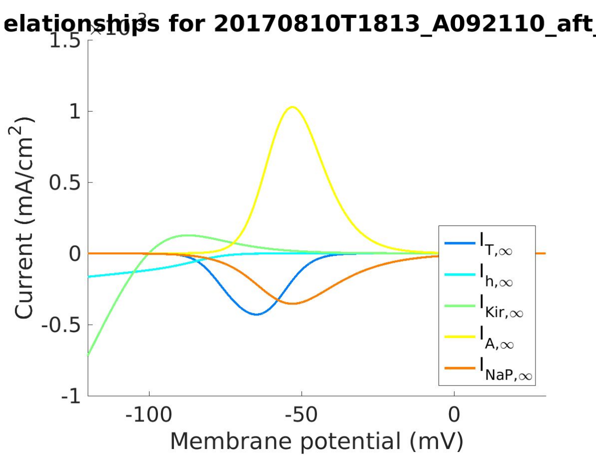
All traces:



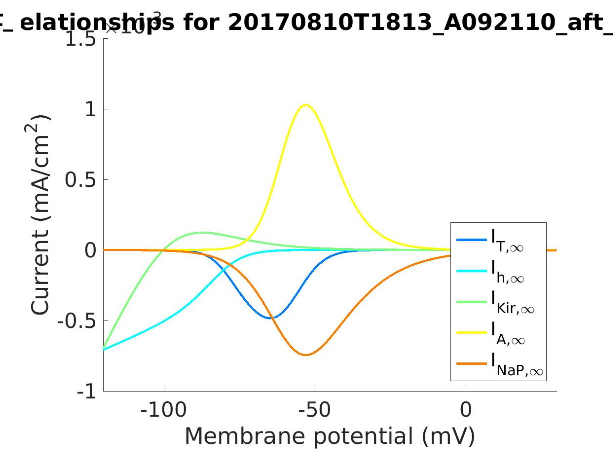
Steady-state I-V curves for **soma, dend0**:



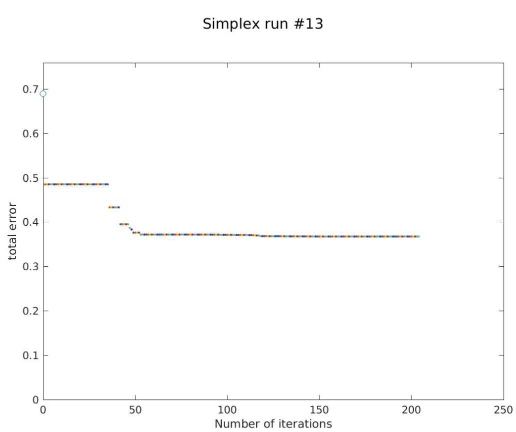
Steady-state I-V curves for **dend1**:



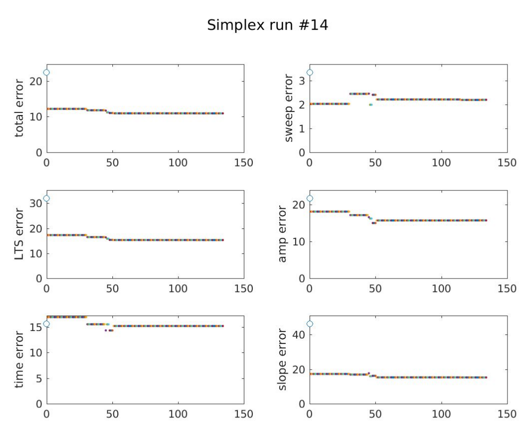
Steady-state I-V curves for **dend2**:



Passive fitting history:

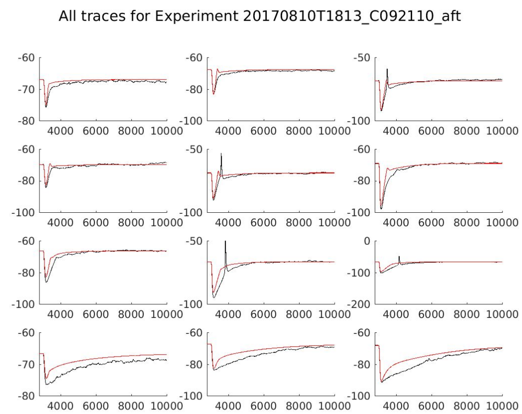


Active fitting history:

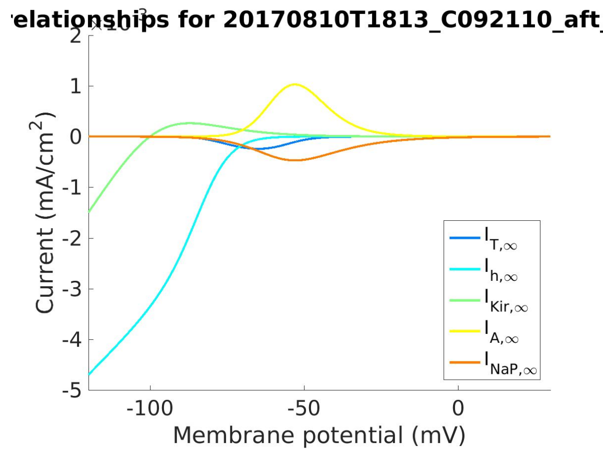


C092110

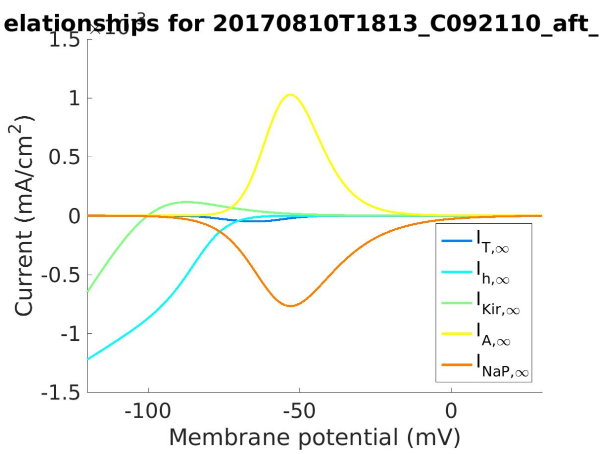
All traces:



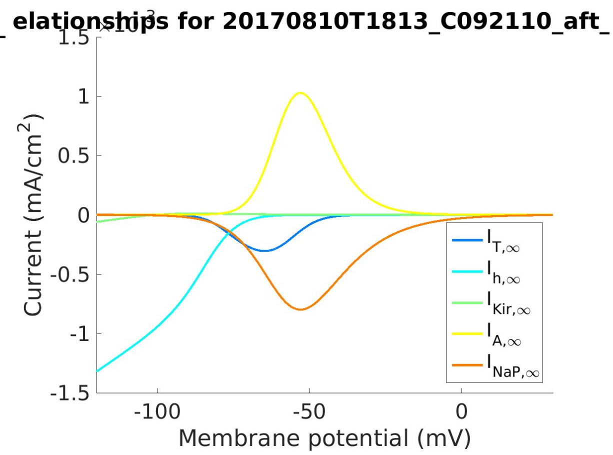
Steady-state I-V curves for **soma, dend0**:



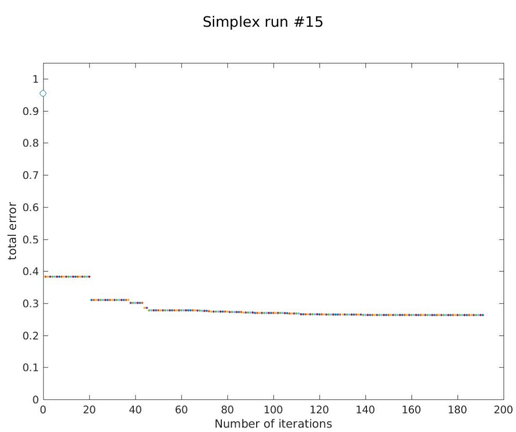
Steady-state I-V curves for **dend1**:



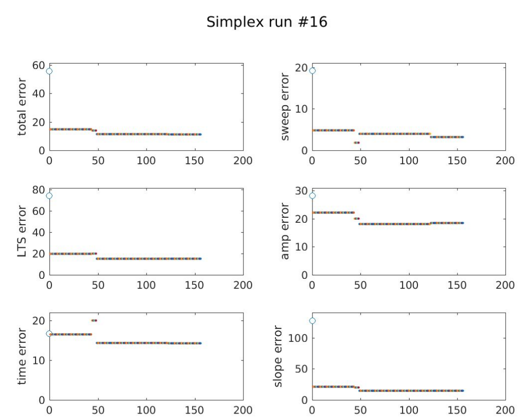
Steady-state I-V curves for **dend2**:



Passive fitting history:

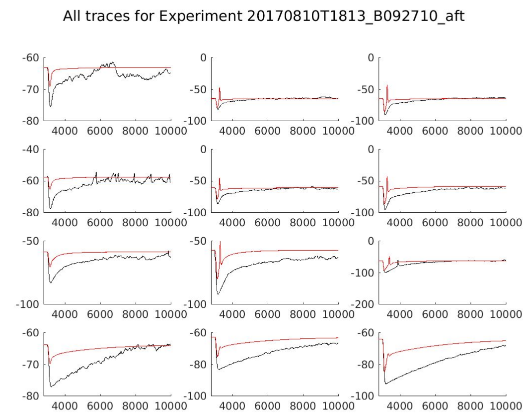


Active fitting history:

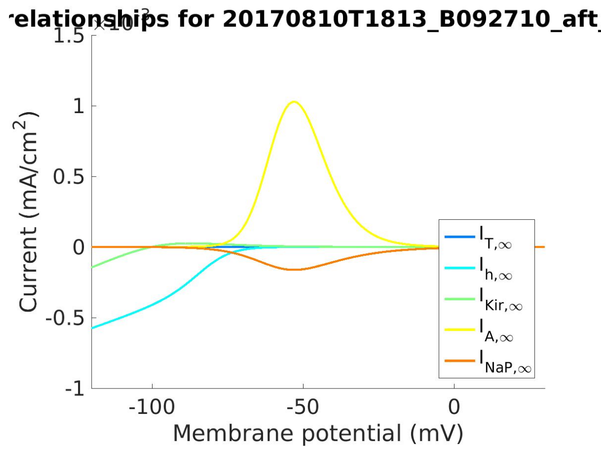


B092710

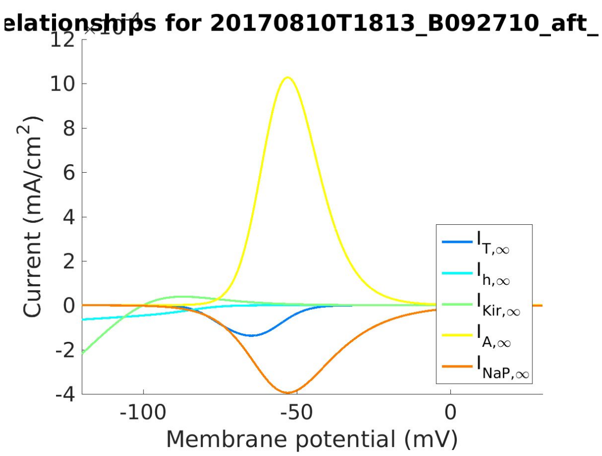
All traces:



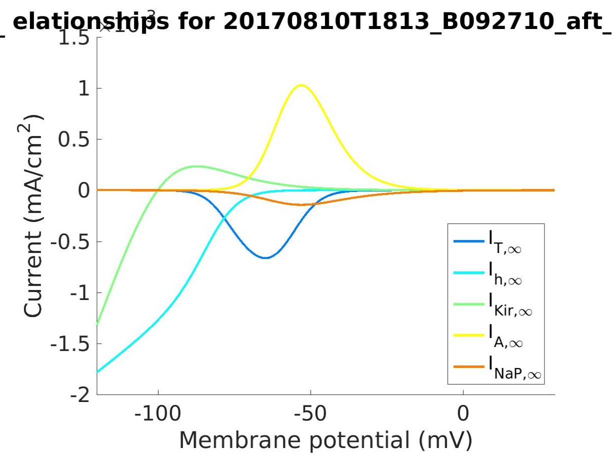
Steady-state I-V curves for **soma, dend0**:



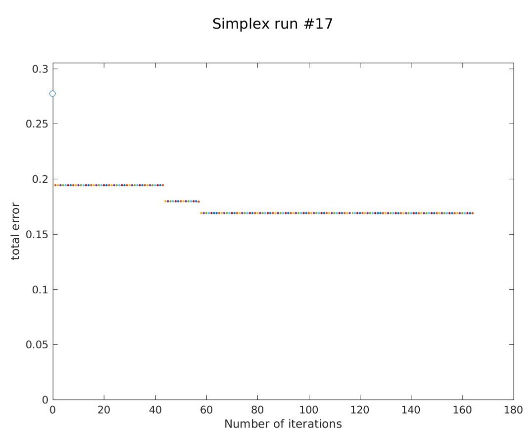
Steady-state I-V curves for **dend1**:



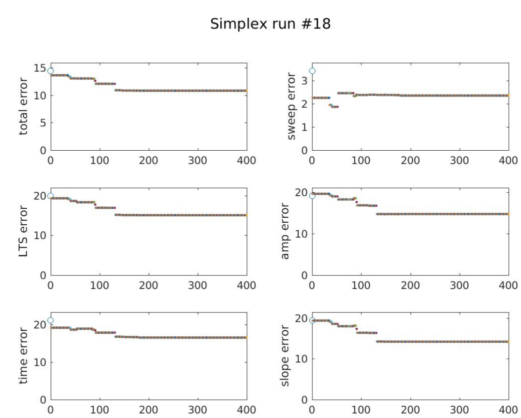
Steady-state I-V curves for **dend2**:



Passive fitting history:

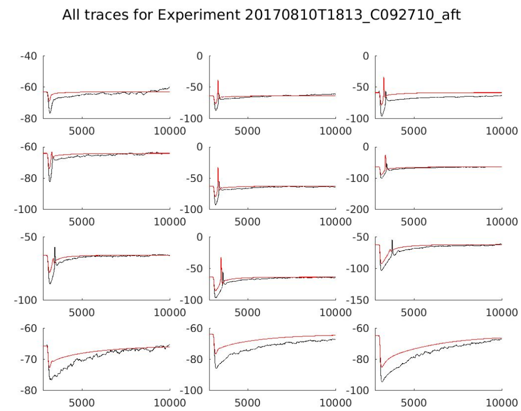


Active fitting history:

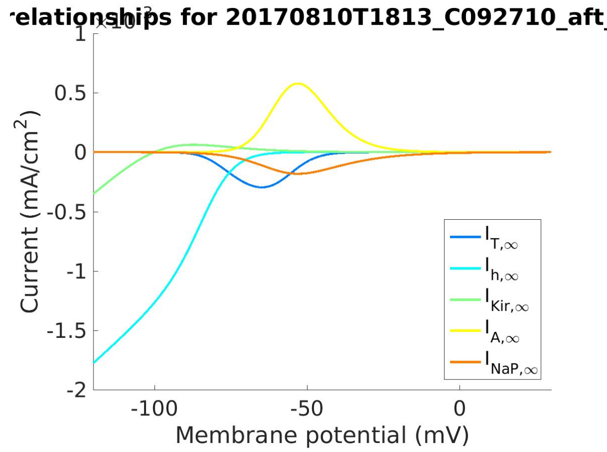


C092710

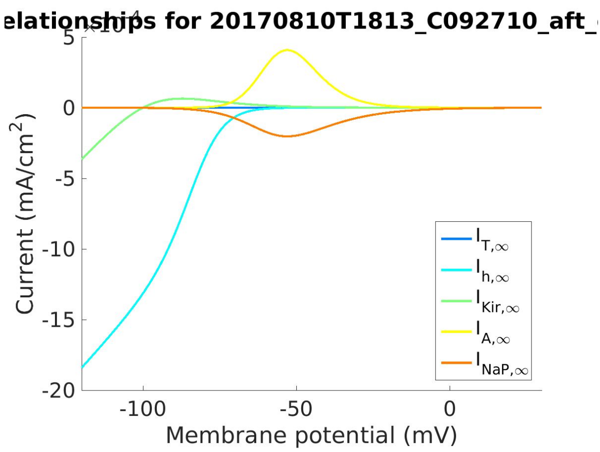
All traces:



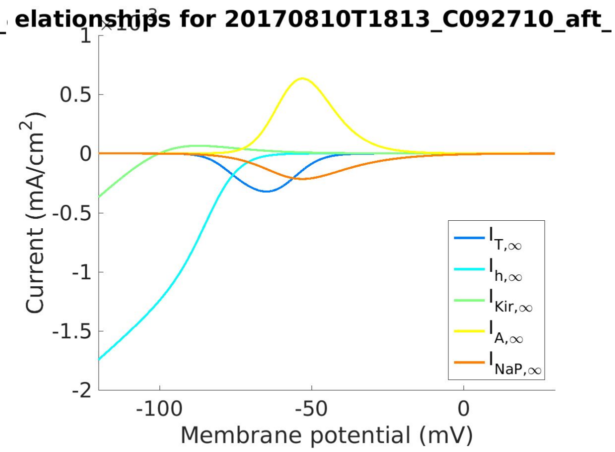
Steady-state I-V curves for **soma, dend0**:



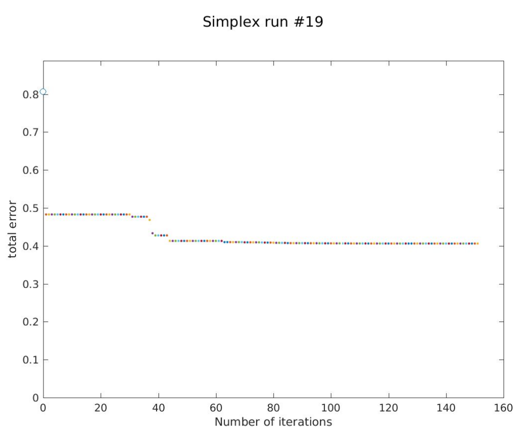
Steady-state I-V curves for **dend1**:



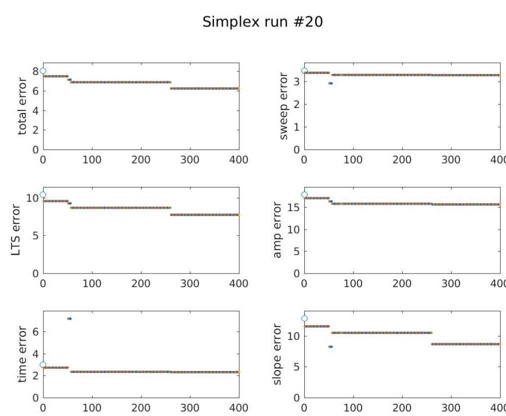
Steady-state I-V curves for **dend2**:



Passive fitting history:

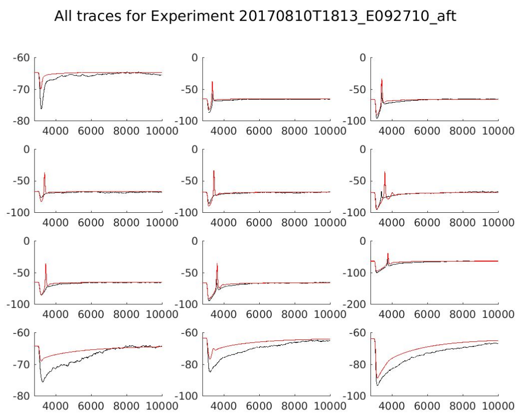


Active fitting history:

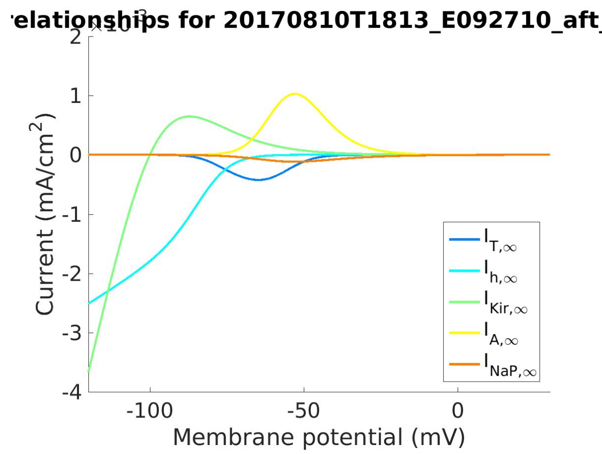


E092710

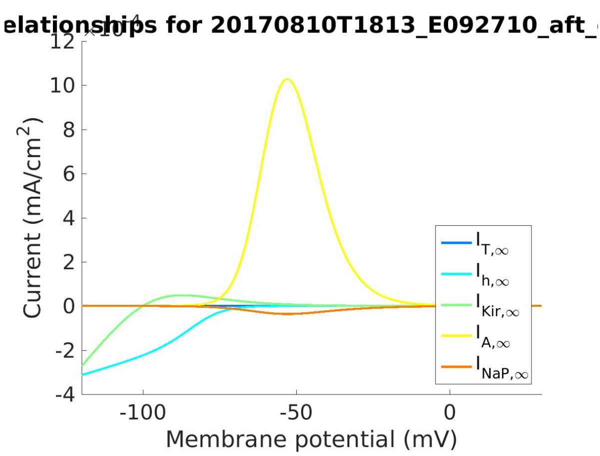
All traces:



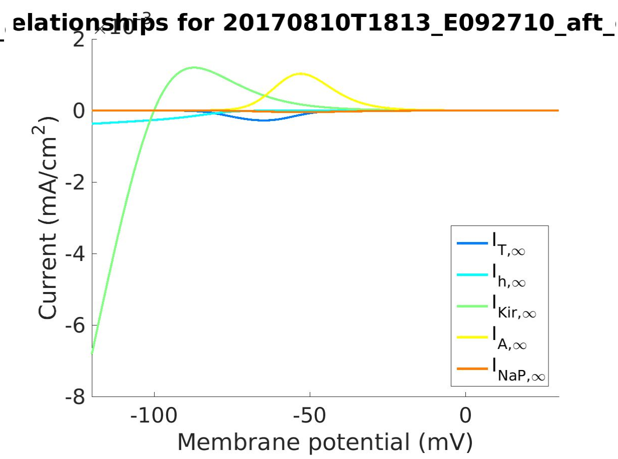
Steady-state I-V curves for **soma, dend0**:



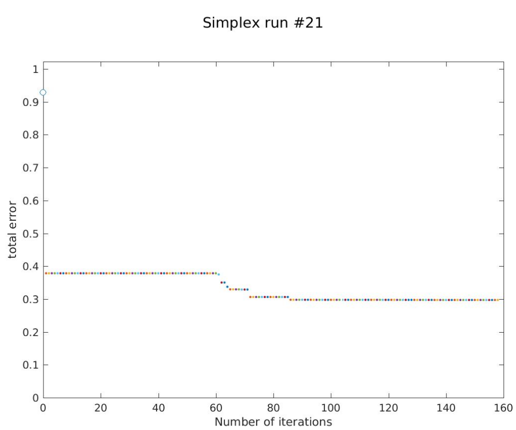
Steady-state I-V curves for **dend1**:



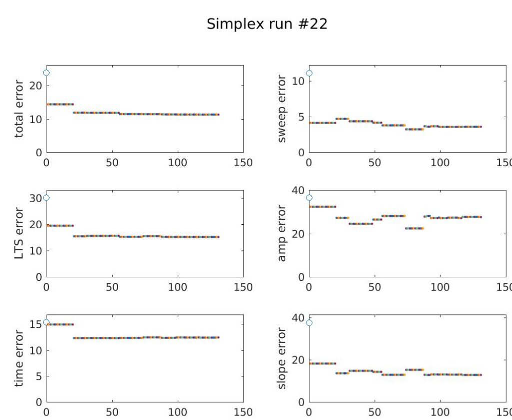
Steady-state I-V curves for **dend2**:



Passive fitting history:

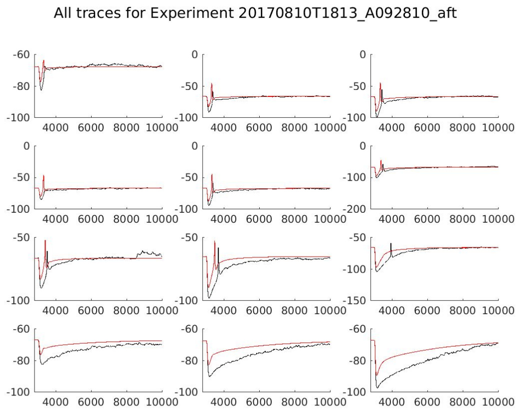


Active fitting history:

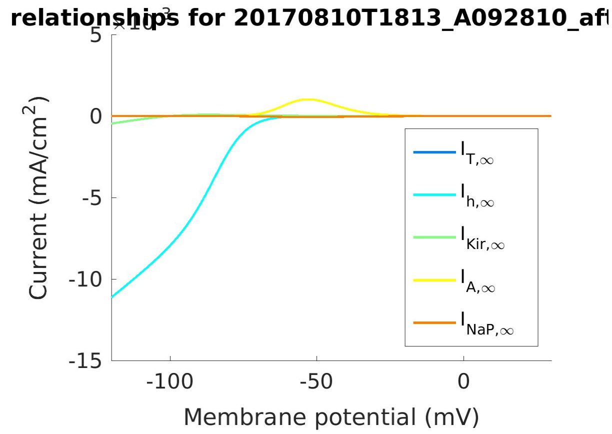


A092810

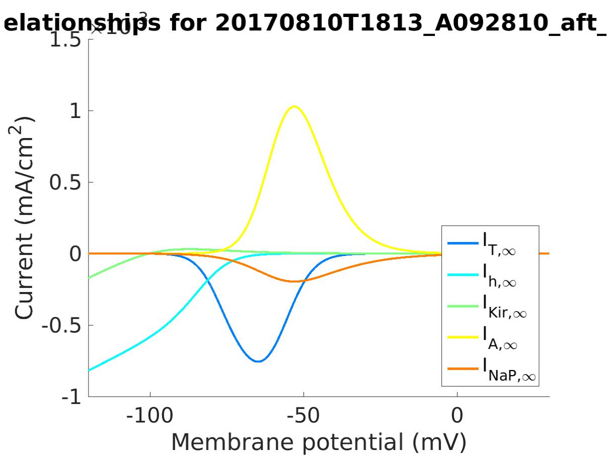
All traces:



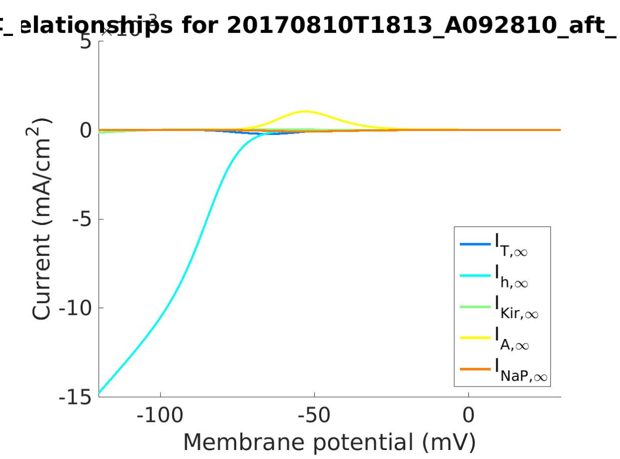
Steady-state I-V curves for **soma, dend0**:



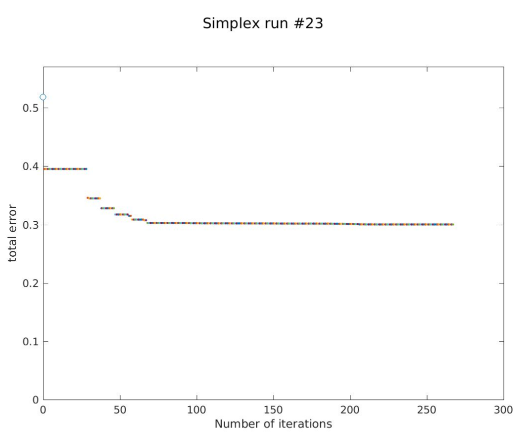
Steady-state I-V curves for **dend1**:



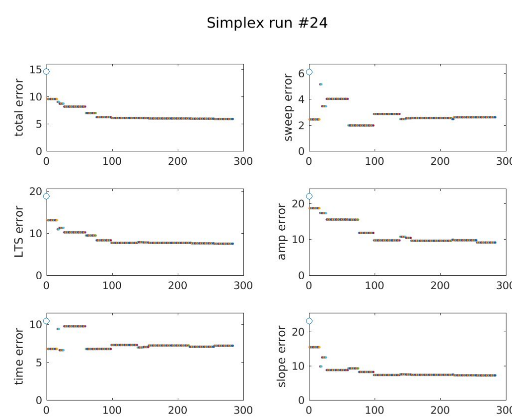
Steady-state I-V curves for **dend2**:



Passive fitting history:

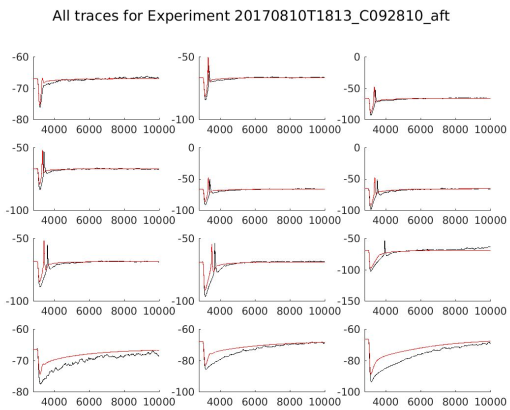


Active fitting history:

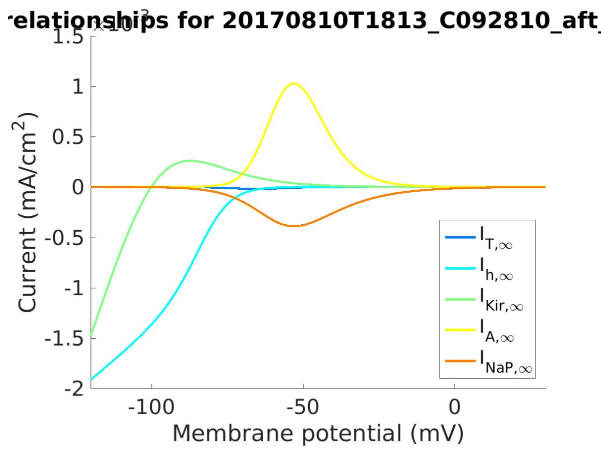


C092810

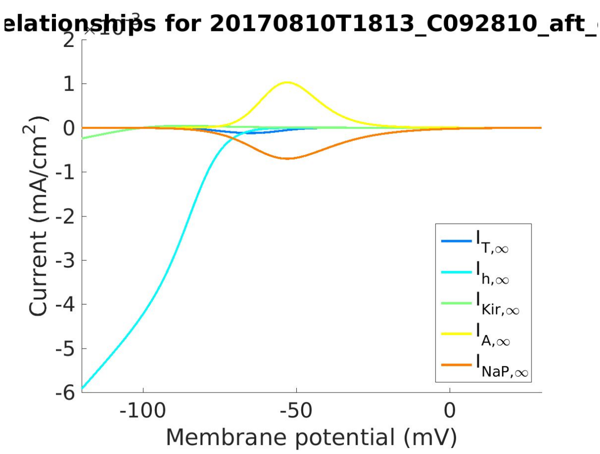
All traces:



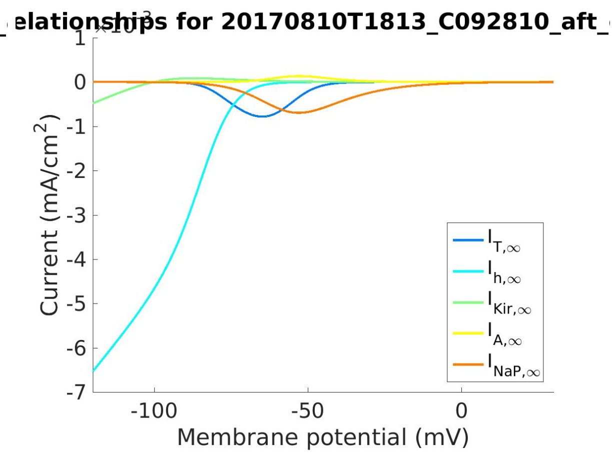
Steady-state I-V curves for **soma, dend0**:



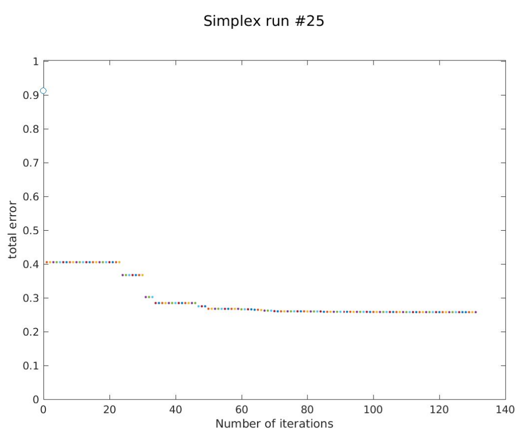
Steady-state I-V curves for **dend1**:



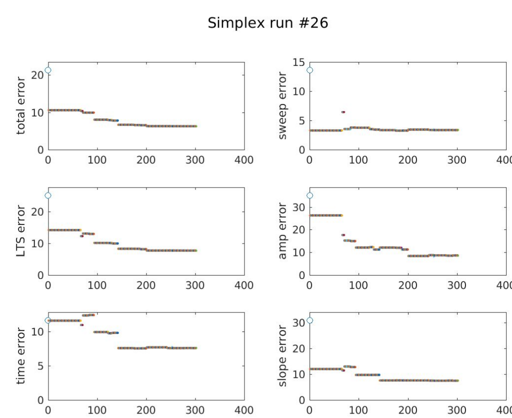
Steady-state I-V curves for **dend2**:



Passive fitting history:

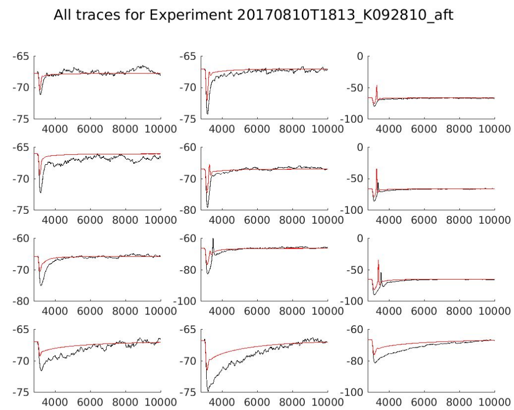


Active fitting history:

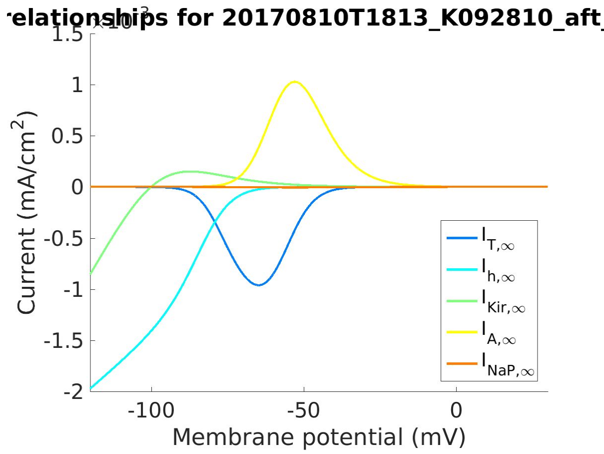


K092810

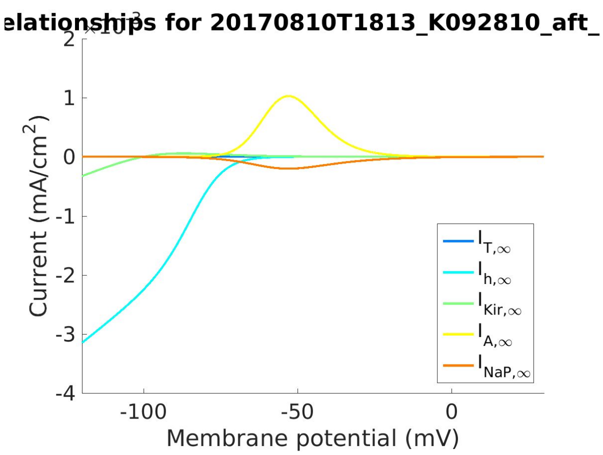
All traces:



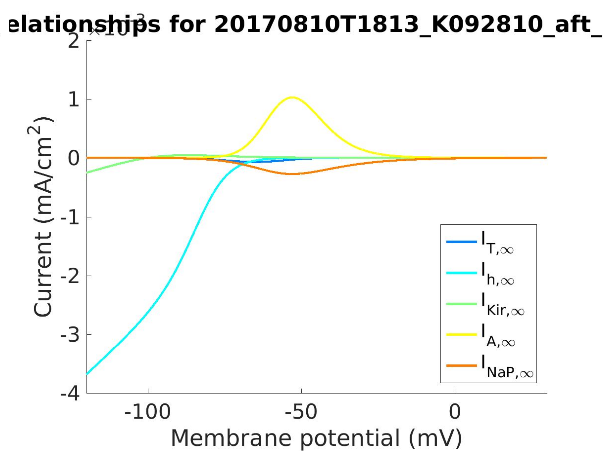
Steady-state I-V curves for **soma, dend0**:



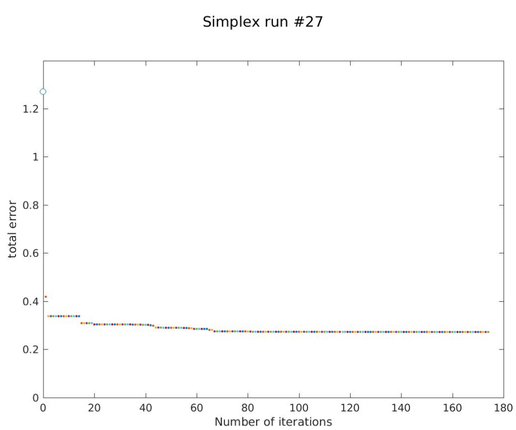
Steady-state I-V curves for **dend1**:



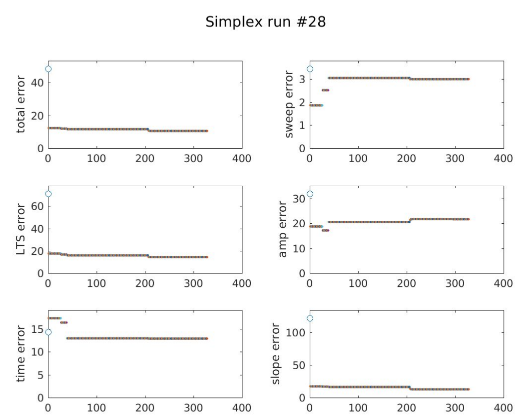
Steady-state I-V curves for **dend2**:



Passive fitting history:

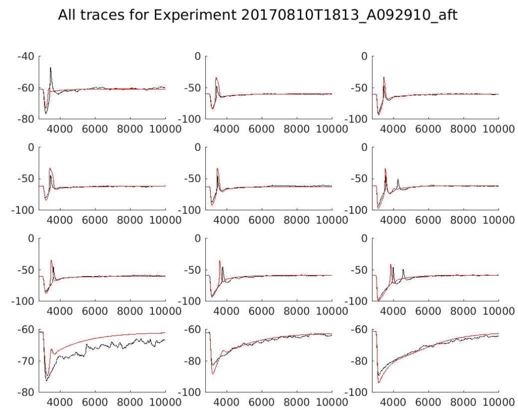


Active fitting history:

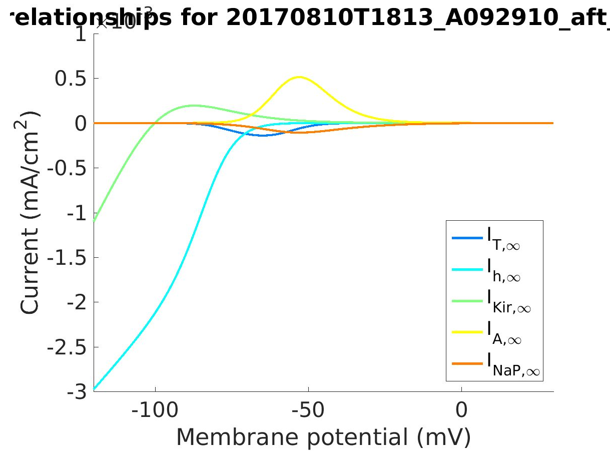


A092910

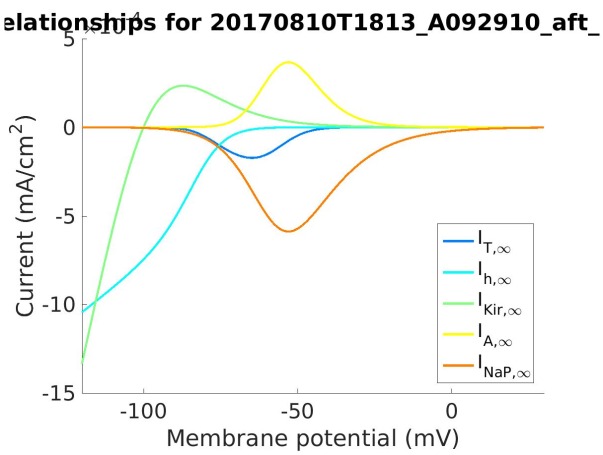
All traces:



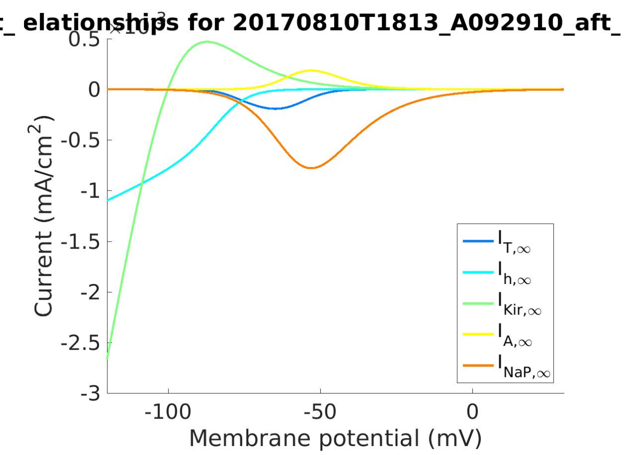
Steady-state I-V curves for **soma, dend0**:



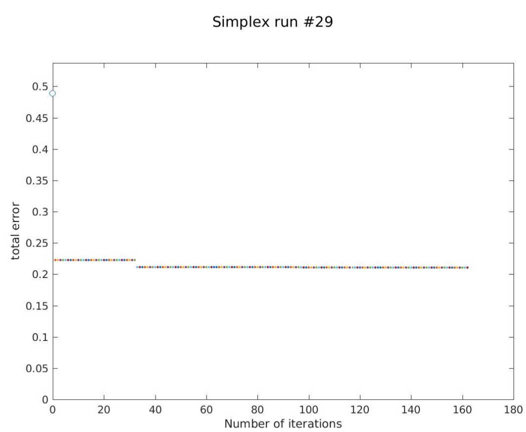
Steady-state I-V curves for **dend1**:



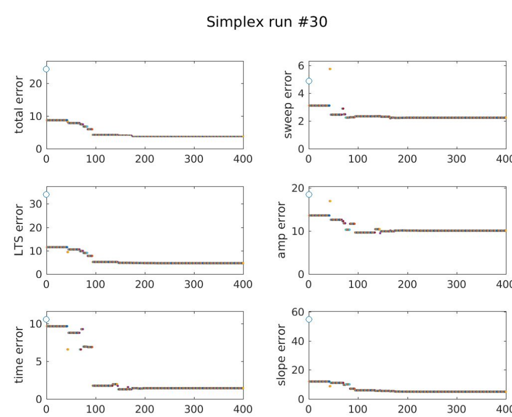
Steady-state I-V curves for **dend2**:



Passive fitting history:

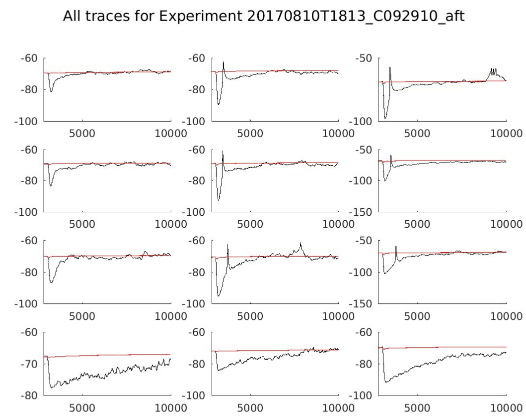


Active fitting history:

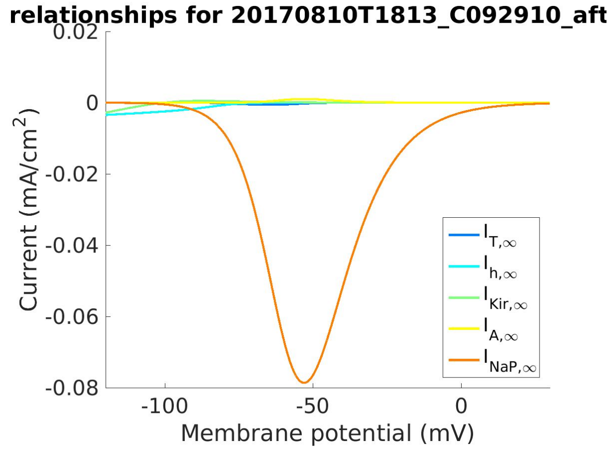


C092910

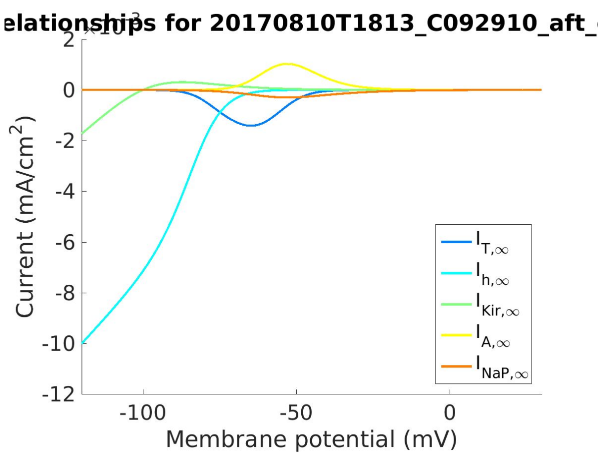
All traces:



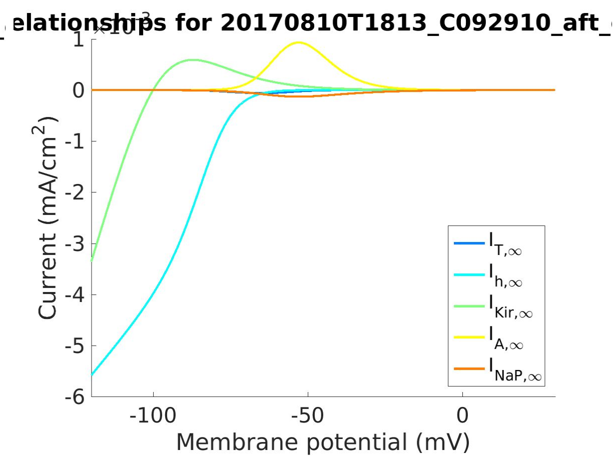
Steady-state I-V curves for **soma, dend0**:



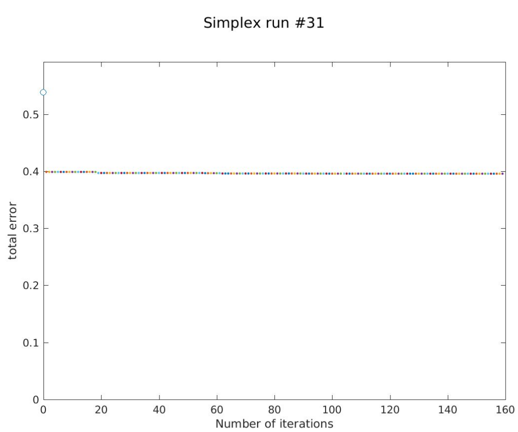
Steady-state I-V curves for **dend1**:



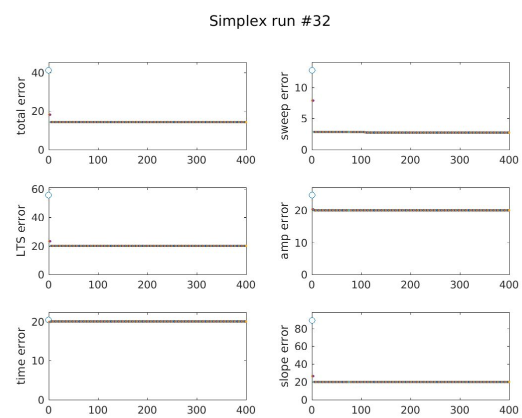
Steady-state I-V curves for **dend2**:



Passive fitting history:

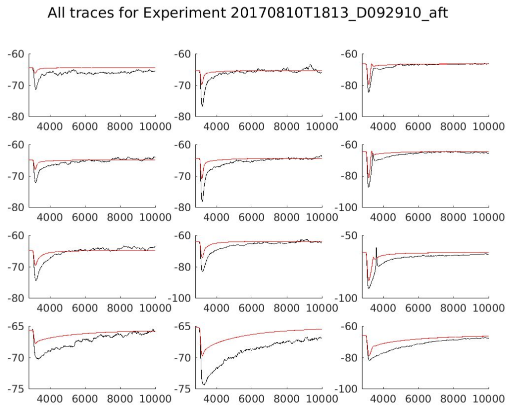


Active fitting history:

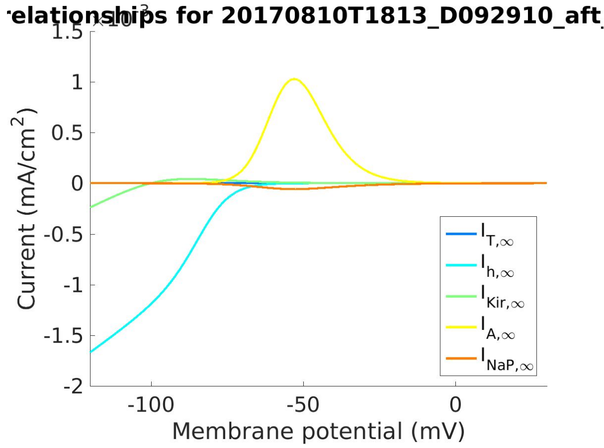


D092910

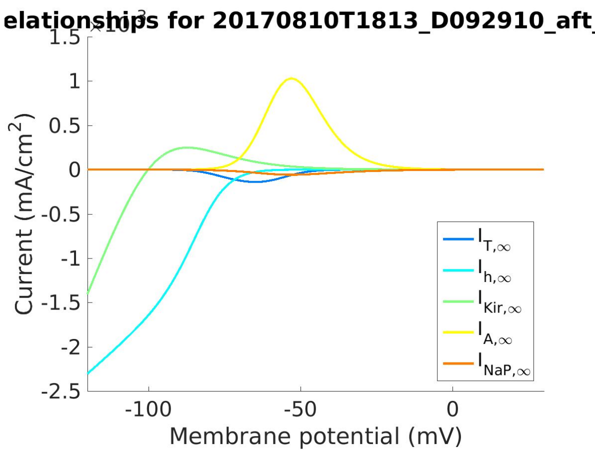
All traces:



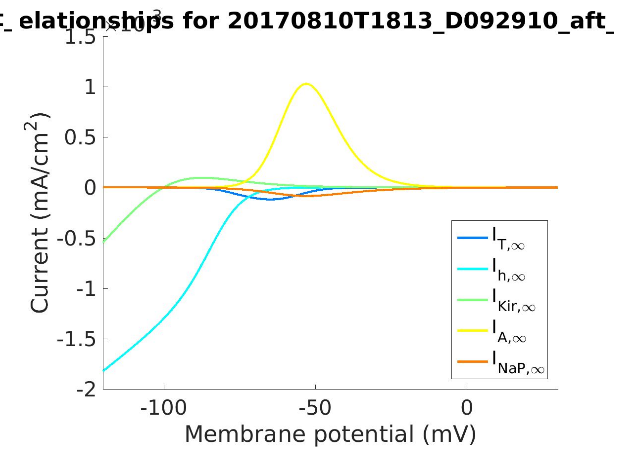
Steady-state I-V curves for **soma, dend0**:



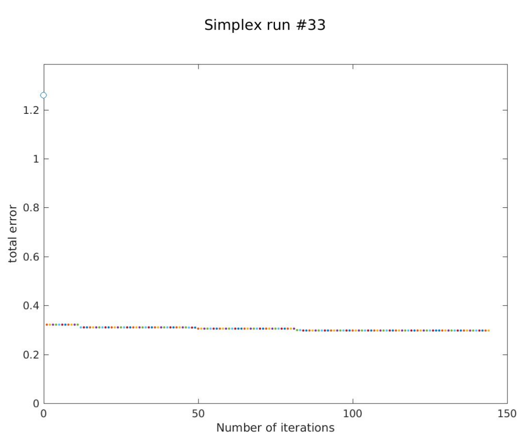
Steady-state I-V curves for **dend1**:



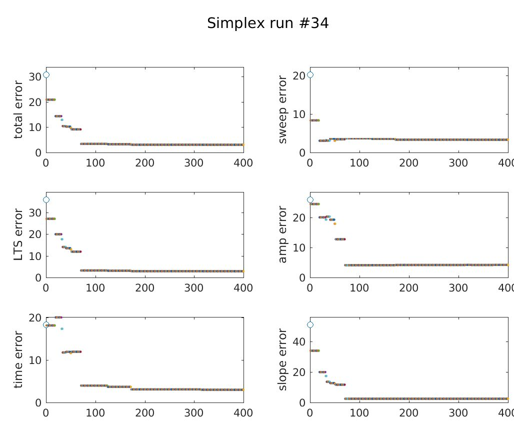
Steady-state I-V curves for **dend2**:



Passive fitting history:

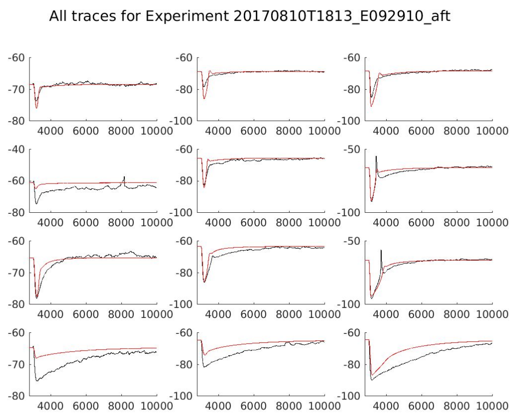


Active fitting history:

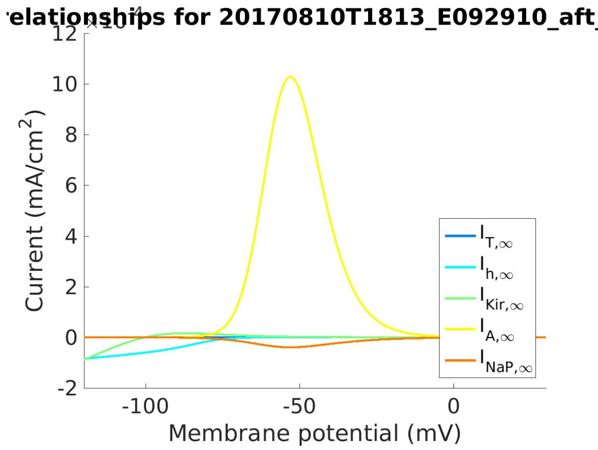


E092910

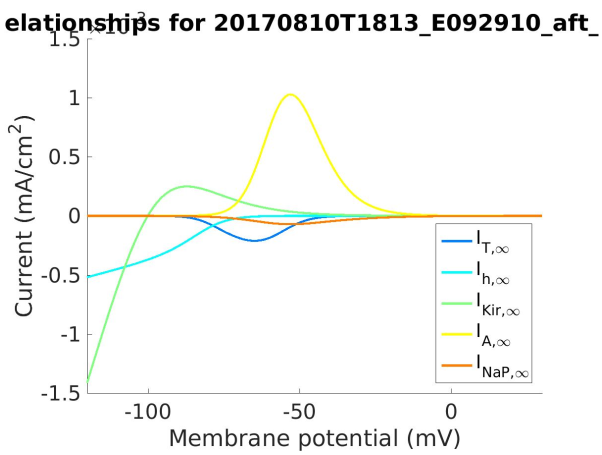
All traces:



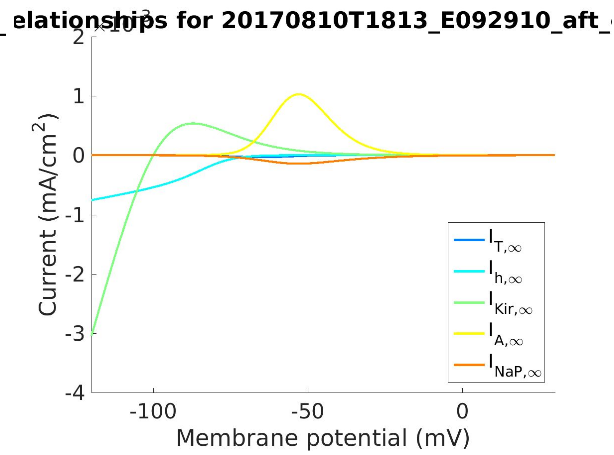
Steady-state I-V curves for **soma, dend0**:



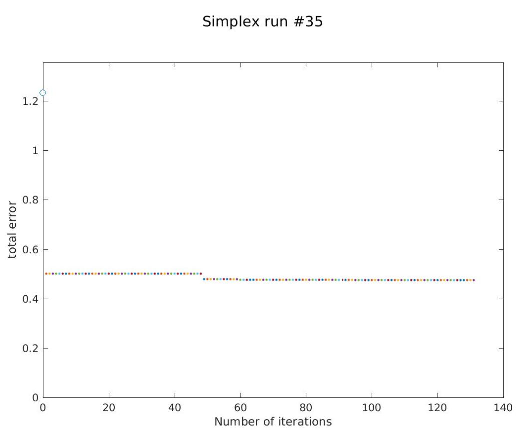
Steady-state I-V curves for **dend1**:



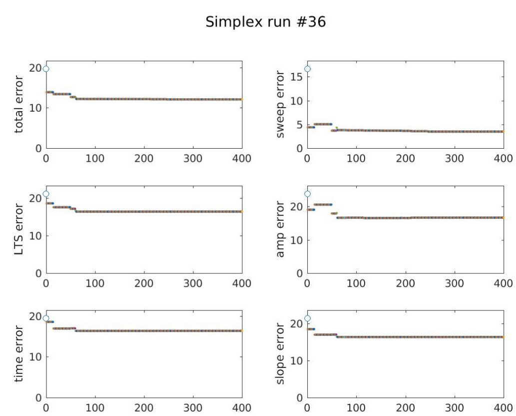
Steady-state I-V curves for **dend2**:



Passive fitting history:

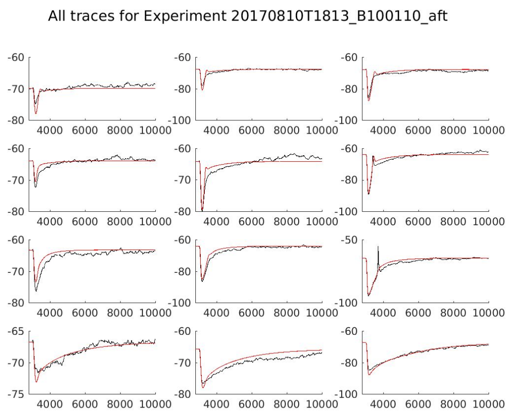


Active fitting history:

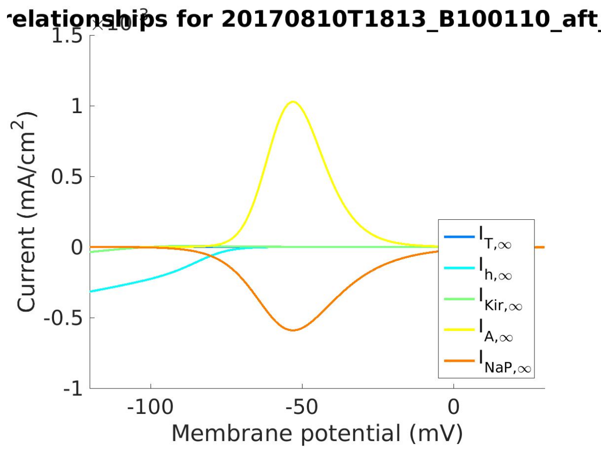


B100110

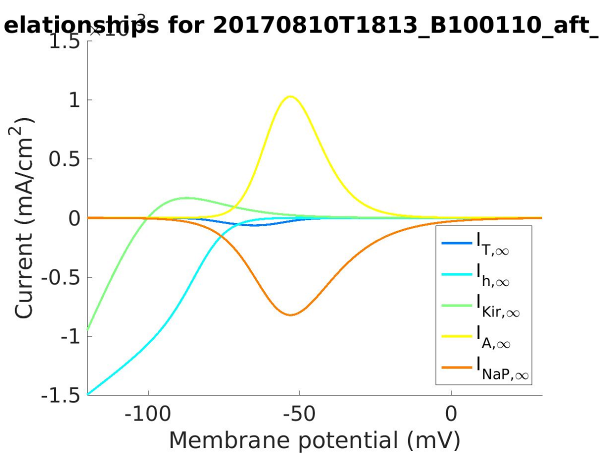
All traces:



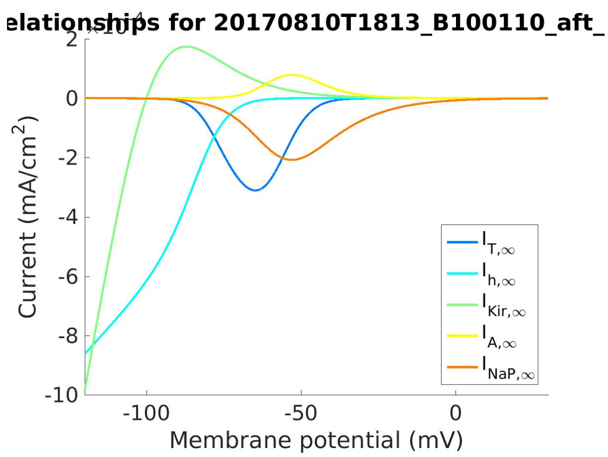
Steady-state I-V curves for **soma, dend0**:



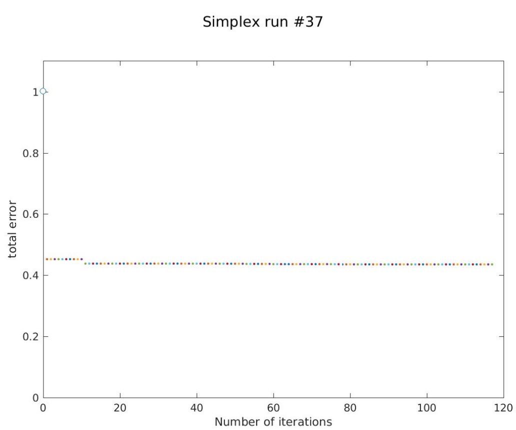
Steady-state I-V curves for **dend1**:



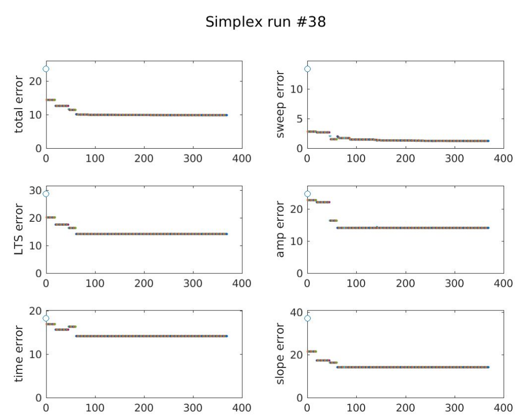
Steady-state I-V curves for **dend2**:



Passive fitting history:

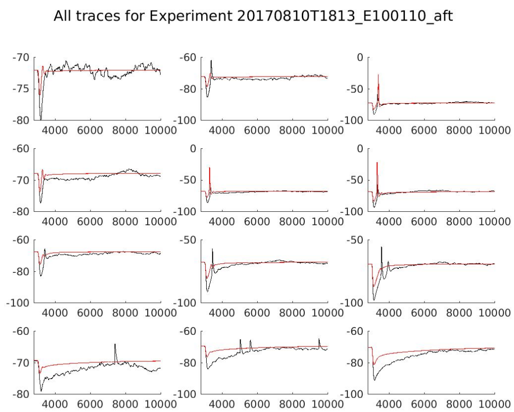


Active fitting history:

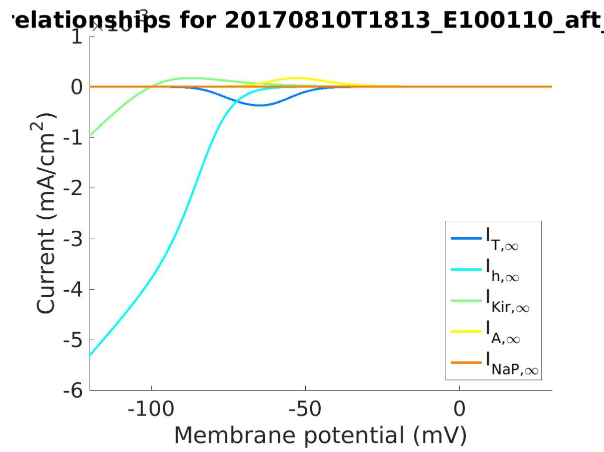


E100110

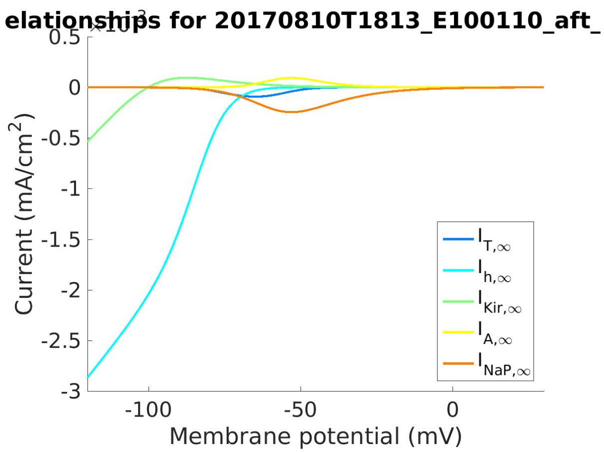
All traces:



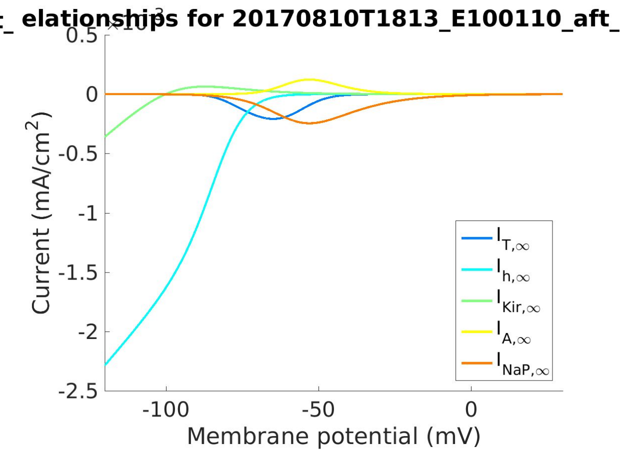
Steady-state I-V curves for **soma, dend0**:



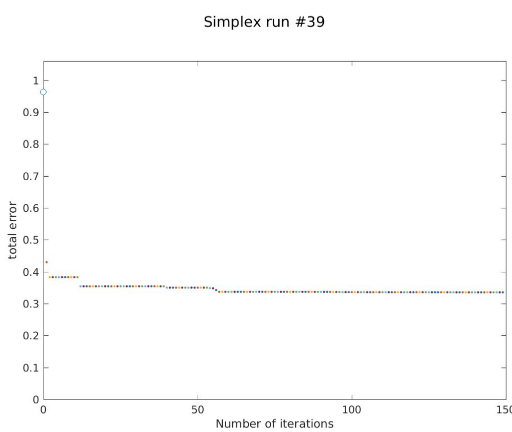
Steady-state I-V curves for **dend1**:



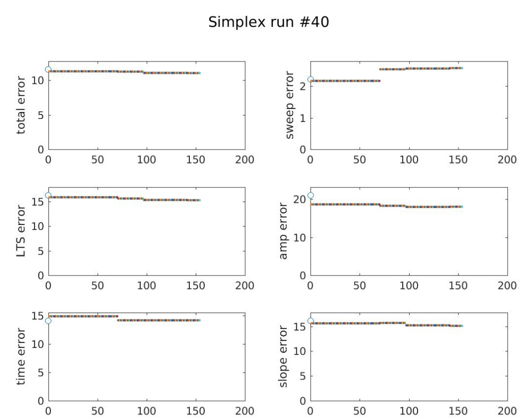
Steady-state I-V curves for **dend2**:



Passive fitting history:

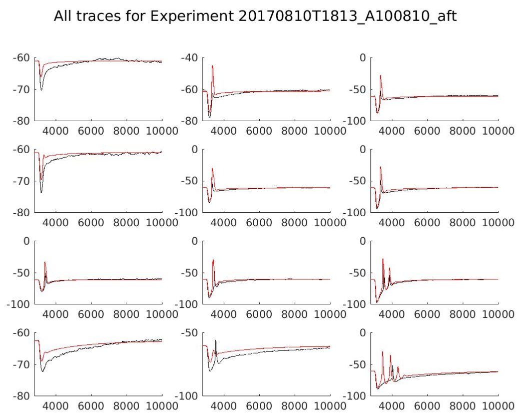


Active fitting history:

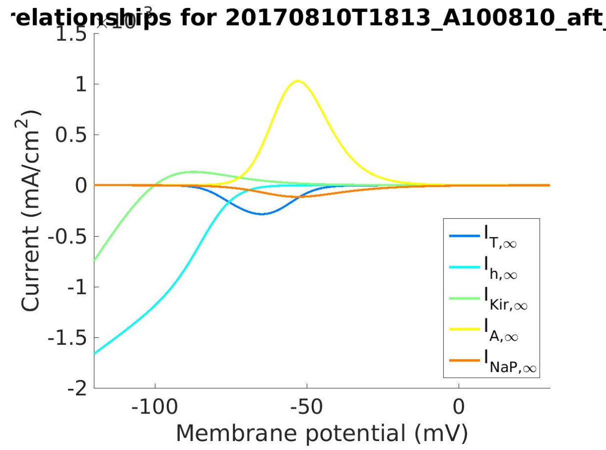


A100810

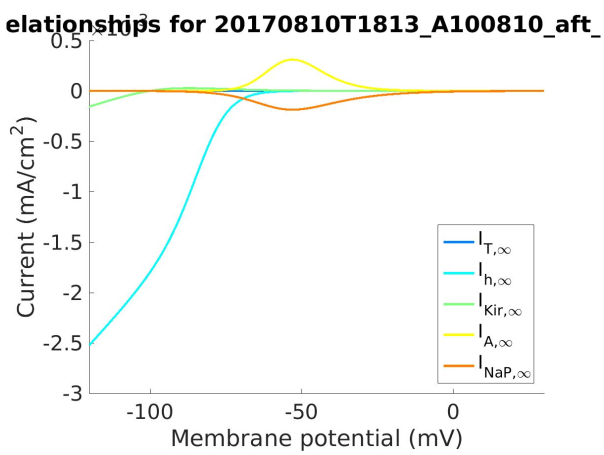
All traces:



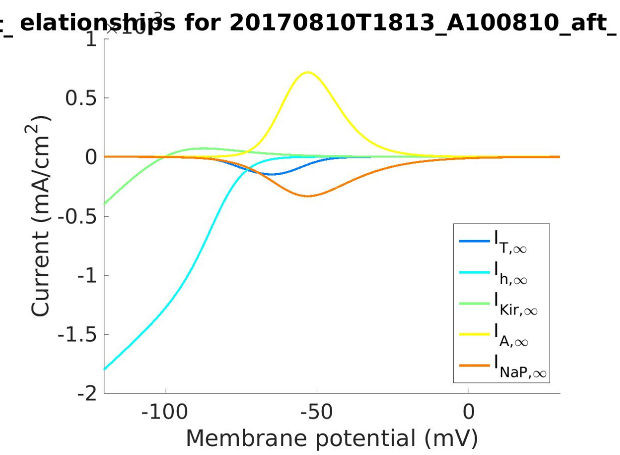
Steady-state I-V curves for **soma, dend0**:



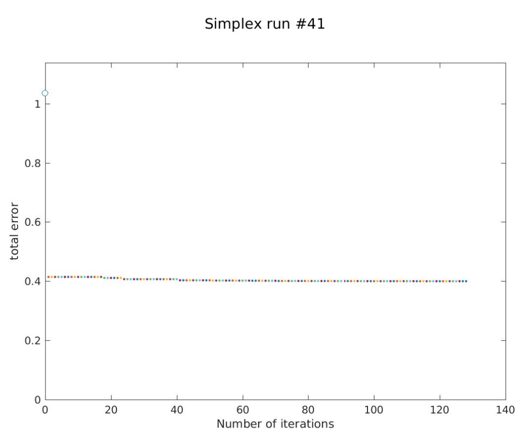
Steady-state I-V curves for **dend1**:



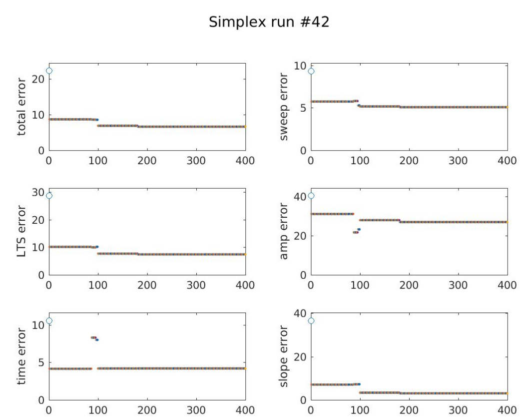
Steady-state I-V curves for **dend2**:



Passive fitting history:

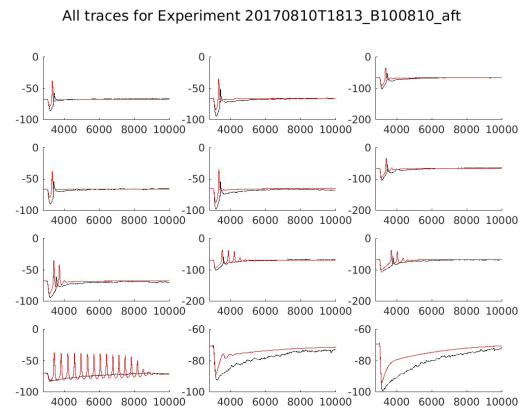


Active fitting history:

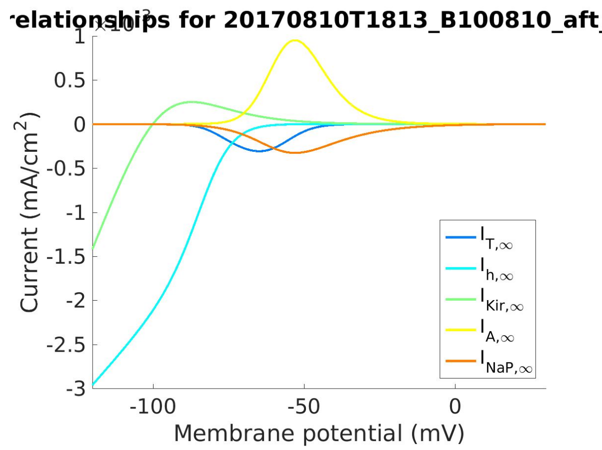


B100810

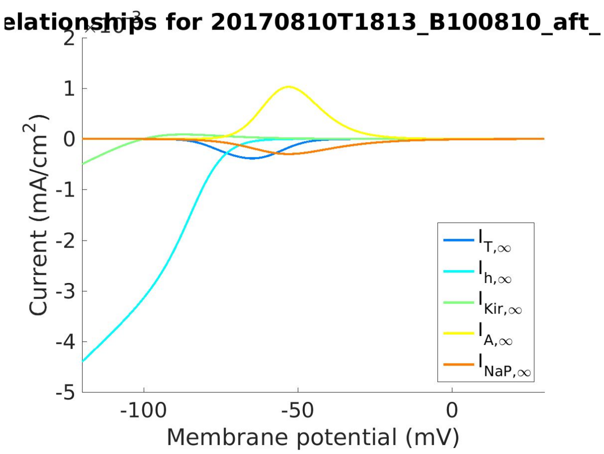
All traces:



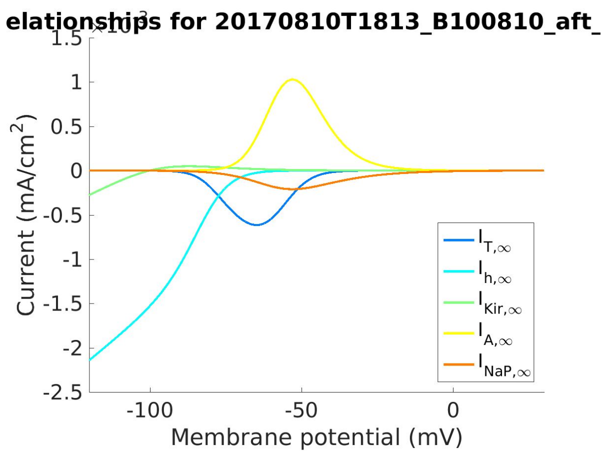
Steady-state I-V curves for **soma, dend0**:



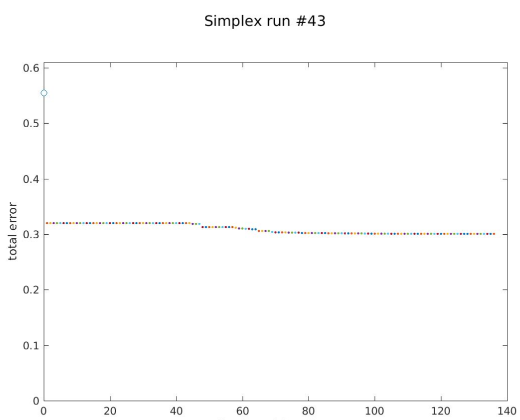
Steady-state I-V curves for **dend1**:



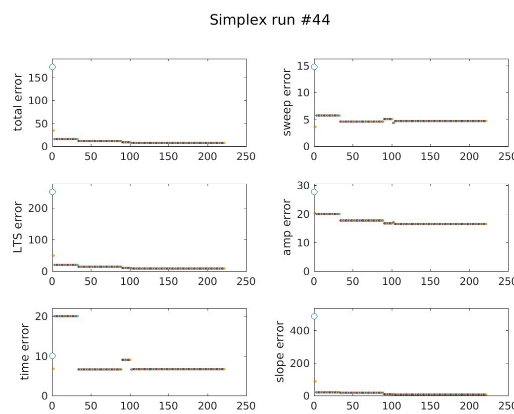
Steady-state I-V curves for **dend2**:



Passive fitting history:

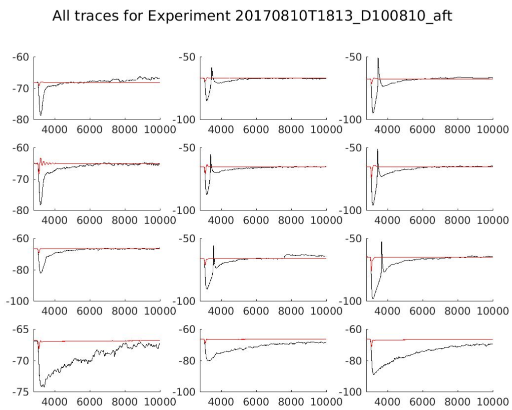


Active fitting history:

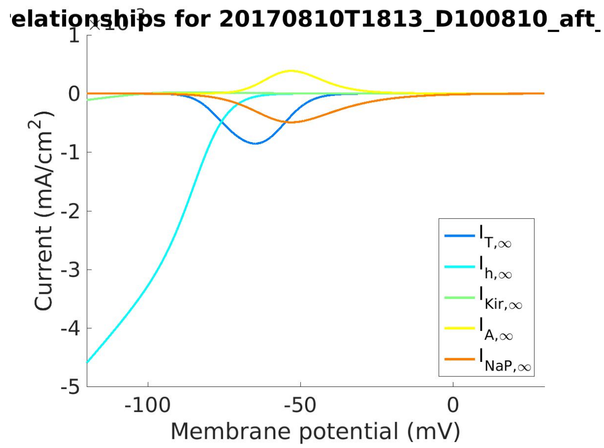


D100810

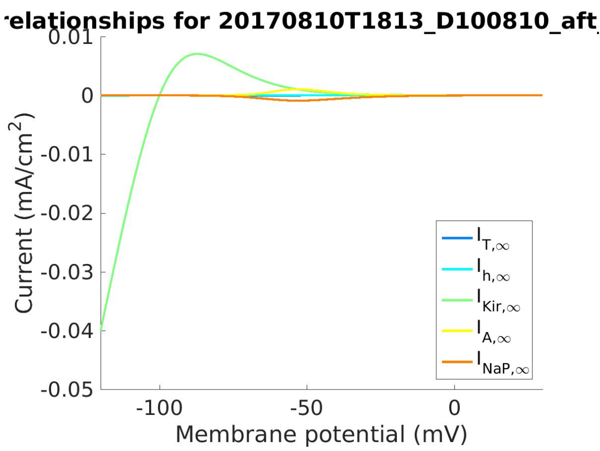
All traces:



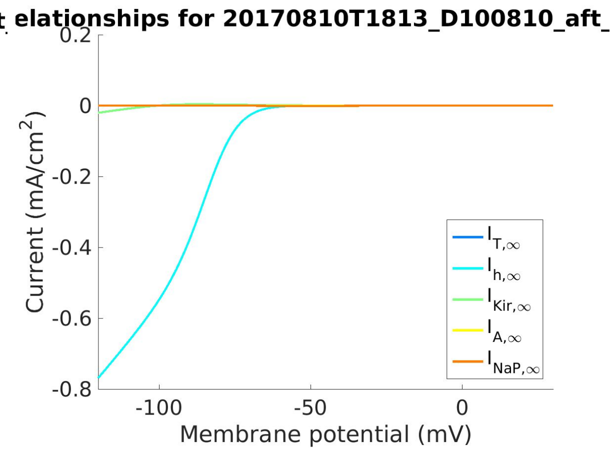
Steady-state I-V curves for **soma, dend0**:



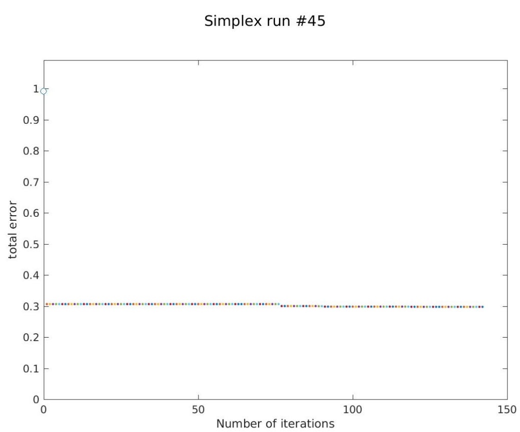
Steady-state I-V curves for **dend1**:



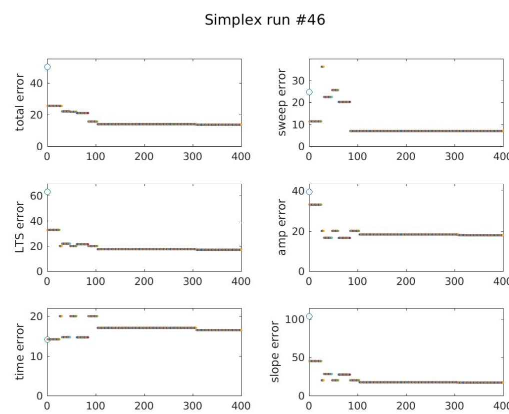
Steady-state I-V curves for **dend2**:



Passive fitting history:

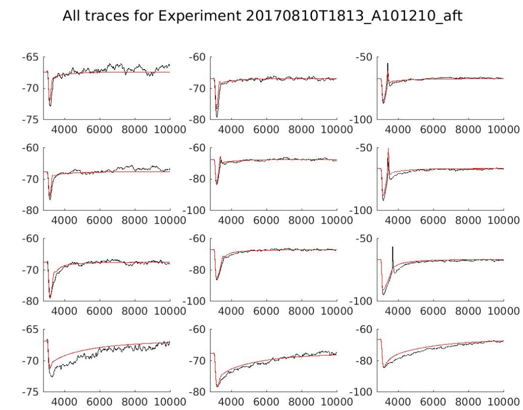


Active fitting history:

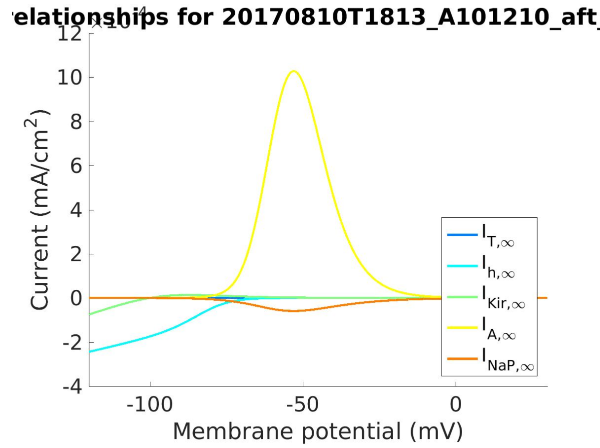


A101210

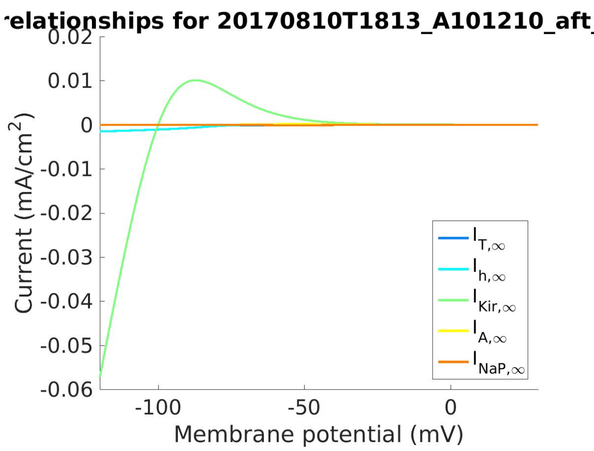
All traces:



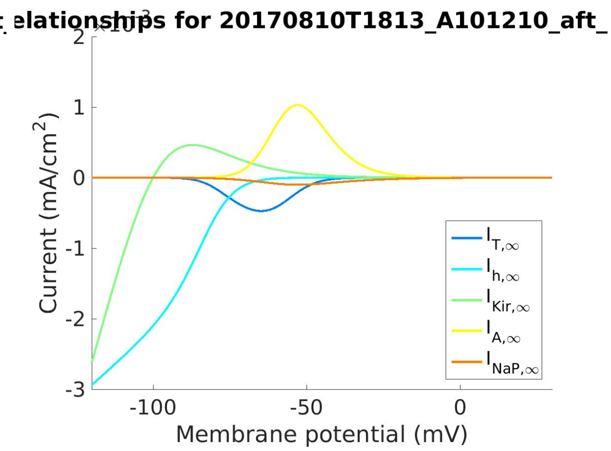
Steady-state I-V curves for **soma, dend0**:



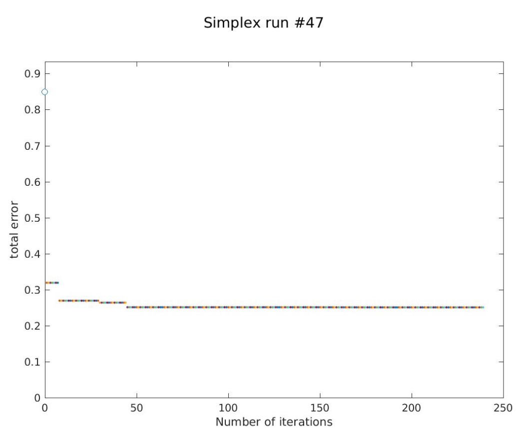
Steady-state I-V curves for **dend1**:



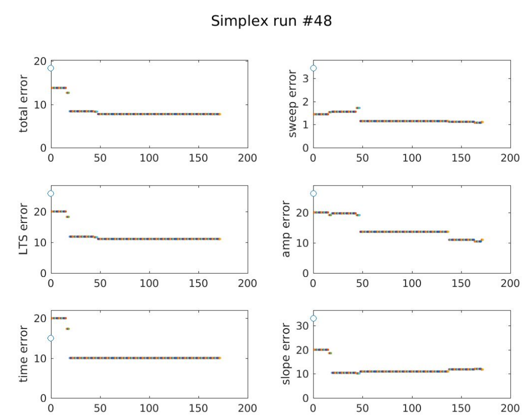
Steady-state I-V curves for **dend2**:



Passive fitting history:

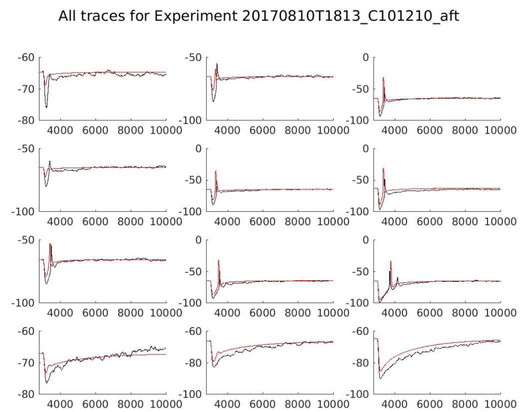


Active fitting history:

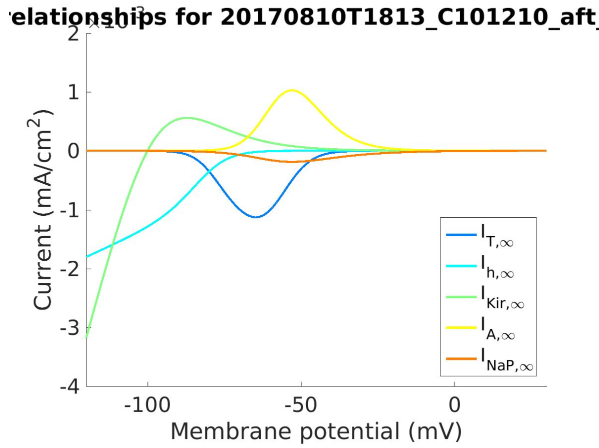


C101210

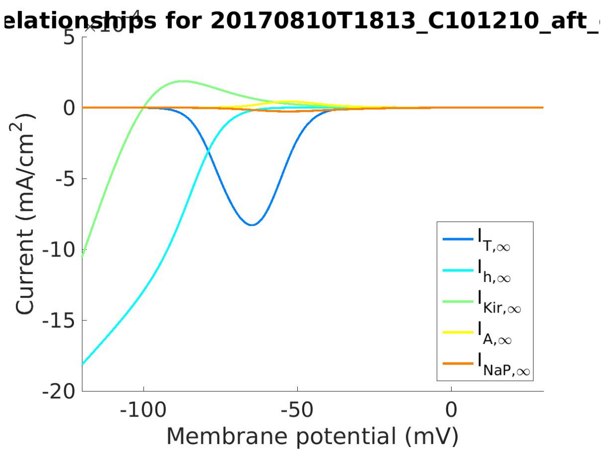
All traces:



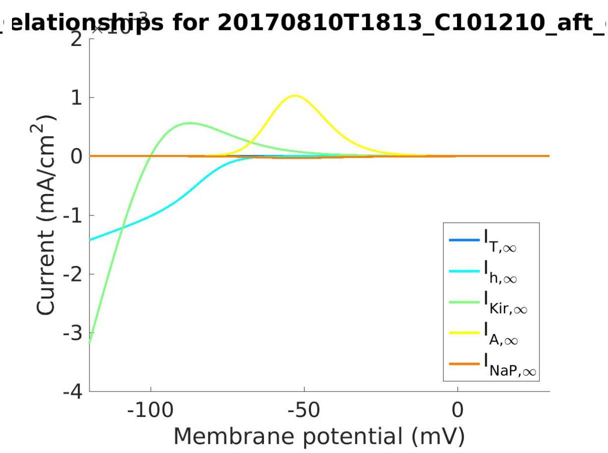
Steady-state I-V curves for **soma, dend0**:



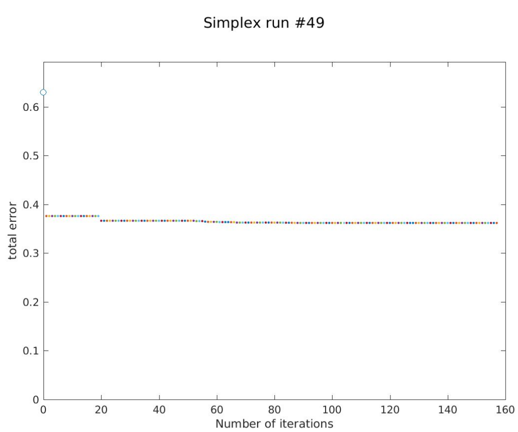
Steady-state I-V curves for **dend1**:



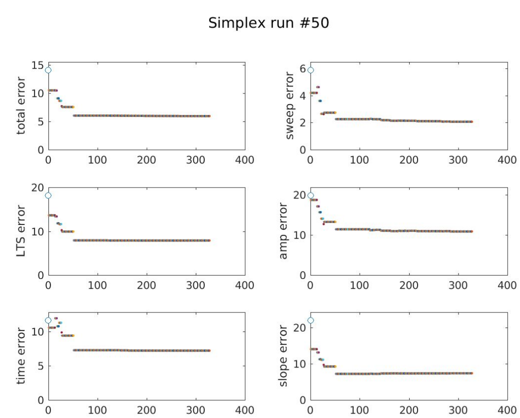
Steady-state I-V curves for **dend2**:



Passive fitting history:

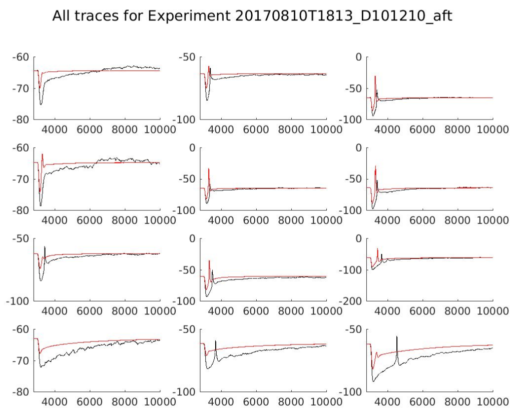


Active fitting history:

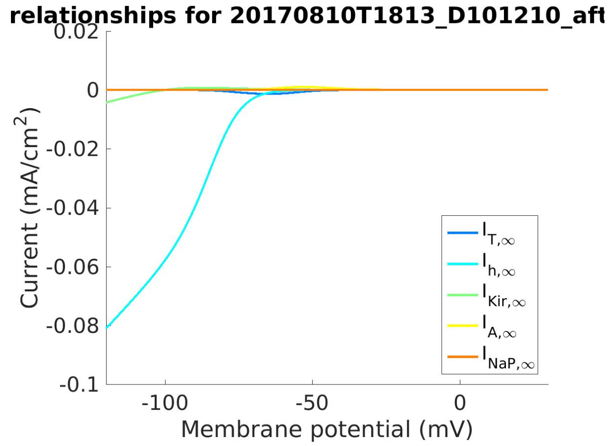


D101210

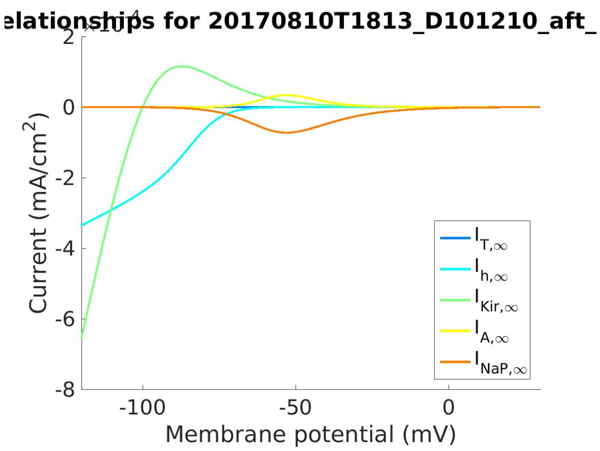
All traces:



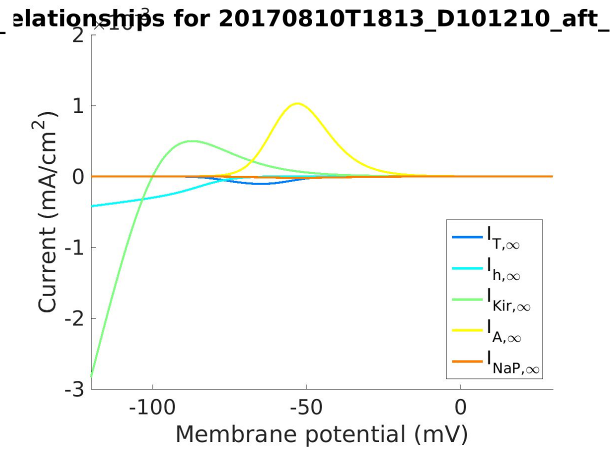
Steady-state I-V curves for **soma, dend0**:



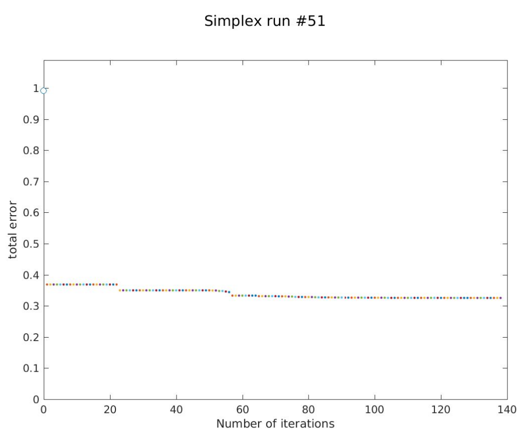
Steady-state I-V curves for **dend1**:



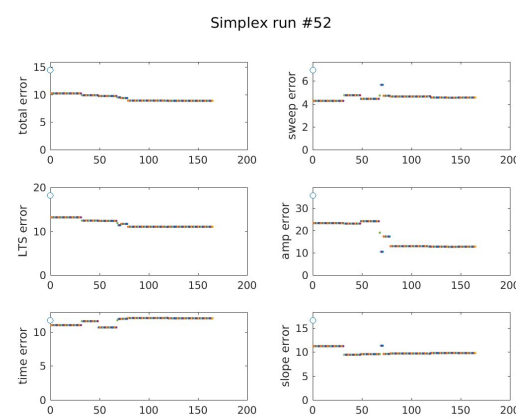
Steady-state I-V curves for **dend2**:



Passive fitting history:

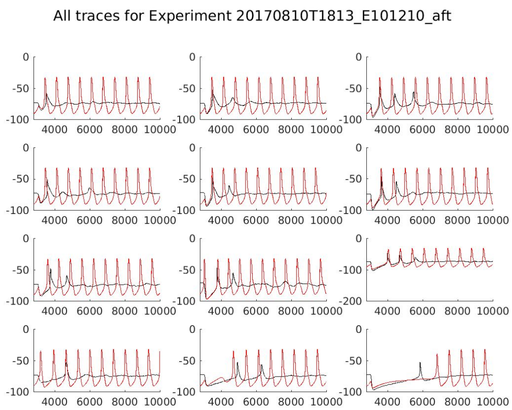


Active fitting history:

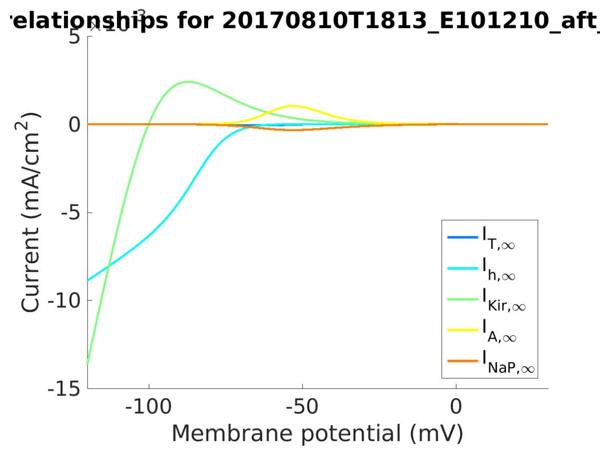


E101210

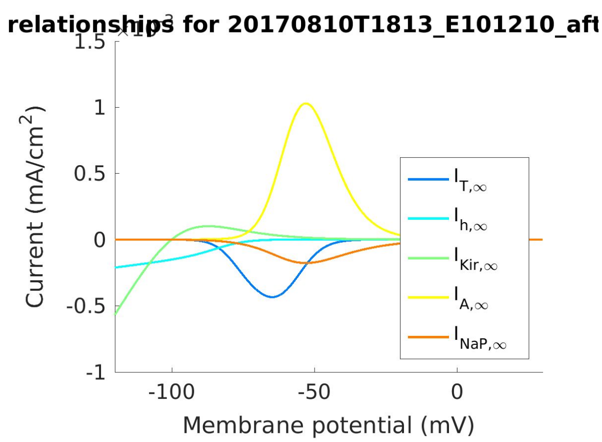
All traces:



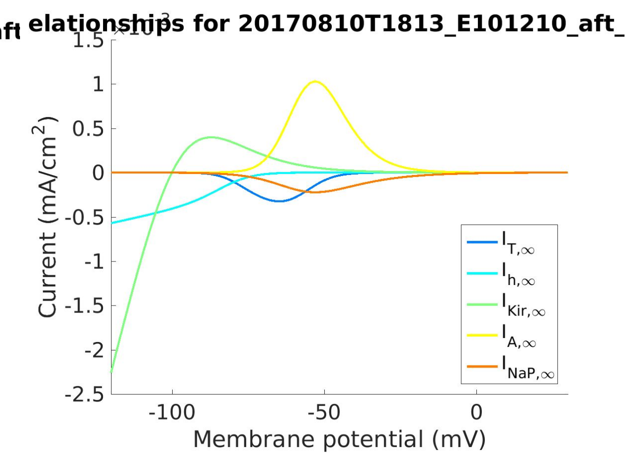
Steady-state I-V curves for **soma, dend0**:



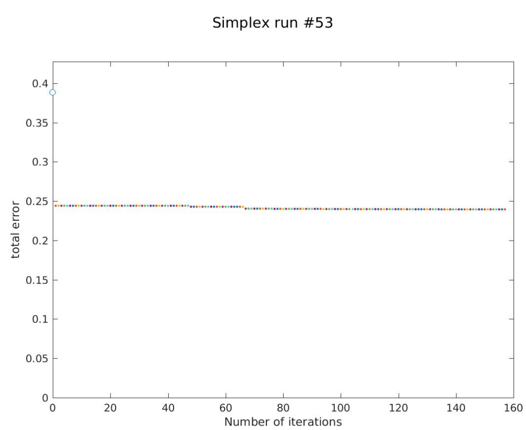
Steady-state I-V curves for **dend1**:



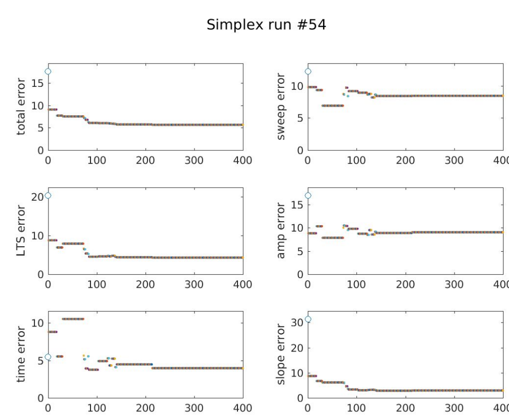
Steady-state I-V curves for **dend2**:



Passive fitting history:

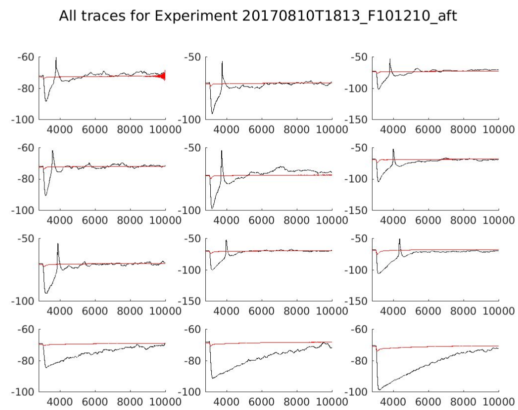


Active fitting history:

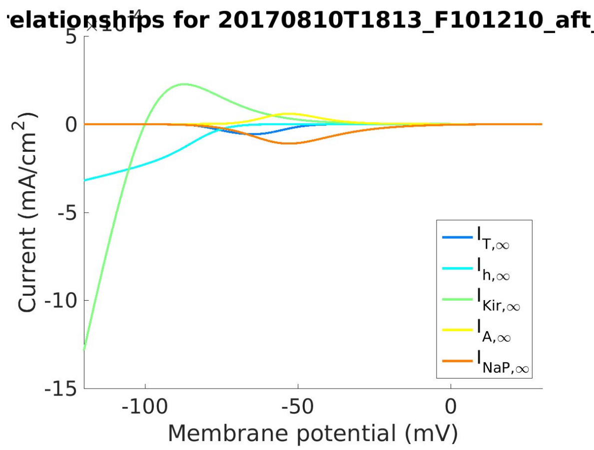


F101210

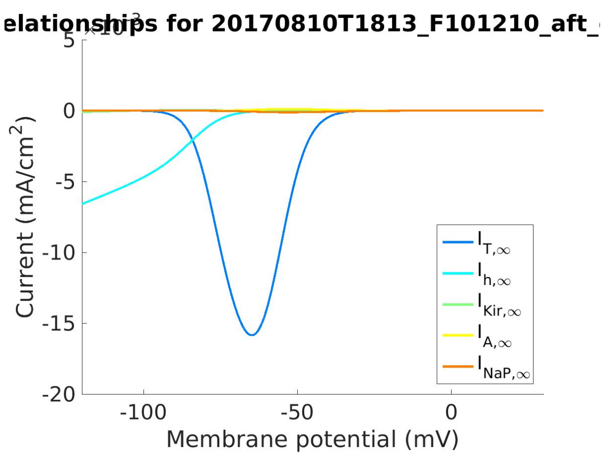
All traces:



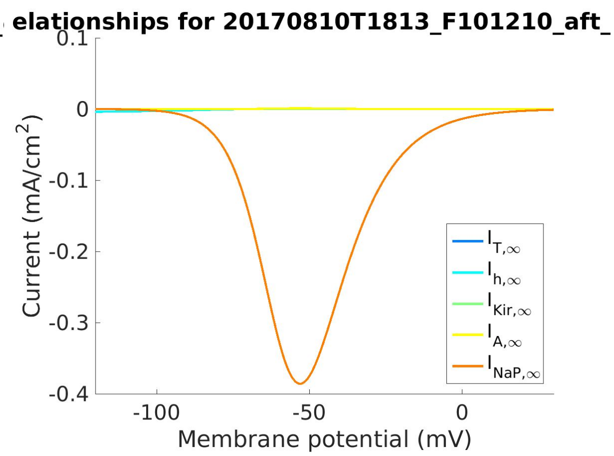
Steady-state I-V curves for **soma, dend0**:



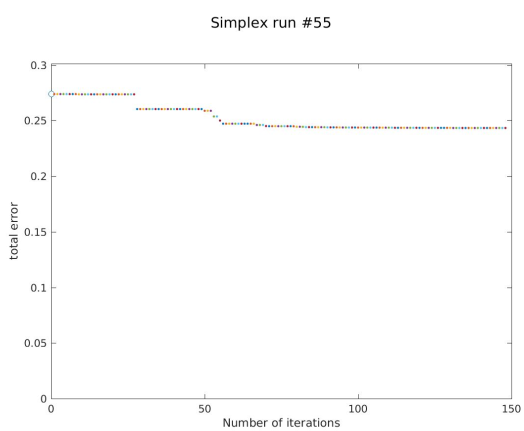
Steady-state I-V curves for **dend1**:



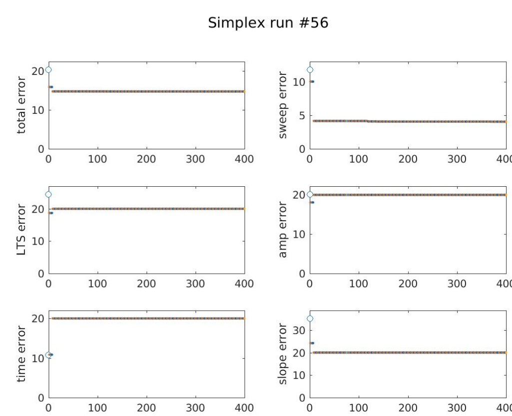
Steady-state I-V curves for **dend2**:



Passive fitting history:

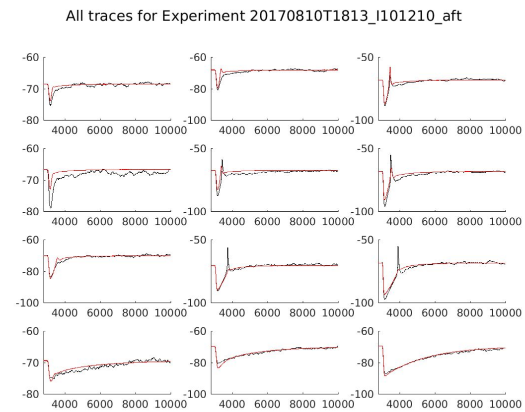


Active fitting history:

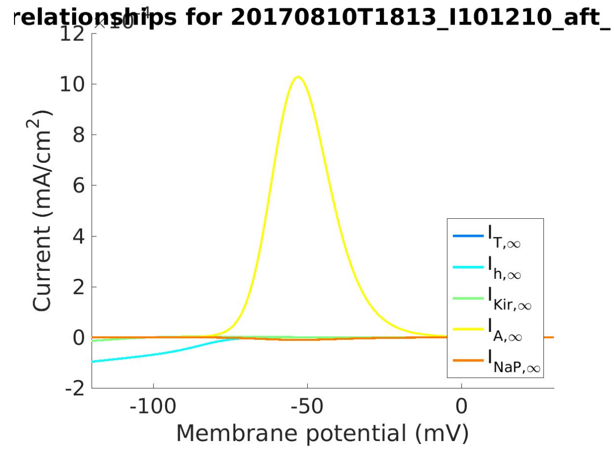


I101210

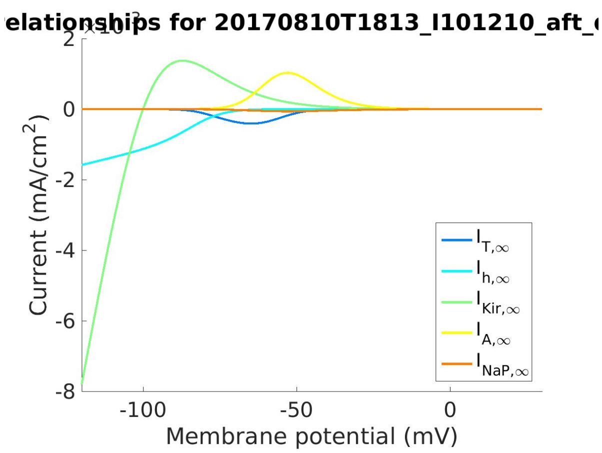
All traces:



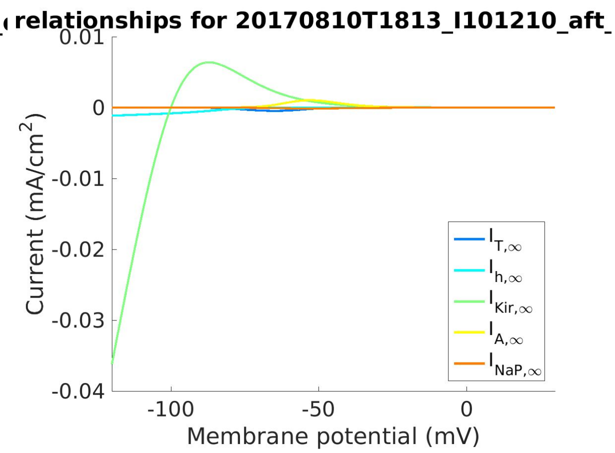
Steady-state I-V curves for **soma, dend0**:



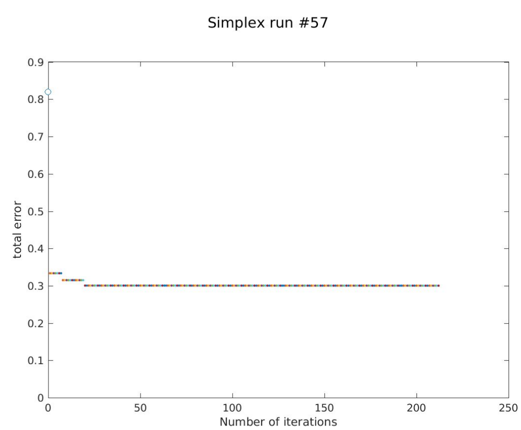
Steady-state I-V curves for **dend1**:



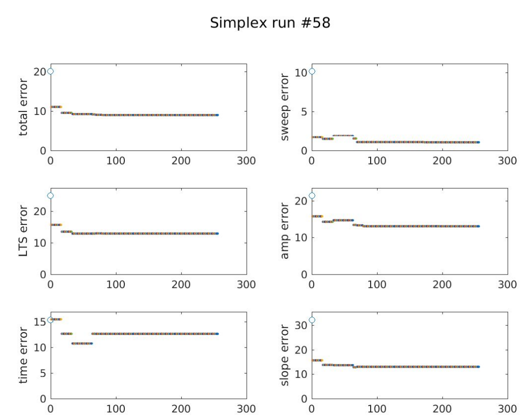
Steady-state I-V curves for **dend2**:



Passive fitting history:

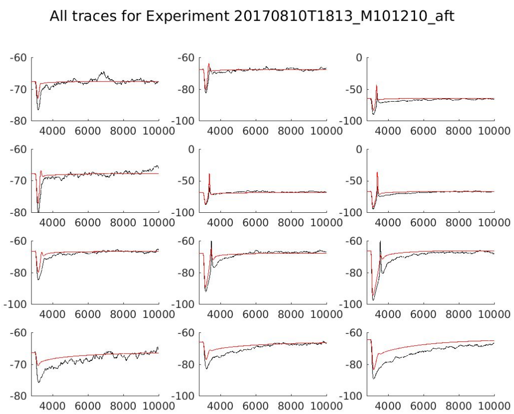


Active fitting history:

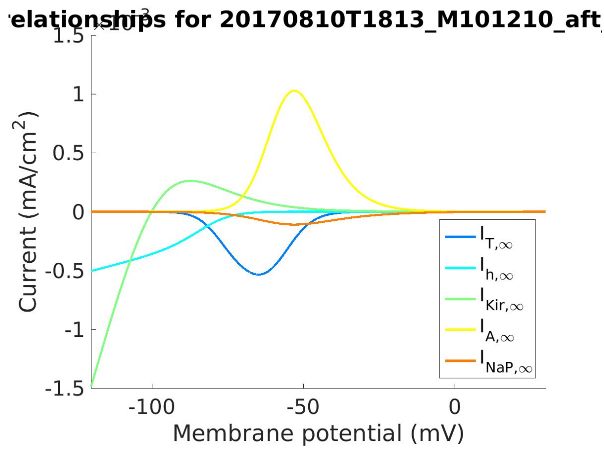


M101210

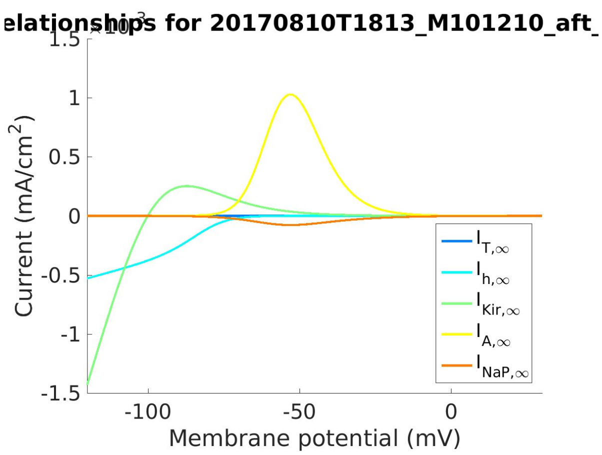
All traces:



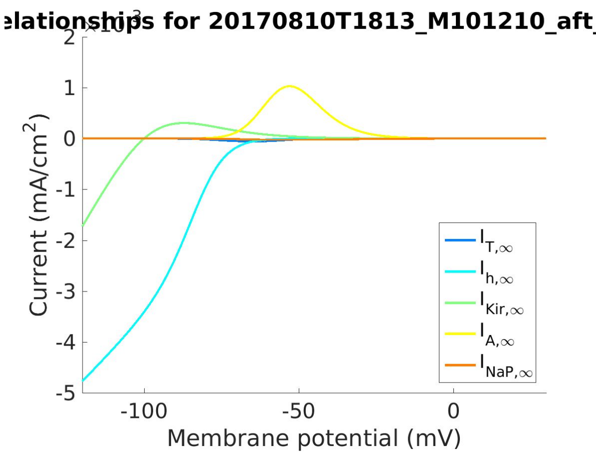
Steady-state I-V curves for **soma, dend0**:



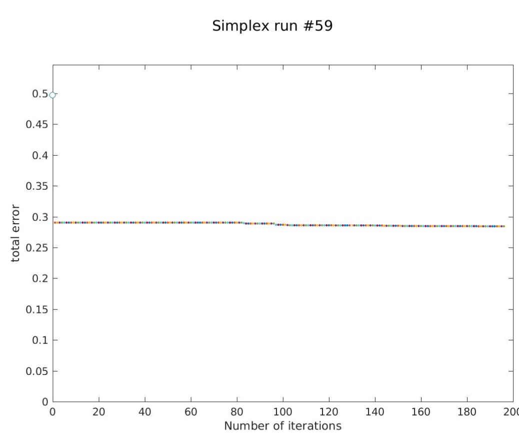
Steady-state I-V curves for **dend1**:



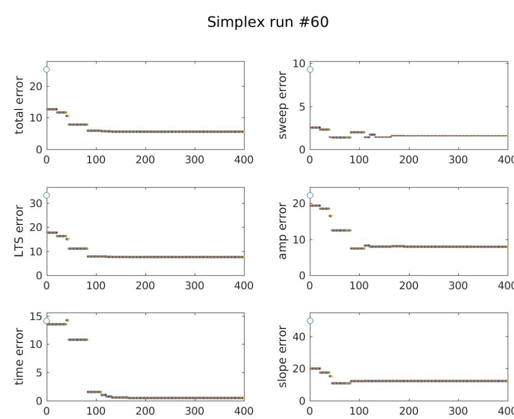
Steady-state I-V curves for **dend2**:



Passive fitting history:

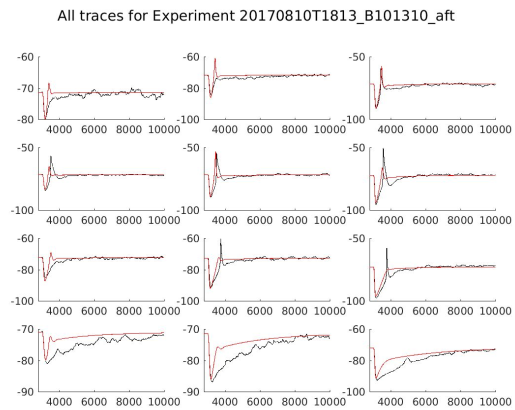


Active fitting history:

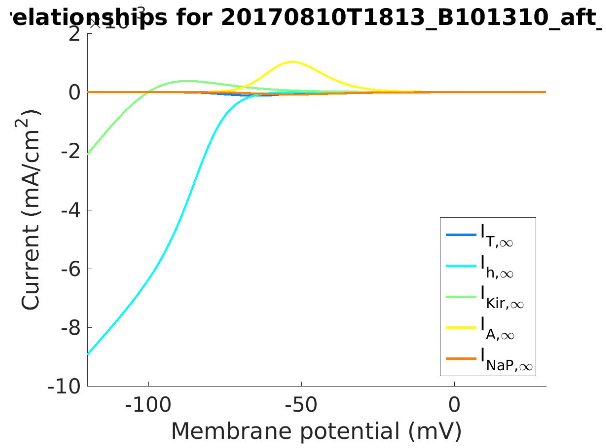


B101310

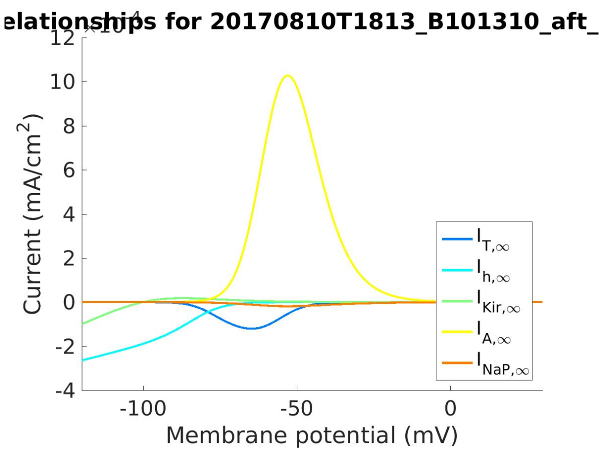
All traces:



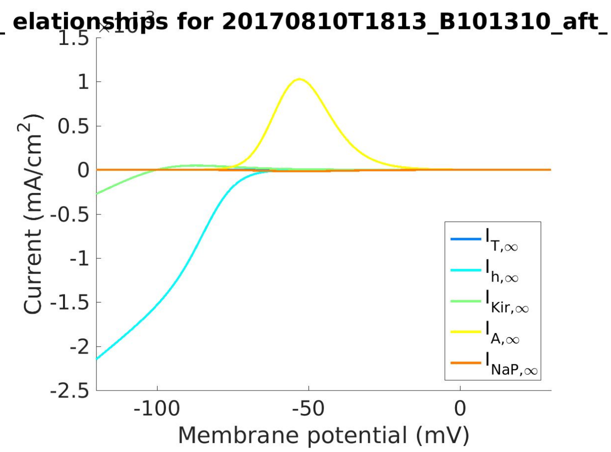
Steady-state I-V curves for **soma, dend0**:



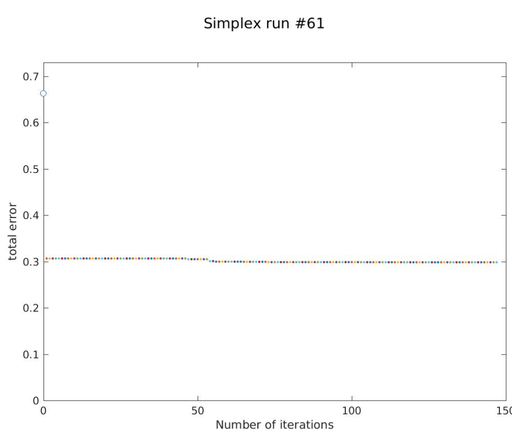
Steady-state I-V curves for **dend1**:



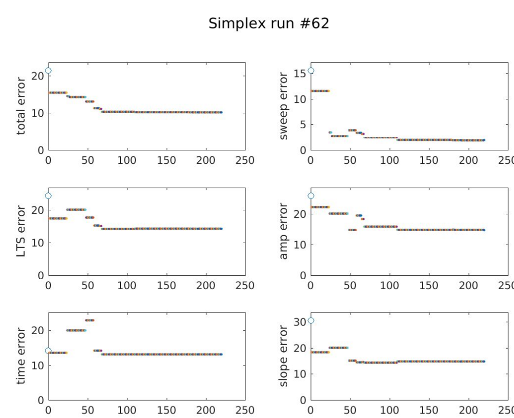
Steady-state I-V curves for **dend2**:



Passive fitting history:

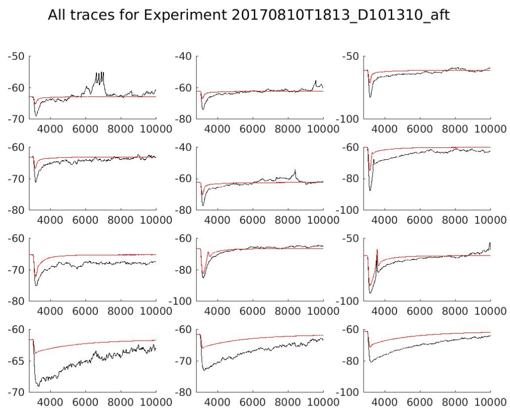


Active fitting history:

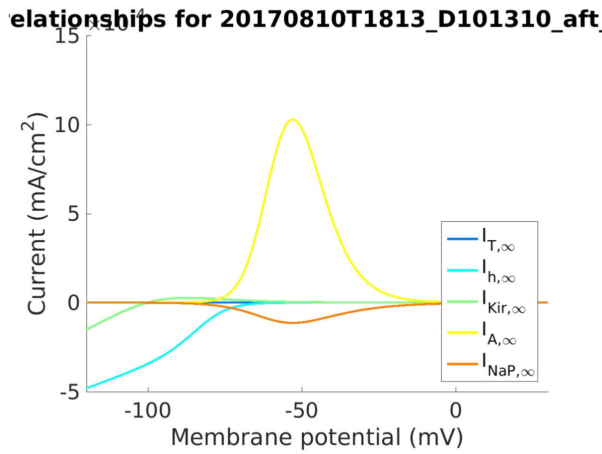


D101310

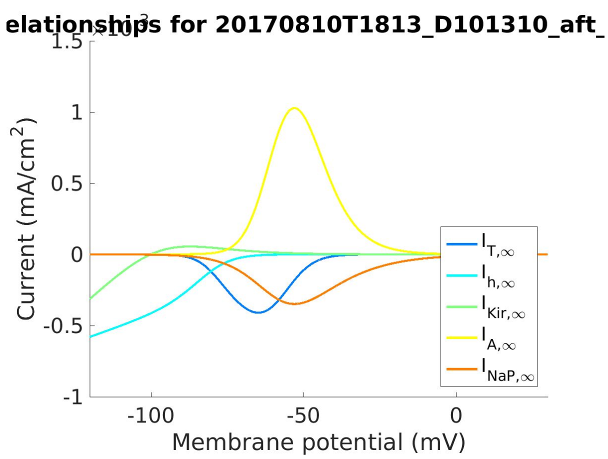
All traces:



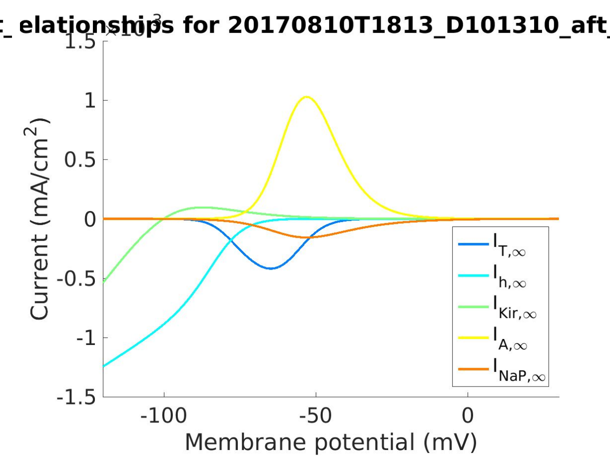
Steady-state I-V curves for **soma, dend0**:



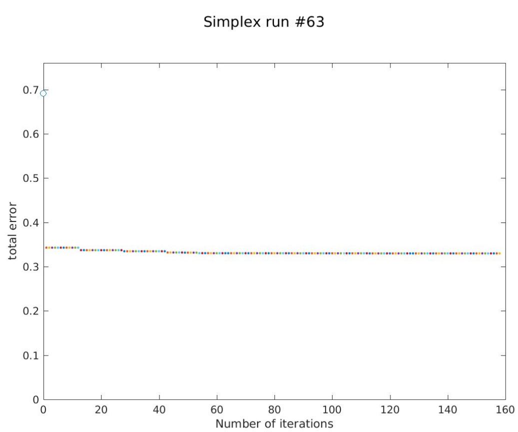
Steady-state I-V curves for **dend1**:



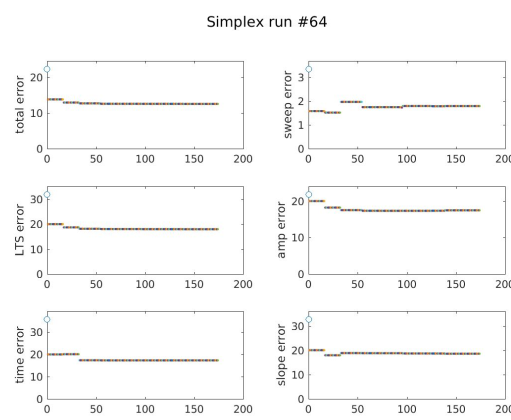
Steady-state I-V curves for **dend2**:



Passive fitting history:

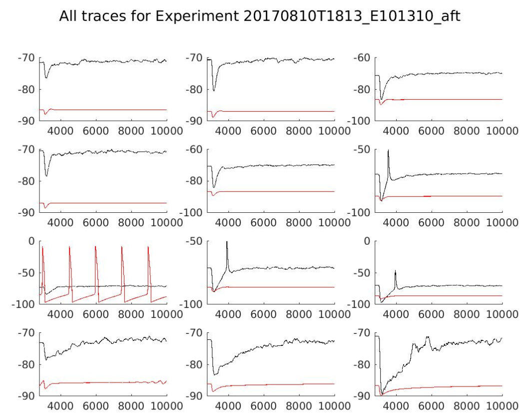


Active fitting history:

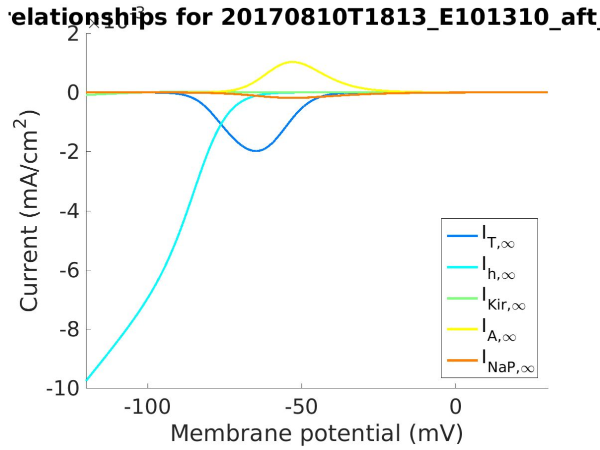


E101310

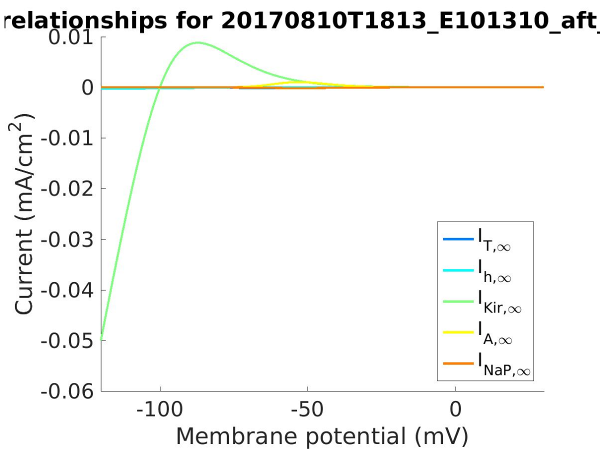
All traces:



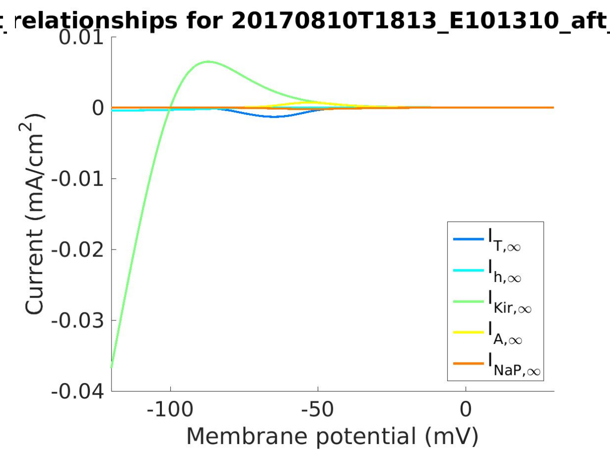
Steady-state I-V curves for **soma, dend0**:



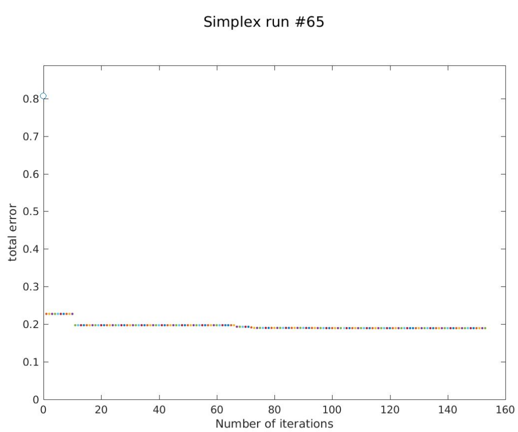
Steady-state I-V curves for **dend1**:



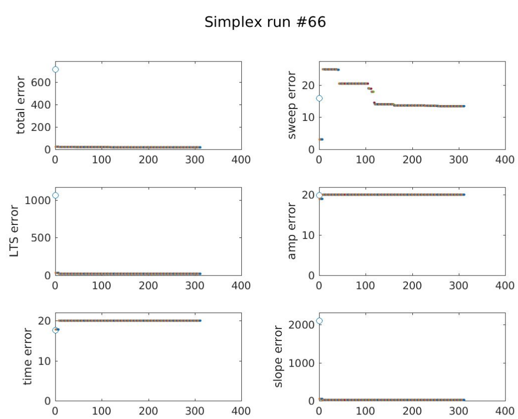
Steady-state I-V curves for **dend2**:



Passive fitting history:



Active fitting history:



Plan for next week

- Area paper:
    - Send out emails to committee members about defense date
    - Work on **Area Paper outline**
    - Browse recent literature on GABA-B receptors & HCN channels
    - Prepare PPT slides for qualifying exam

- Single Neuron Model:
    - Try different initial conditions and fit **across cells** again
    - Make plots of the **geometry** before and after fitting
    - Start with default parameters for those to be fitted across trials, and best parameters for those that were fitted across cells, fit across trials using the "**most representative trace**" (Of all trials of the same condition, see if most have bursts or LTS or neither. If neither, choose one without LTS with minimum noise. If most have LTSs but not bursts, choose one with LTS but not bursts with minimum noise. If most have bursts, choose one with bursts with minimum noise)
    - Write out the voltage relationships between compartments. Is the **cable equation** used by NEURON? No. Are the diameters tapered? No.
    - Try ball-and-stick model with 2 nodes for the stick instead? Use theory to estimate build parameters and fit only epas & gpas?
    - Try writing out an **explicit objective function**
    - Investigate where **shiftm, shifth, slopem, slopeh** should be placed. Should we make T_1/2 and k parameters instead? (Perhaps no, because taum and minf should vary together, see Pinsky-Rinzel model.)
    - Make g's and p's linearly vary from soma->dend1->dend2?
    - Explore Ed's way of **parallelizing Matlab without using a toolbox license**.

- Knowledge buildup:
    - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)

7/31/2017

<u>minEASE (updates)</u>

- Now skips to the next unchecked event when using keyboard to increment/decrement event number
- Now reads .mat files that contain a **data matrix**.
- Added **DataType** (**'abf'** or **'mat'**) as an optional parameter-value pair argument. If no data type is provided, the program first searches for **ABF files** in the data subdirectory, then searches for **MAT files** if abf files don't exist.
- Added **SiMs** (the sampling interval in ms) as an optional parameter-value pair argument. The default SiMs for mat files is **0.1 ms**. If ABF files are read, any user-defined SiMs is overridden by what is stored in the file.
- A function **abf2mat.m** under Adams_Functions is updated to save data matrices directly and to accept a directory as an argument (all abf files in the directory will be converted in this case).
- Added **sweepsToAnalyze** as an input parameter (a column in the input Excel file) so that the user can select the sweeps they want from an ABF file if there are multiple sweeps per file.
- Now makes a **subdirectory** in the output directory for each file if there are multiple sweeps per file

7/30/2017~8/6/2017

Details of our current TC neuron model

- **IT.mod**
  - **T-type calcium current** responsible for low-threshold spikes (LTS)
  - *History:* Modified from ITGHK.mod of the **Destexhe et al 1998a model**, based on the model of Huguenard & McCormick, J Neurophysiol 68: 1373-1383, 1992.
  - *Current-voltage relationship:* Described by **Goldman-Hodgkin-Katz equations**.
  - *Gating:* Uses **2 activation gates** and **1 inactivation gate** (**m^2h**). Voltage dependence and kinetics of activation/inactivation at **23 ℃** from voltage-clamp data (whole cell patch clamp) of Huguenard & Prince, J. Neurosci. 12: 3804-3817, 1992. Updated to reflect values in Destexhe et al, 1998.
  - The activation and inactivation functions can be empirically corrected to account for the contamination of inactivation, to compensate for screening charge, etc. The correction terms are denoted **shiftm** and **shifth** and cause depolarizing (rightward) shifts.
  - The steepness of the activation and inactivation functions can be varied with the parameters **slopem** and **slopeh**, respectively.
  - Suffix: “**IT**”
  - Input/Output: reads **cai** [mM] & **cao** [mM], writes **ica** [mA/cm^2]
  - Parameters - GLOBAL variables whose values are fixed:

Name	Description	Default value	Range/ global
qm	Q_{10} for activation [1]	3.6*	global
qh	Q_{10} for inactivation [1]	2.5*	global

    - *Q_{10}s are from Coulter et al., J Physiol 414: 587, 1989. However, Destexhe et al 1998 used **2.5** in the simulations.
  - Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
pcabar	default maximum Ca++ permeability [cm/s]	0.2e-3	range
shiftm	depolarizing shift of activation curve [mV]	1*	range
shifth	depolarizing shift of inactivation curve [mV]	1*	range
slopem	scaling factor for slope of activation curve [mV]	1	range
slopeh	scaling factor for slope of inactivation curve [mV]	1	range

    - *Default shifts corresponds to 2 mM ext Ca++ (compensates for screening charge) and was used by Destexhe et al 1998.

- Assigned variables - Variables that are assigned outside the mod file:

Name	Description	Dependent Parameters	Range/ global
v	membrane potential [mV]	N/A	range
celsius	temperature [℃]	N/A	global
cai	calcium concentration inside the cell [mM]	N/A	range
cao	calcium concentration outside the cell [mM]	N/A	range

- Assigned variables - GLOBAL variables that are assigned in the INITIAL block:

Name	Description	Dependent Parameters	Range/ global
phim	temperature adjustment to taum [1]	qm, celsius	global
phih	temperature adjustment to tauh [1]	qh, celsius	global

- Assigned variables - RANGE variables that are assigned in the INITIAL & DERIVATIVE blocks:

Name	Description	Dependent Parameters	Range/ global
minf	steady state value of activation gating variable [1]	v, shiftm, slopem	range
hinf	steady state value of inactivation gating variable [1]	v, shifth, slopeh	range
taum	time constant for activation [ms]	v, shiftm, slopem, phim	range
tauh	time constant for inactivation [ms]	v, shifth, slopeh, phih	range

- Assigned variables - RANGE variables that are assigned in the BREAKPOINT block:

Name	Description	Dependent Parameters	Range/ global
ica	calcium current generated [mA/cm²]	pcabar, m, h, v, cai, cao	range

- States:

Name	Description	Dependent Parameters	Initialization
m	activation gating variable [1]	minf, taum	minf
h	inactivation gating variable [1]	hinf, tauh	hinf

- Equations:
  - First, update gating variables:

$$\frac{dm}{dt} = \frac{m_\infty - m}{\tau_m}$$

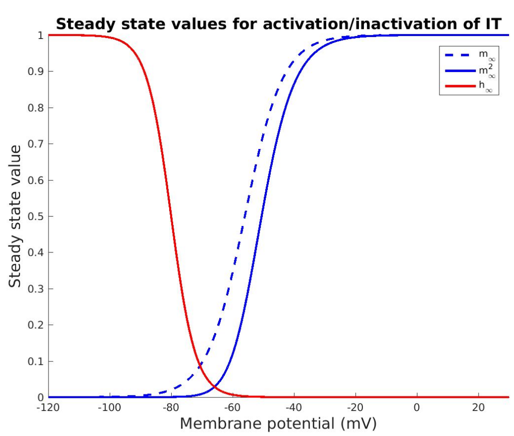
$$\frac{dh}{dt} = \frac{h_\infty - h}{\tau_h}$$

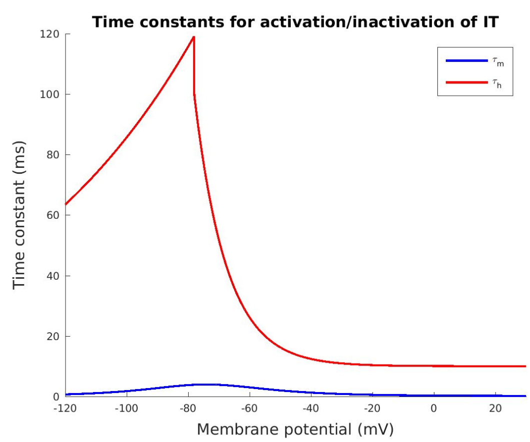
$$m_\infty = \frac{1}{1 + e^{(V+57-shift_m)/(-6.2 slope_m)}}$$

(Here, $\mathbf{V_{1/2}}$ is assumed to be **-57 mV**, but can be modified by $\boldsymbol{shift_m}$, the slope **-6.2** is modified by $\boldsymbol{slope_m}$)

$$h_\infty = \frac{1}{1 + e^{(V+81-shift_h)/(4.0 slope_h)}}$$

(Here, $\mathbf{V_{1/2}}$ is assumed to be **-81 mV**, but can be modified by $\boldsymbol{shift_h}$, the slope **4.0** is modified by $\boldsymbol{slope_h}$)





$$\tau_m = \frac{1}{\Phi_m slope_m}\left(0.612 + \frac{1}{e^{(V+132-shift_m)/-16.7} + e^{(V+16.8-shift_m)/18.2}}\right)$$

For $V - shift_h < -80\,\mathrm{mV}$,

$$\tau_h = \frac{1}{\Phi_h slope_h} e^{(V+467-shift_h)/66.6}$$

For $V - shift_h >= -80\,\mathrm{mV}$,

$$\tau_h = \frac{1}{\Phi_h slope_h}(28 + e^{(V+22-shift_h)/(-10.5)})$$

$$\Phi_m = Q_{10,m}^{(T-23)/10}$$

In all simulations, $Q_{10,m}$ = **3.6**. Since T = **33°C**, $1/Phi_m$ = **0.277**.

$$\Phi_h = Q_{10,h}^{(T-23)/10}$$

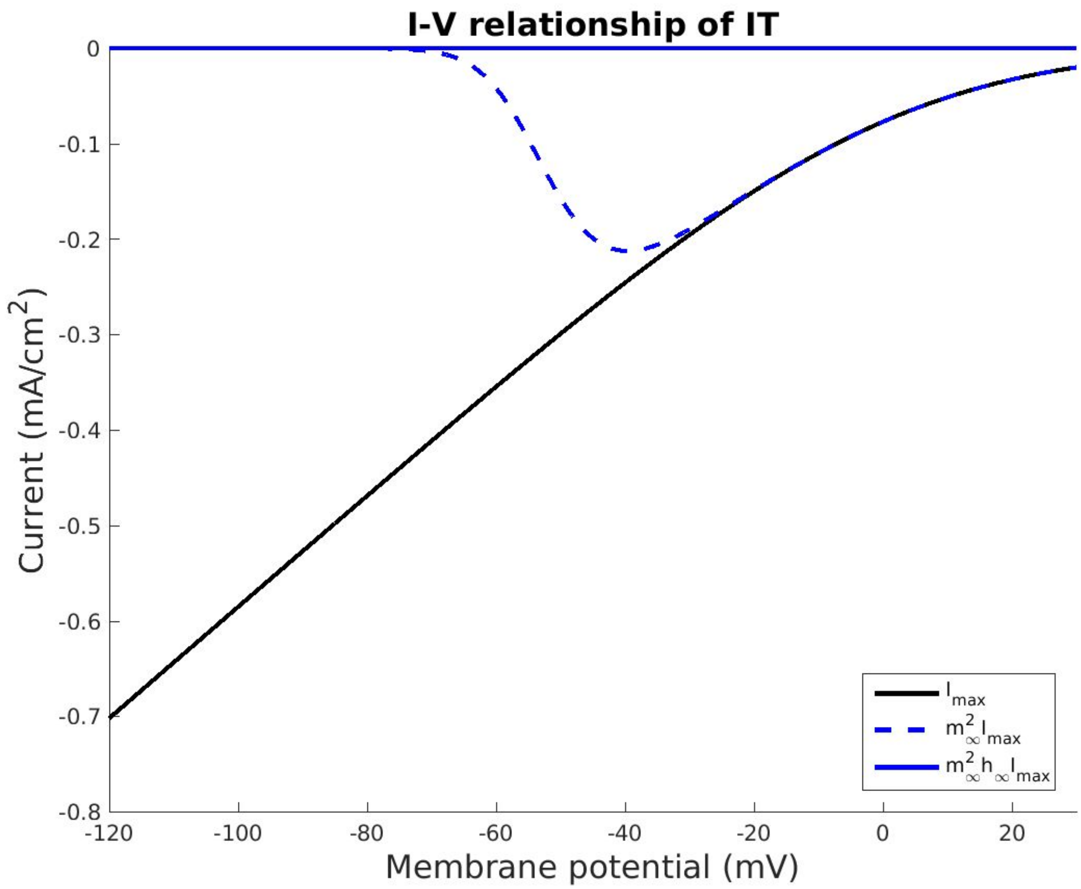
In all simulations, $Q_{10,h}$ = **2.5**. Since T = **33°C**, $1/Phi_h$ = **0.400**.

- Next, update currents:

$$I_\mathrm{T} = I_\mathrm{Ca} = \bar{P}_\mathrm{Ca} m^2 h G(V, [\mathrm{Ca}]_o, [\mathrm{Ca}]_i)$$

$$G(V, [\mathrm{Ca}]_o, [\mathrm{Ca}]_i) = \frac{Z^2 F^2 V}{RT} \frac{[\mathrm{Ca}]_i - [\mathrm{Ca}]_o e^{-ZFV/RT}}{1 - e^{-ZFV/RT}}$$

where Z = 2, T is in [K], V is in [V]. This is based on the **Goldman–Hodgkin–Katz flux equation**



- Procedures and functions:

Name & Arguments	Description	Called by
evaluate_fct(v(mV))	Update **minf, hinf, taum, tauh** based on current voltage	INITIAL, DERIVATIVE
ghk(v(mV), ci(mM), co(mM)) (.001 coul/cm3)	Computes the **Goldman-Hodgkin-Katz flux** based on current voltage, concentration inside the cell, concentration outside the cell	BREAKPOINT, **nongat()**
efun(z)	z/(exp(z) - 1) with Taylor approximation when |z| < 1e-4, z is a floating point number (uses NMODL intrinsic function **fabs**)	**ghk()**
nongat(v,cai,cao)	**Non-gated** version of the calcium current nongat = pcabar * ghk(v, cai, cao)	NONE

  - **ghk** has the structure:
    (.001)*2*FARADAY*(ci*efun(-z) - co*efun(z))
    where
    efun(z) = z/(exp(z) - 1)
    and
    z = (1e-3 [V/mV])*2*FARADAY*v/(R*(celsius+273.15))
    For |z| < **1e-4**, the **1st order Taylor approximation**
    z/(exp(z) - 1) ~ 1 - z/2 is used

- **Ih.mod**
  - **Hyperpolarization-activated nonspecific cationic current**
  - *History:* Modified from Ih.mod of Amarillo et al., J Neurophysiol, 2014. Based on the model of Huguenard & McCormick, J Neurophysiol 68: 1373-1383, 1992, with updated kinetics from Santoro et al., 2000 & Amarillo et al., 2014.
  - *Current-voltage relationship:* Described by **Ohm's Law**.
  - *Gating:* Uses **1 activation gate** (**m**). Voltage dependence and kinetics of activation at **34 ℃** from Amarillo et al., 2014. Note: Huguenard & McCormick originally had $V_{1/2}$ = **-75 mV** and k = **5.5 mV**. Santoro et al. had $V_{1/2}$ = **-82 mV**
  - *Permeability ratio:* **K^+:Na^+** is about **3:1~4:1,** Santoro et al., 1999.
  - *Approximate reversal potential:* Based on [Na+]out = 127.25 mM, [Na+]in = 4.5 mM, [K+]out = 2.5 mM, [K+]in = 113 mM & celsius = 33 degC, the GHK voltage equation yields **-24 ~ -32 mV.** Santoro et al., 1999 had **-35 mV**. Amarillo et al., 2014 used **-43 mV**.
  - *Identity:* HCN channels (Hyperpolarization-activated cyclic-nucleotide dependent cation-nonspecific channels). **mHCN2** & **mHCN4** found in thalamocortical relay neurons. See Santoro et al., 2000.
  - Suffix: "**Ih**"

- Input/Output: writes **ih** [mA/cm²] as a **nonspecific current**
- Parameters - GLOBAL variables whose values are fixed:

Name	Description	Default value	Range/ global
qm	Q_{10} for activation [1]	4.0*	global

  - *Q_{10} is from Santoro & Tibbs, 1999, based on values of 3.13 (sheep Purkinje fibers), 4.5 (rat CA1 pyramidal neurons), 5 (guinea pig CA1 pyramidal neurons)

- Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
ghbar	default maximum conductance of Ih [S/cm^2]	2.2e-5	range
eh	reversal potential of Ih [mV]	-43	range
shiftm	depolarizing shift of activation curve [mV]	0	range

- Assigned variables - Variables that are assigned outside the mod file:

Name	Description	Dependent Parameters	Range/ global
v	membrane potential [mV]	N/A	range
celsius	temperature [°C]	N/A	global

- Assigned variables - GLOBAL variables that are assigned in the INITIAL block:

Name	Description	Dependent Parameters	Range/ global
phim	temperature adjustment to taum [1]	qm, celsius	global

- Assigned variables - RANGE variables that are assigned in the INITIAL & DERIVATIVE blocks:

Name	Description	Dependent Parameters	Range/ global
minf	steady state value of activation gating variable [1]	v, shiftm	range
taum	time constant for activation [ms]	v, shiftm, phim	range

- Assigned variables - RANGE variables that are assigned in the BREAKPOINT block:

Name	Description	Dependent Parameters	Range/ global
ih	H current generated [mA/cm2]	ghbar, m, v, eh	range

- States:

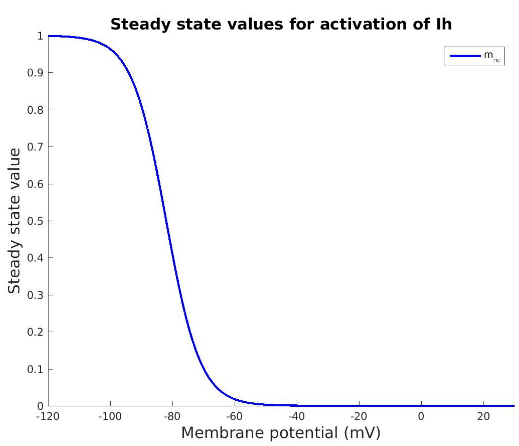
Name	Description	Dependent Parameters	Initialization
m	activation gating variable [1]	minf, taum	minf

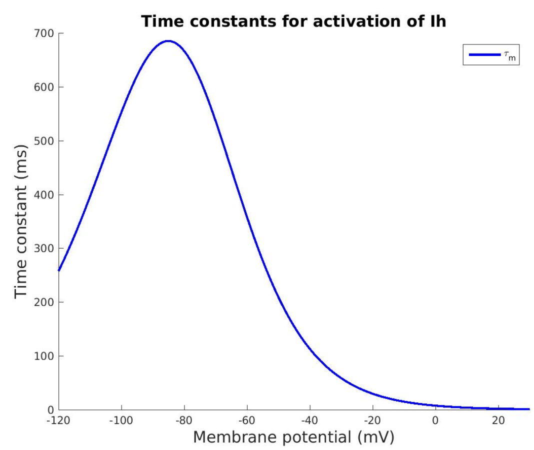
- Equations:
  - First, update gating variables:

$$\frac{dm}{dt} = \frac{m_\infty - m}{\tau_m}$$

$$m_\infty = \frac{1}{1 + e^{(V+82-shift_m)/5.5}}$$

(Here, $\mathbf{V_{1/2}}$ is assumed to be **-82 mV**, but can be modified by $\boldsymbol{shift_m}$)





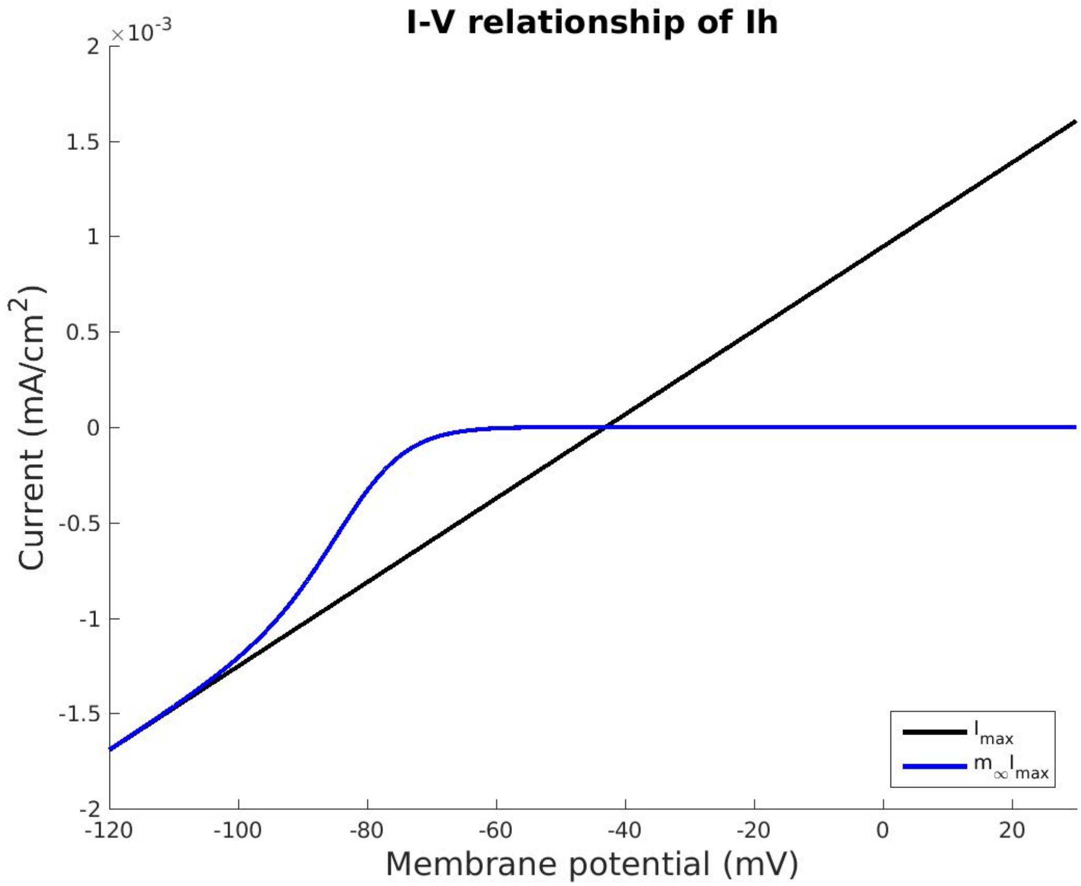
$$\tau_m = \frac{1}{\Phi_m(0.0008 + (3.5\times 10^{-6})e^{-0.05787(V-shift_m)} + e^{-1.87+0.0701(V-shift_m)})}$$

$$\Phi_m = Q_{10,m}^{(T-34)/10}$$

In all simulations, $Q_{10,m}$ = **4.0**. Since T = **33°C**, 1/Phi_m = **0.871**.

  - Next, update currents:

$$I_\text{h} = \bar{g}_\text{h} m(V - E_\text{h})$$



- Procedures and functions:

Name & Arguments	Description	Called by
settables(v(mV))	Update **minf, taum** based on current voltage	INITIAL, DERIVATIVE

- **IA.mod**
  - **Fast transient potassium current**
  - *History:* Modified from IA.mod of Amarillo et al., J Neurophysiol, 2014, based on the model of Huguenard & McCormick, J Neurophysiol 68: 1373-1383, 1992.
  - *Current-voltage relationship:* Described by **Ohm's Law**.
  - *Gating:* Uses **4 activation gates** and **1 inactivation gate** (**m^4h**). There are two types of activation gates, each paired with a type of inactivation gates. The ratio of contribution is **3:2**.
  - Voltage dependence and kinetics of activation/inactivation at **23 ℃** from voltage-clamp data (whole cell patch clamp) of Huguenard & Prince, J. Neurosci. 12: 3804-3817, 1992.
  - Suffix: "**IA**"
  - Input/Output: reads **ek** [mV], writes **ik** [mA/cm²]

- Parameters - GLOBAL variables whose values are fixed:

Name	Description	Default value	Range/ global
q10	Q_{10} for both activation and inactivation [1]	2.8*	global

  - *from Huguenard et al, 1991.

- Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
gkbar	default maximum conductance of IA [S/cm^2]	5.5e-3	range

- Assigned variables - Variables that are assigned outside the mod file:

Name	Description	Dependent Parameters	Range/ global
v	membrane potential [mV]	N/A	range
celsius	temperature [°C]	N/A	global
ek	reversal potential of potassium [mV]	N/A	range

- Assigned variables - GLOBAL variables that are assigned in the INITIAL block:

Name	Description	Dependent Parameters	Range/ global
phi	temperature adjustment to taum & tauh [1]	q10, celsius	global

- Assigned variables - RANGE variables that are assigned in the INITIAL & DERIVATIVE blocks:

Name	Description	Dependent Parameters	Range/ global
m1inf	steady state value of activation gating variable #1 [1]	v	range
m2inf	steady state value of activation gating variable #2 [1]	v	range
hinf	steady state value of inactivation gating variables [1]	v	range
taum	time constant for activation gating variables [ms]	v, phi	range
tauh1	time constant for inactivation gating variable #1 [ms]	v, phi	range

tauh2	time constant for inactivation gating variable #2 [ms]	v, phi	range

- Assigned variables - RANGE variables that are assigned in the BREAKPOINT block:

Name	Description	Dependent Parameters	Range/ global
ik	potassium current generated [mA/cm²]	gkbar, m1, m2, h1, h2, ek, v	range

- States:

Name	Description	Dependent Parameters	Initialization
m1	activation gating variable #1 [1]	m1inf, taum	m1inf
m2	activation gating variable #2 [1]	m2inf, taum	m2inf
h1	inactivation gating variable #1 [1]	hinf, tauh1	hinf
h2	inactivation gating variable #2 [1]	hinf, tauh2	hinf

- Equations:
  - First, update gating variables:

$$\frac{dm_1}{dt} = \frac{m_{1,\infty} - m_1}{\tau_m}$$

$$\frac{dm_2}{dt} = \frac{m_{2,\infty} - m_2}{\tau_m}$$

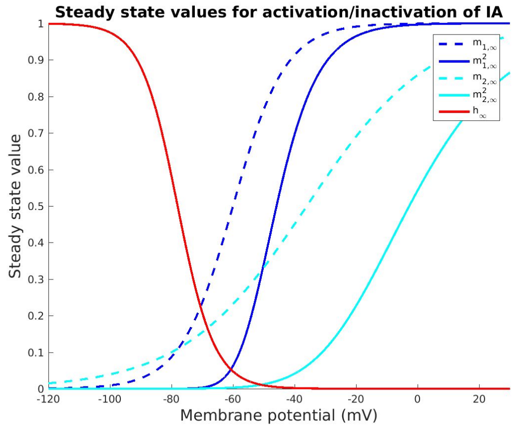
$$\frac{dh_1}{dt} = \frac{h_\infty - h_1}{\tau_{h_1}}$$

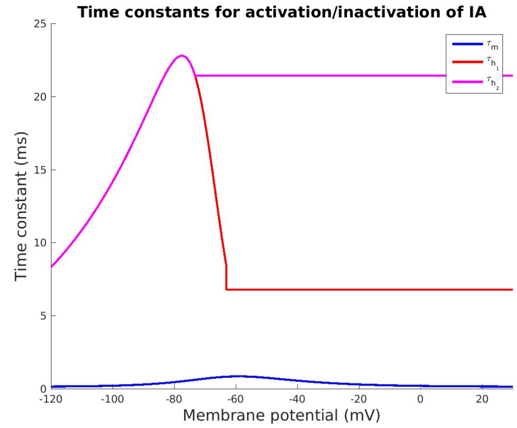
$$\frac{dh_2}{dt} = \frac{h_\infty - h_2}{\tau_{h_2}}$$

$$m_{1,\infty} = \frac{1}{1 + e^{(V+60)/(-8.5)}}$$

$$m_{2,\infty} = \frac{1}{1 + e^{(V+36)/(-20)}}$$

$$h_\infty = \frac{1}{1 + e^{(V+78)/6.0}}$$





$$\tau_m = \frac{1}{\Phi_m}(0.37 + \frac{1.0}{e^{(V+35.8)/19.7} + e^{(V+79.7)/(-12.7)}}$$

For $V < -63\,\mathrm{mV}$,

$$\tau_{h_1} = \frac{1}{\Phi(e^{(V+46)/5.0} + e^{(V+238)/(-37.5)})}$$

For $V \geq -63\,\mathrm{mV}$,

$$\tau_{h_1} = \frac{19}{\Phi}$$

For $V < -73\,\mathrm{mV}$,

$$\tau_{h_2} = \frac{1}{\Phi(e^{(V+46)/5.0} + e^{(V+238)/(-37.5)})}$$

For $V \geq -73\,\mathrm{mV}$,

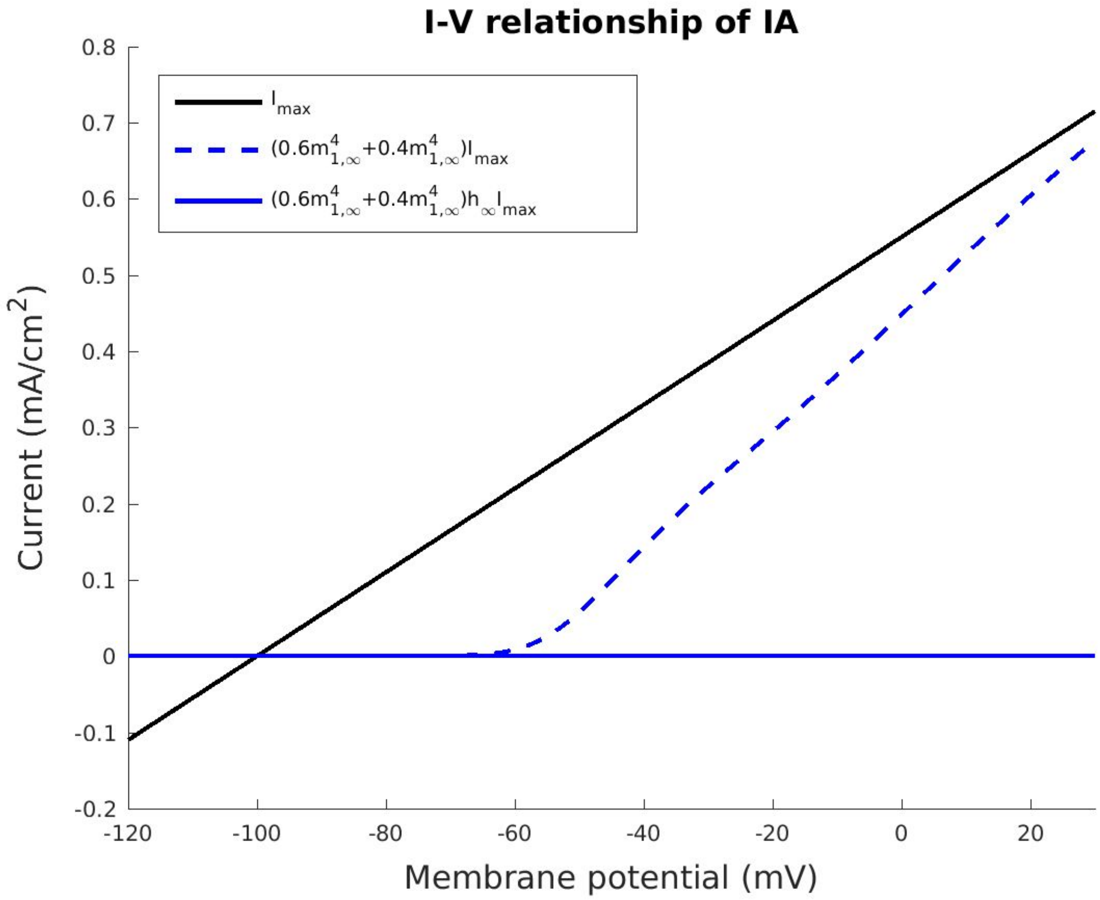
$$\tau_{h_2} = \frac{60}{\Phi}$$

$$\Phi_m = Q_{10,m}^{(T-23)/10}$$

In all simulations, $Q_{10,m}$ = **2.8**. Since T = **33°C**, 1/Phi_m = **0.357**.

- Next, update currents:

$$I_\mathrm{A} = \bar{g}_\mathrm{K}(0.6m_1^4h_1 + 0.4m_2^4h_2)(V - E_\mathrm{K})$$



- Procedures and functions:

Name & Arguments	Description	Called by
settables(v(mV))	Update **m1inf, m2inf, hinf, taum, tauh1, tauh2** based on current voltage	INITIAL, DERIVATIVE

- **IKir.mod**
  - **Potassium strong inward rectifier current**
  - *History:* Modified from IKir.mod of Amarillo et al., J Neurophysiol, 2014.
  - *Current-voltage relationship:* Described by **Ohm's Law**..
  - *Gating:* Uses an instantaneous activation gate. Voltage dependence from Amarillo et al., J Neurophysiol, 2014.
  - Suffix: "**IKir**"
  - Input/Output: reads **ek** [mV], writes **ik** [mA/cm²]
  - Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
gkbar	default maximum conductance of IKir [S/cm^2]	2.0e-5	range

- Assigned variables - Variables that are assigned outside the mod file:

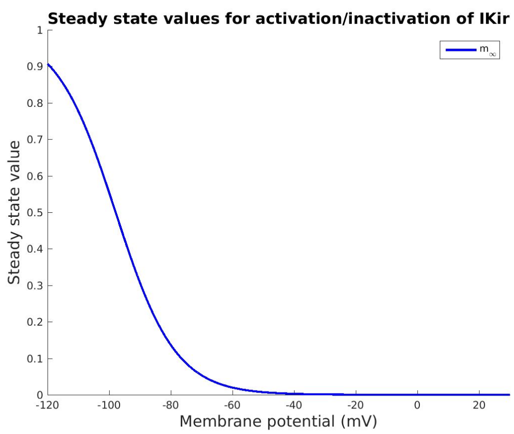
Name	Description	Dependent Parameters	Range/ global
v	membrane potential [mV]	N/A	range
ek	reversal potential of potassium [mV]	N/A	range

- Assigned variables - RANGE variables that are assigned in the BREAKPOINT block:

Name	Description	Dependent Parameters	Range/ global
minf	steady state value of activation gating variable [1]	v	range
ik	potassium current generated [mA/cm²]	gkbar, minf, ek, v	range

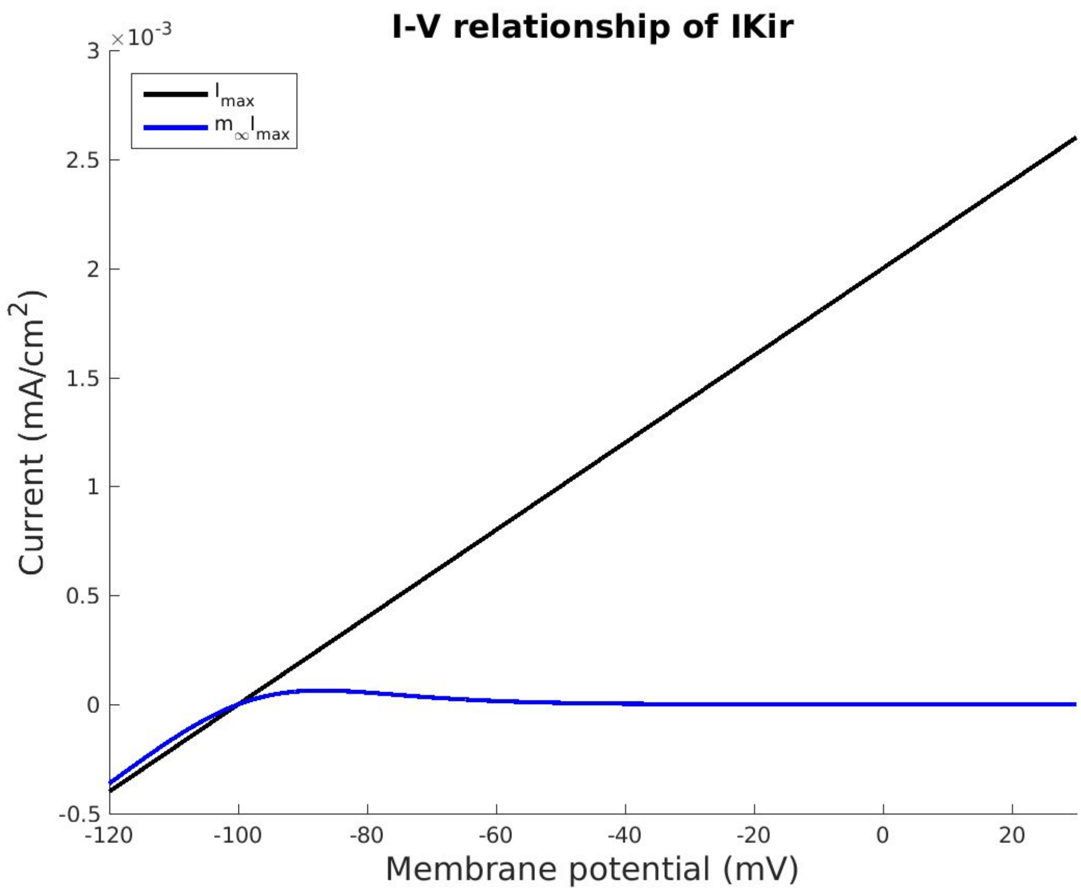
- Equations:
  - Update gating variable:

$$m_\infty = \frac{1}{1+e^{(V+97.9)/9.7}}$$



  - Update current:

$$I_{\text{Kir}} = \bar{g}_{\text{K}} m_\infty (V - E_{\text{K}})$$



- **INaP.mod**
  - **Persistent sodium current**
  - *History:* Modified from INaP.mod of Amarillo et al., J Neurophysiol, 2014. Based on the model by Wu et al, 2005 on mesencephalic trigeminal sensory neurons.
  - *Current-voltage relationship:* Described by **Ohm's Law**.
  - *Gating:* Uses **1 activation gate** and **1 inactivation gate** (**mh**). The activation is instantaneous whereas the inactivation is slow and time-dependent. Voltage dependence and kinetics of activation/inactivation at **23 ℃** from voltage-clamp data (whole cell patch clamp) of Wu et al, 2005.
  - Suffix: "**INaP**"
  - Input/Output: reads **ena** [mV], writes **ina** [mA/cm²]
  - Parameters - GLOBAL variables whose values are fixed:

Name	Description	Default value	Range/ global
qh	Q_{10} for inactivation [1]	3*	global

  - *Q_{10} is assumed by Amarillo et al

- Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
gnabar	default maximum conductance of INaP [S/cm^2]	5.5e-6	range

- Assigned variables - Variables that are assigned outside the mod file:

Name	Description	Dependent Parameters	Range/ global
v	membrane potential [mV]	N/A	range
celsius	temperature [°C]	N/A	global
ena	reversal potential of sodium [mV]	N/A	range

- Assigned variables - GLOBAL variables that are assigned in the INITIAL block:

Name	Description	Dependent Parameters	Range/ global
phih	temperature adjustment to tauh [1]	qh, celsius	global

- Assigned variables - RANGE variables that are assigned in the INITIAL & DERIVATIVE blocks:

Name	Description	Dependent Parameters	Range/ global
minf	steady state value of activation gating variable [1]	v	range
hinf	steady state value of activation gating variable [1]	v	range
tauh	time constant for inactivation [ms]	v, phih	range

- Assigned variables - RANGE variables that are assigned in the BREAKPOINT block:

Name	Description	Dependent Parameters	Range/ global
ina	sodium current generated [mA/cm2]	gnabar, minf, h, v, ena	range

- States:

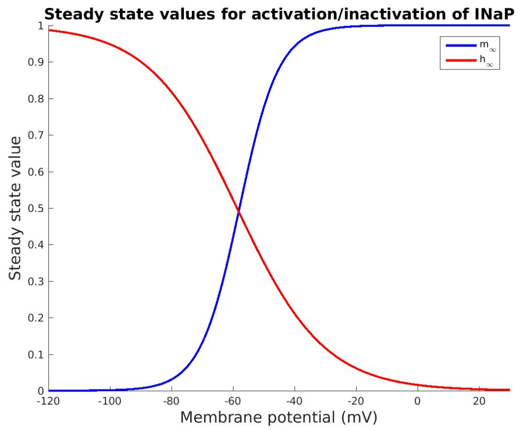
Name	Description	Dependent Parameters	Initialization
h	inactivation gating variable [1]	hinf, tauh	hinf

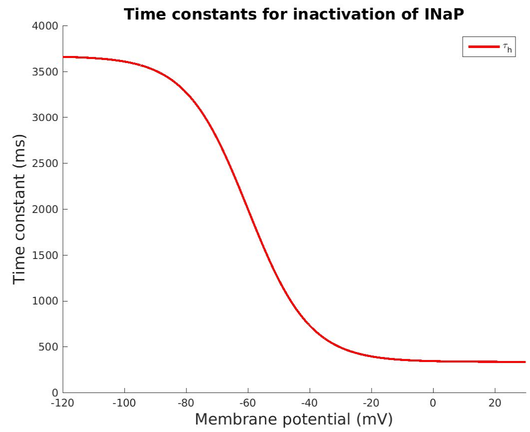
- Equations:
  - First, update gating variables:

$$m_\infty = \frac{1}{1 + e^{(V+57.9)/(-6.4)}}$$

$$\frac{dh}{dt} = \frac{h_\infty - h}{\tau_h}$$

$$h_\infty = \frac{1}{1 + e^{(V+58.7)/14.2}}$$





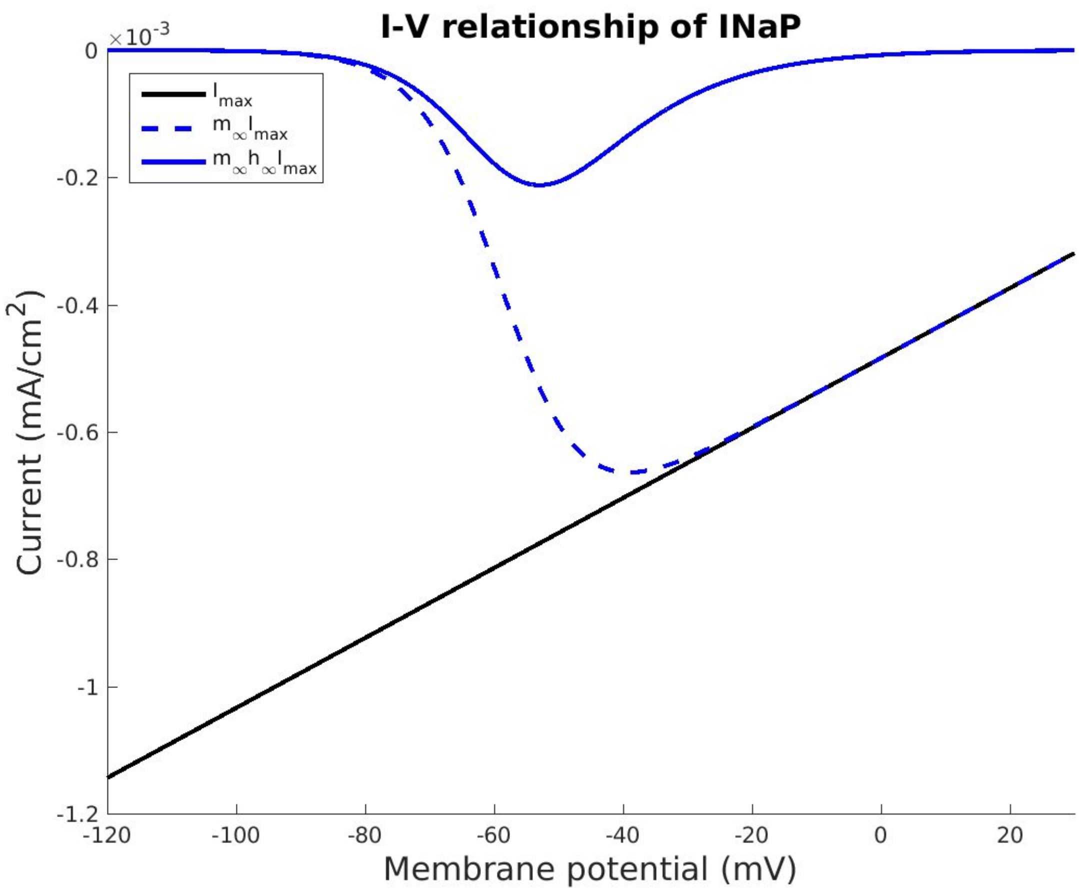
$$\tau_h = \frac{1}{\Phi_h}(1000 + \frac{10000}{1 + e^{(V+60)/10}})$$

$$\Phi_h = Q_{10,h}^{(T-23)/10}$$

In all simulations, $Q_{10,m}$ = **3**. Since T = **33°C**, 1/Phi_m = **0.333**.

  - Next, update currents:

$$I_{\text{NaP}} = \bar{g}_{\text{Na}} m_\infty h (V - E_{\text{Na}})$$



- Procedures and functions:

Name & Arguments	Description	Called by
setvalues(v(mV))	Update **minf, hinf, tauh** based on current voltage	INITIAL, DERIVATIVE

- **cadecay.mod**
  - **Fast mechanism for submembranal Ca++ concentration (cai)**
  - Suffix: “**cad**” (same as calcium pump)
  - Input/Output: reads **ica** ([mA/cm²]) & **cai**, writes **cai**
  - Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
depth	Depth of the shell just beneath the membrane [μm]	0.1	range
cainf	Equilibrium concentration of calcium [mM]	2.4e-4	range

taur	Time constant of calcium extrusion, must be fast) [ms]	24*	range

        - *Sohal & Huguenard 2003 (@ 34 degC). Note: Destexhe used 5 ms, Amarillo used 1 ms.
    - Assigned variables - Variables that are assigned outside the mod file:

Name	Description	Dependent Parameters	Range/ global
ica	calcium current [mA/cm2]	N/A	range

    - Assigned variables - RANGE variables that are assigned in the DERIVATIVE block:

Name	Description	Dependent Parameters	Range/ global
drive_channel	calcium flux due to ica [mM/ms]	ica, depth	range

    - States & initialization:

Name	Description	Initialization
cai	submembranal Ca++ concentration [mM]	cainf

    - Equations:
        - Differential equation:

$$\frac{d[\mathrm{Ca}]_i}{dt} = -\frac{I_{\mathrm{Ca}}}{2Fd} + \frac{([\mathrm{Ca}]_\infty - [\mathrm{Ca}]_i)}{\tau_r}$$ (using implicit integration)

where *F* is Faraday's constant, *d* is the depth of the shell just beneath the membrane.

- **gabab_m3ha.mod**
    - **Simple GABA-B receptor**
    - Point Process: "**gabab**"
    - Input/Output: writes a nonspecific current **i**
    - Parameters - GLOBAL variables whose values are fixed:

Name	Description	Default value	Range/ global
p	power of rising phase [1]	8	global
q10	Q10 for all phases [1]	2.1*	global

        - *Q10 is from Otis et al, 1993. However, not used here since Christine did everything at 33 degC

- Parameters - RANGE variables whose values are specified in hoc:

Name	Description	Default value	Range/ global
Erev	Reversal potential [mV]	-115	range
amp	maximum amplitude of gabab conductance [uS]	15.92*	range
Trise	rise time constant [ms]	52*	range
TfallFast	fast decay time constant [ms]	140.02*	range
TfallSlow	slow decay time constant [ms]	1073*	range
w	weight of fast decay [1]	0.952*	range
Ninputs	number of input streams [1]	1	range

  - *these are changed across pharmacological conditions

- Assigned variables - Variables that are assigned outside the mod file:

Name	Description	Dependent Parameters	Range/ global
v	postsynaptic membrane potential [mV]	N/A	range
celsius	temperature [℃]	N/A	global

- Assigned variables - GLOBAL variables that are assigned in the INITIAL block:

Name	Description	Dependent Parameters	Range/ global
phi	temperature adjustment for rates [1]	q10, celsius	global

- Assigned variables - RANGE variables that are assigned in the BREAKPOINT block:

Name	Description	Dependent Parameters	Range/ global
g	conductance generated [uS]	Ron, RoffFast, RoffSlow, w, p, amp	range
i	current generated [nA]	g, v, Erev	range

- States:

Name	Description	Dependent Parameters	Initialization

Ron	slow decay variable [1]	Trise, phi, weight, Ninputs	0
RoffSlow	fast decay variable [1]	TfallFast, phi, weight, Ninputs	0
RoffFast	rise variable [1]	TfallSlow, phi, weight, Ninputs	0

- These have a maximum value of 1 for an isolated IPSC

○ *Obsolete* - Internal variables in the NET_RECEIVE block that are called by reference:

Name	Description	Dependent Parameters	Initialization
Rlast	amount of activation right after the last synaptic event [1]	Rlast, Tlast, p, amp, Trise, TfallFast, TfallSlow, w, weight, Ninputs	0
Tlast	time point of the last synaptic event [ms]	t	0

○ Equations:

- Upon receiving a synaptic event, update synaptic variables:

$$R_{\text{off,fast}} = R_{\text{off,fast}} + \frac{weight}{N_{\text{inputs}}}$$

$$R_{\text{off,slow}} = R_{\text{off,slow}} + \frac{weight}{N_{\text{inputs}}}$$

$$R_{\text{on}} = R_{\text{on}} + \frac{weight}{N_{\text{inputs}}}$$

- At each time step, update synaptic variables:

$$\frac{dR_{\text{off,fast}}}{dt} = \frac{-R_{\text{off,fast}}}{T_{\text{off,fast}}/\Phi}$$

$$\frac{dR_{\text{off,slow}}}{dt} = \frac{-R_{\text{off,slow}}}{T_{\text{off,slow}}/\Phi}$$

$$\frac{dR_{\text{on}}}{dt} = \frac{-R_{\text{on}}}{T_{\text{on}}/\Phi}$$

- Finally, update currents:

$$g_{\text{GABA}_\text{B}} = A(1 - R_{\text{on}})^p (wR_{\text{off,fast}} + (1-w)R_{\text{off,slow}})$$

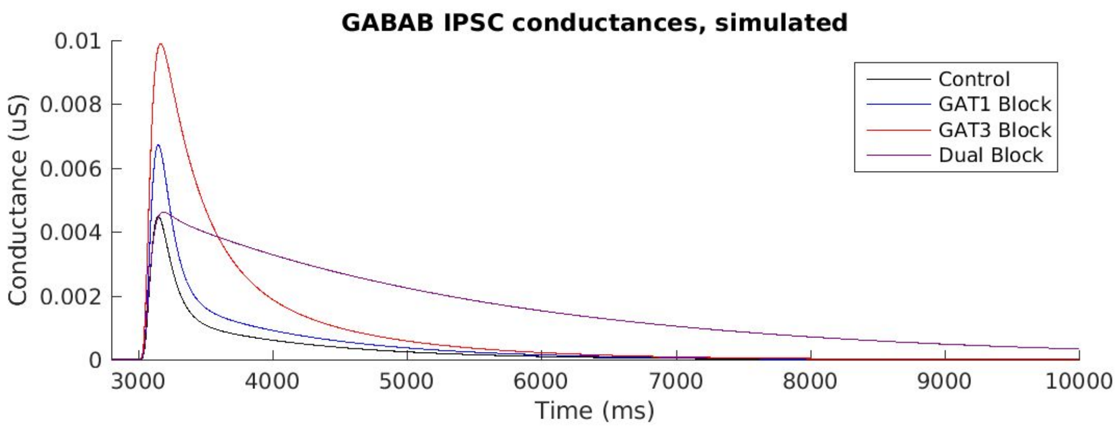
where *A* is the amplitude (not the maximum though)

$$I_{\text{GABA}_\text{B}} = g_{\text{GABA}_\text{B}}(V - E_{\text{rev}})$$

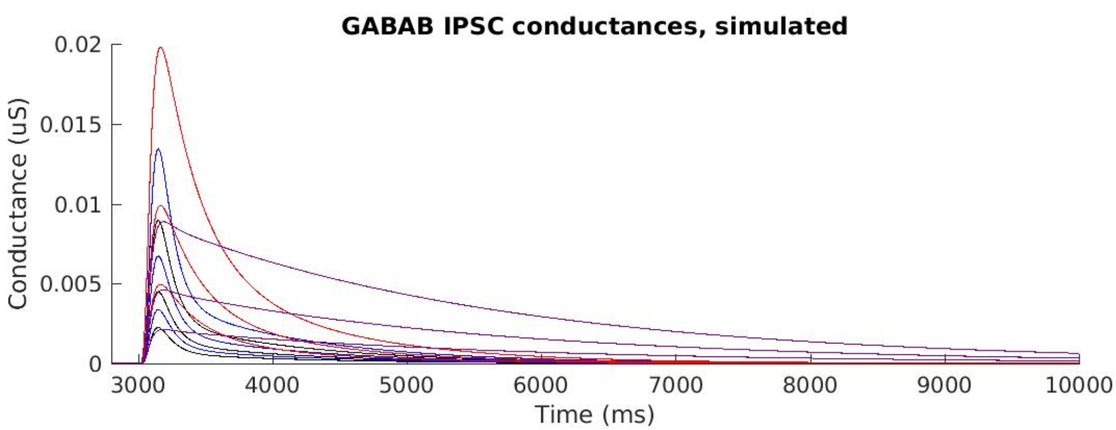
- Parameters for GABA-B conductance curves @ 200 % g incr:

	Control	GAT 1 Block	GAT 3 Block	Dual Block
amp [nS]	32	48	17.76	12.64
Trise [ms]	52	52	38.63	39.88
TfallFast [ms]	90.1	90.1	273.4	65.8
TfallSlow [ms]	1073.2	1073.2	1022	2600
w [1]	0.952	0.952	0.775	0.629

- GABA-B conductance curves @ 200 % g incr:



- GABA-B conductance curves @ 100 %, 200 % & 400% g incr:



Plan for next week

- minEASE:
    - Recompute **IEIs, ISIs, decay times, etc.** after adding/deleting/changing events

- Single Neuron Model:
    - Rerun **singleneuronfitting10.m** for Dexteshe default after changing ek, shifmIT & shiftmIh
    - Finish plotting the **activation/inactivation curves**
    - Plot all **I-V curves** together
    - Write out the voltage relationships between compartments. Is the **cable equation** used by NEURON? Are the diameters tapered?
    - Investigate where **shiftm, shifth, slopem, slopeh** should be placed. Should we make T_1/2 and k parameters instead? (Perhaps no, because taum and minf should vary together, see Pinsky-Rinzel model.)
    - Change **eh** to be bounded by -24~-32 mV?
    - Try ball-and-stick model with 2 nodes for the stick instead? Use theory to estimate build parameters and fit only epas & gpas?
    - Try writing out an **explicit objective function**
    - Write code for **fitting across cells** (pick a **"stereotyped trace"** from all trials, Change parameters for each cell)

- Area paper:
    - Start writing background information for area paper
    - Decide on committee members, defense date and send emails

- Knowledge buildup:
    - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)

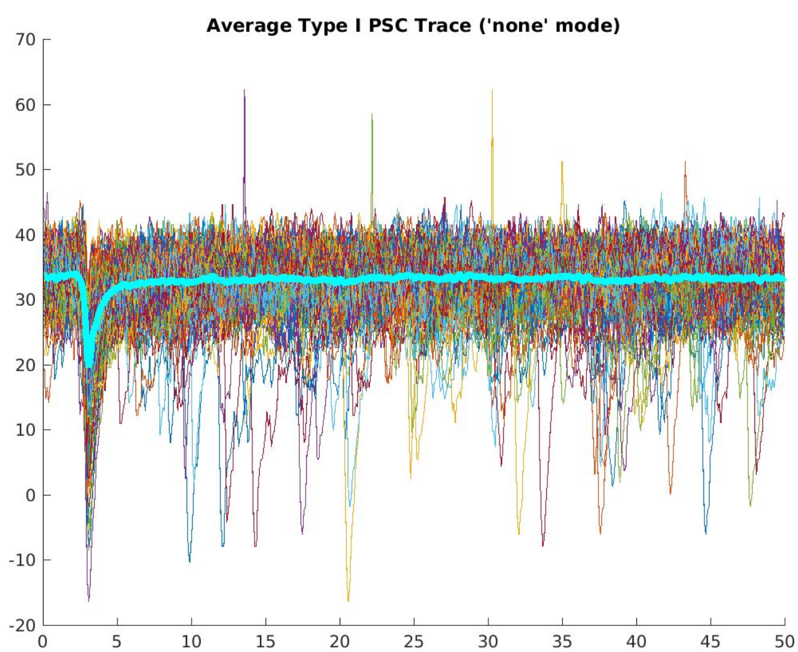
7/24/2017~7/26/2017

<u>minEASE (updates)</u>

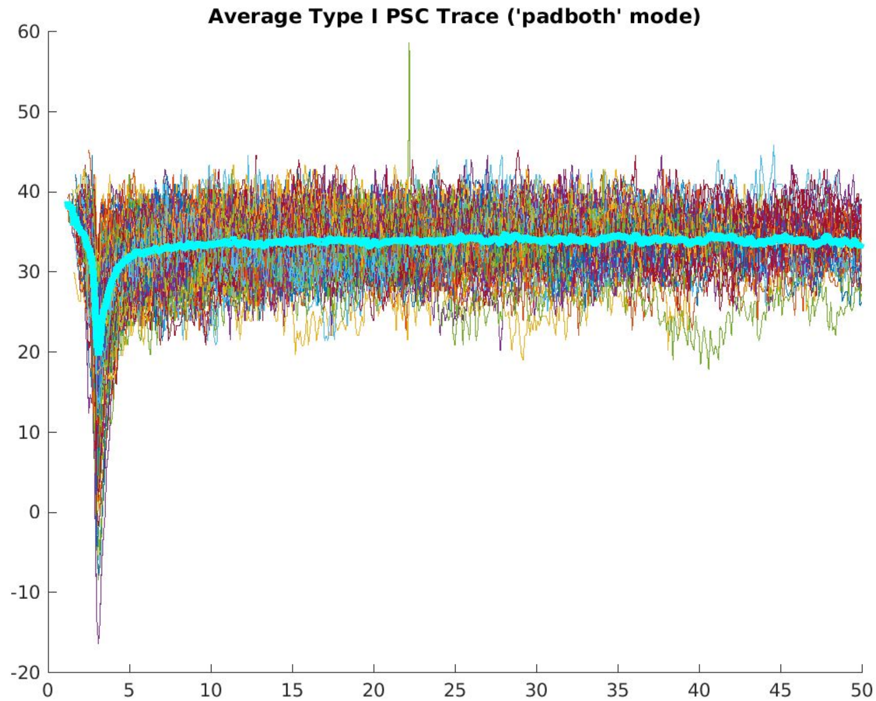
- Fixed bug for 10-90% rise times
- Combine event information from all sweeps that have been analyzed together and change the units of all time/duration values from samples to absolute time (ms).

Peak Time	Breakpoin	Peak Valu	Peak Amp	0-100% Ri	10-90% Ri	Peak to Pe	Peak to Br	50% Deca	Full Decay	Event Clas	Whether I
25.9	31.1298	21.69	9.43987	0.6	0.4	6.3	5.8	1.2	2.7	6	1
32.2	37.7115	28.3664	9.3451	0.5	0.4	8.7	8.4	0.3	8.3	6	1
40.9	40.3224	30.9307	9.39167	0.3	0.2	43.5	42.2	3.8	NaN	6	1
84.4	37.3403	9.90454	27.4357	1.3	0.7	31.1	30.2	0.9	5.4	1	1
115.5	35.0054	25.521	9.48442	0.9	0.8	49.4	48.7	0.9	1.7	6	1
164.9	37.2528	28.5309	8.72189	0.7	0.7	10.5	9.5	0.3	0.9	6	1
175.4	37.3217	28.4304	8.89136	1	0.6	6.9	6.6	0.3	0.6	6	1
182.3	33.0117	24.0007	9.01108	0.3	0.2	41.9	41.6	0.2	1	6	1
224.2	38.8625	29.9925	8.86994	0.3	0.3	11.9	10.6	NaN	NaN	6	1
236.1	31.5741	17.3244	14.2498	1.3	1.1	3.1	2.6	0.5	1.7	1	1
239.2	33.1785	24.1288	9.04967	0.5	0.5	31	30.4	0.6	0.7	6	1
270.2	29.3464	3.83406	25.5123	0.6	0.4	37.4	36.5	0.4	1	1	1
307.6	30.0423	11.0243	19.0179	0.9	0.8	42.3	41.7	0.5	2.4	1	1
349.9	31.1918	17.443	13.7489	0.6	0.6	79.2	78	0.4	0.7	1	1
429.1	33.7981	24.7354	9.06274	1.2	1.2	5.9	5.1	0.6	0.7	6	1
435	38.1053	26.7356	11.3696	0.8	0.8	20.2	18.2	2	NaN	2	1

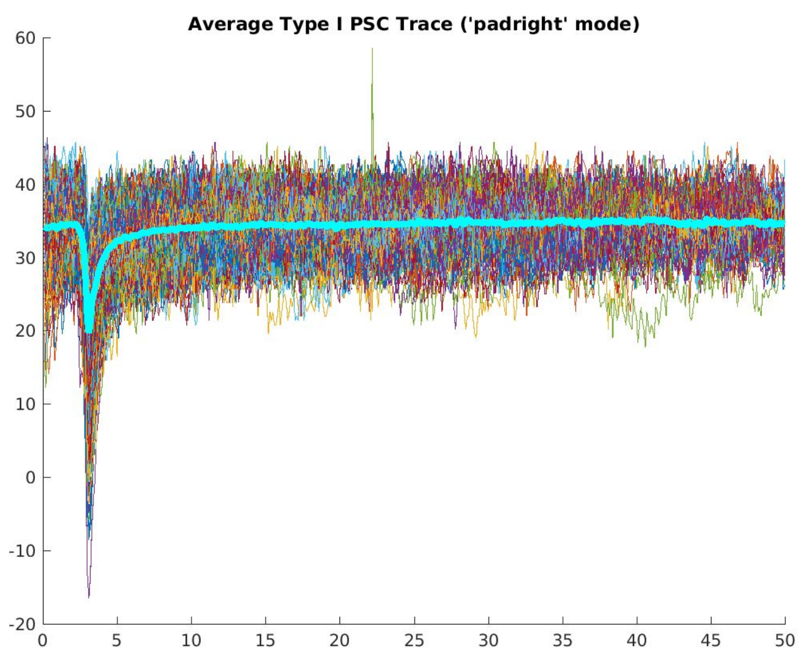
- Averaged Types II & III PSCs too, computed averaged PSCs 4 ways and allowed averaging ***after*** the event info from sweeps are combined:
  - '**None**' mode (keep all PSCs and including leading and trailing traces):



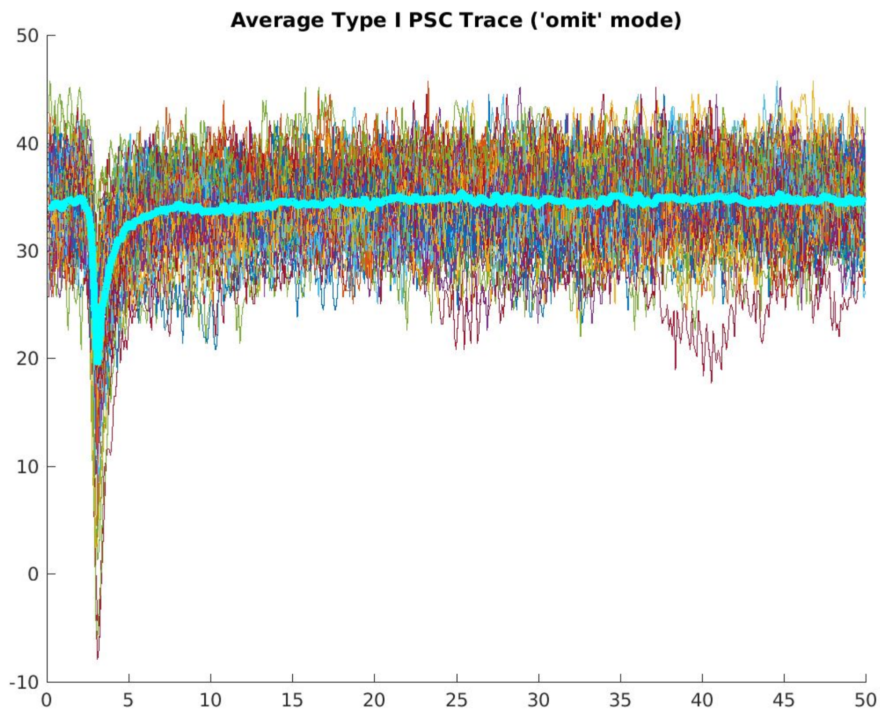
- ‘**Padboth**’ mode (pad **NaNs** to PSCs that are too short on both sides):



- ‘**Padright**’ mode (pad **NaNs** to PSCs that are too short on both sides):



- ‘**Omit**’ mode (omit PSCs that are too short):

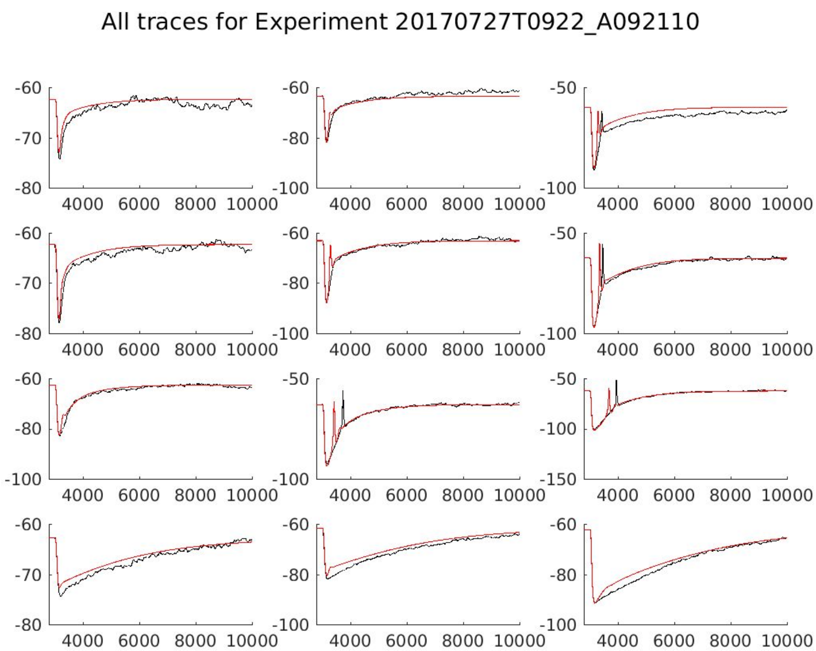


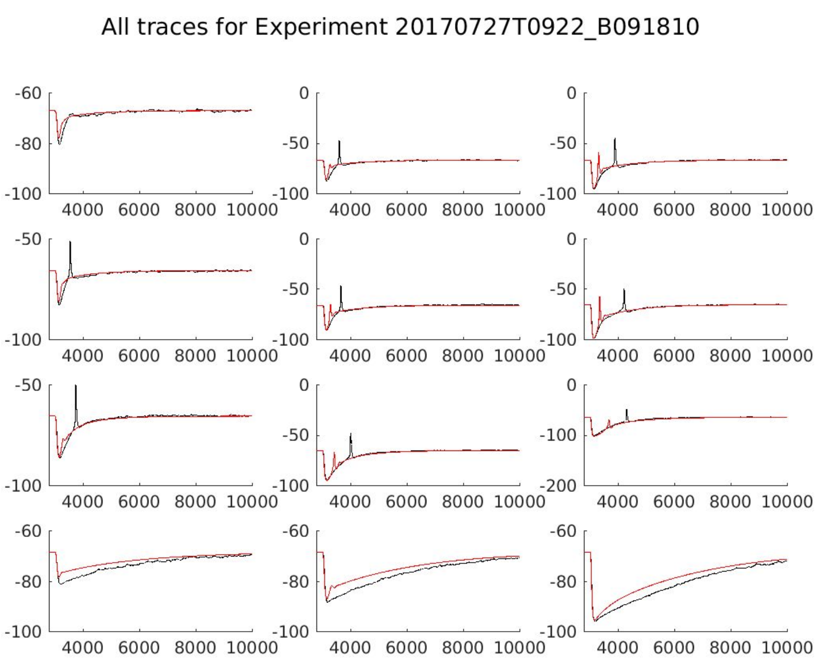
- Allowed loading of previously saved event information
- Fixed the bug that checked events weren’t initialized as filled circles

7/26/2017~7/30/2017

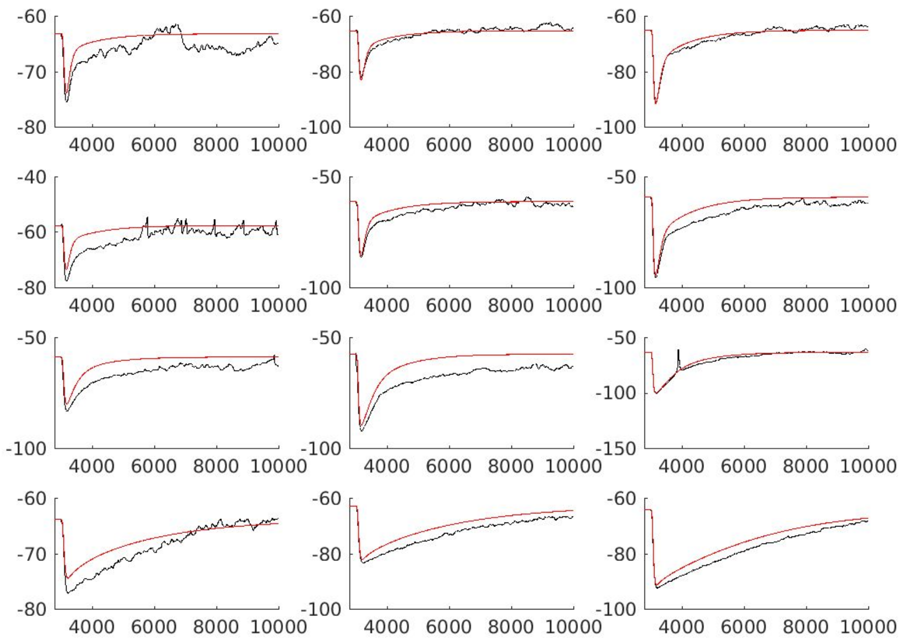
<u>Single Neuron Fitting (continued)</u>

- **singleneuronfitting6_manual**: Took one trace out of each pharm x g incr pair for better visualization. From optimized parameters in **singleneuronfitting5**

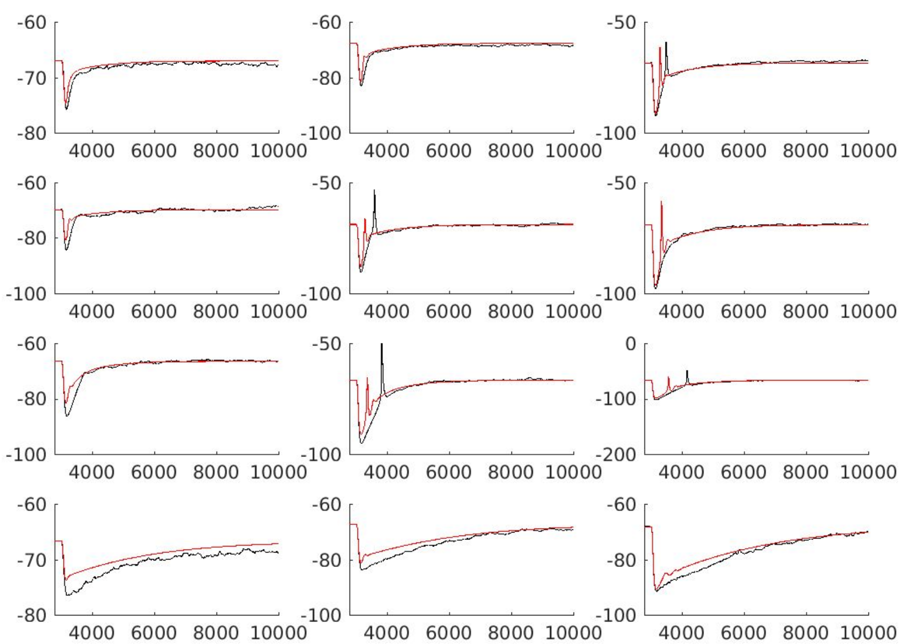




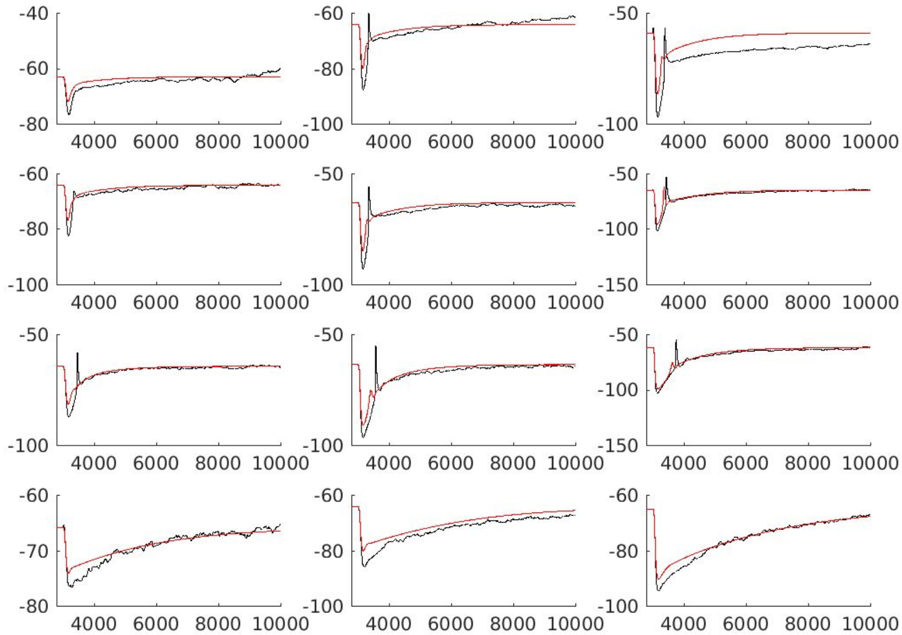
All traces for Experiment 20170727T0922_B092710



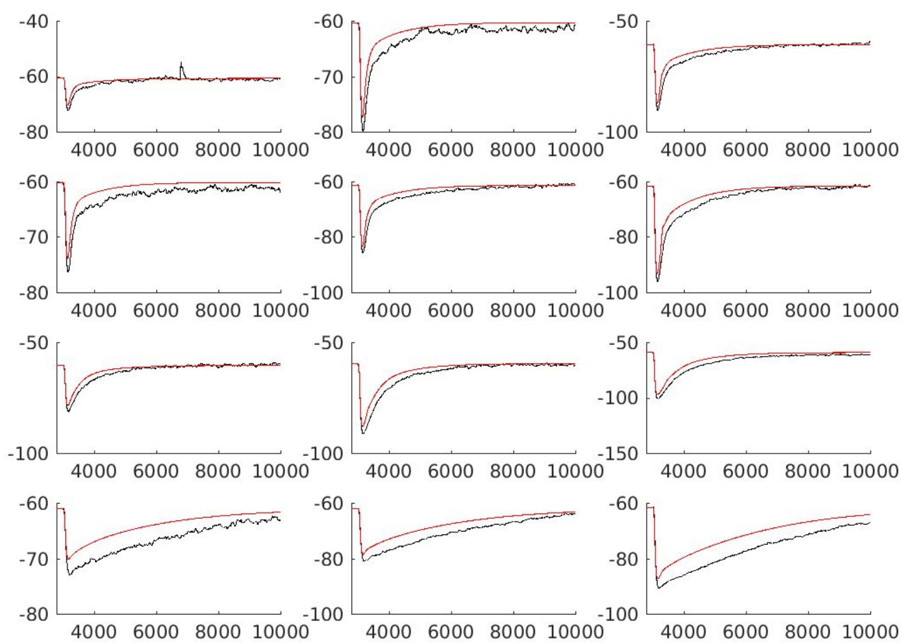
All traces for Experiment 20170727T0922_C092110

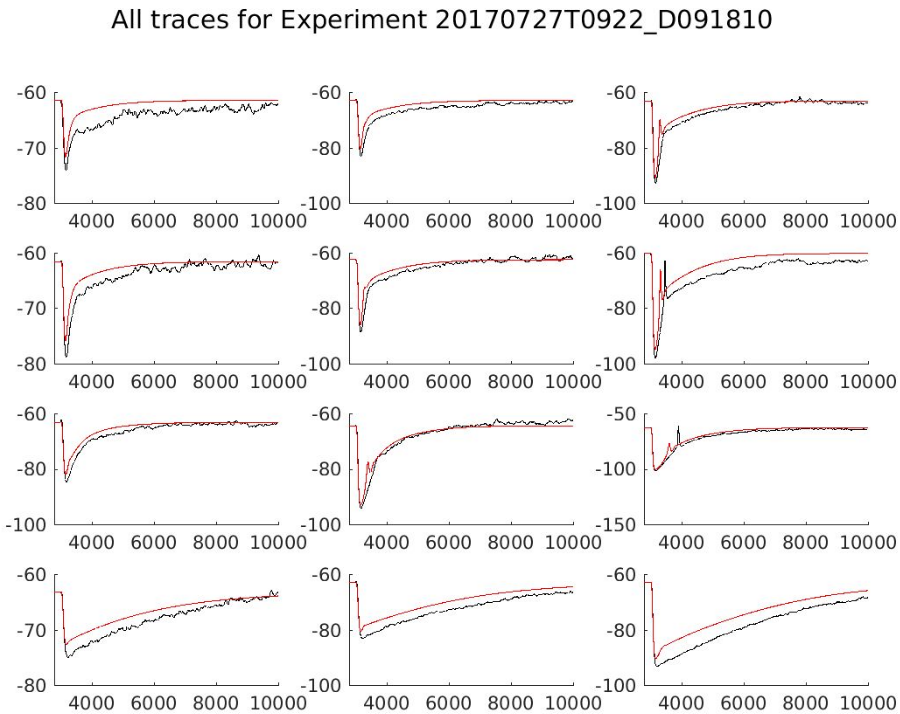


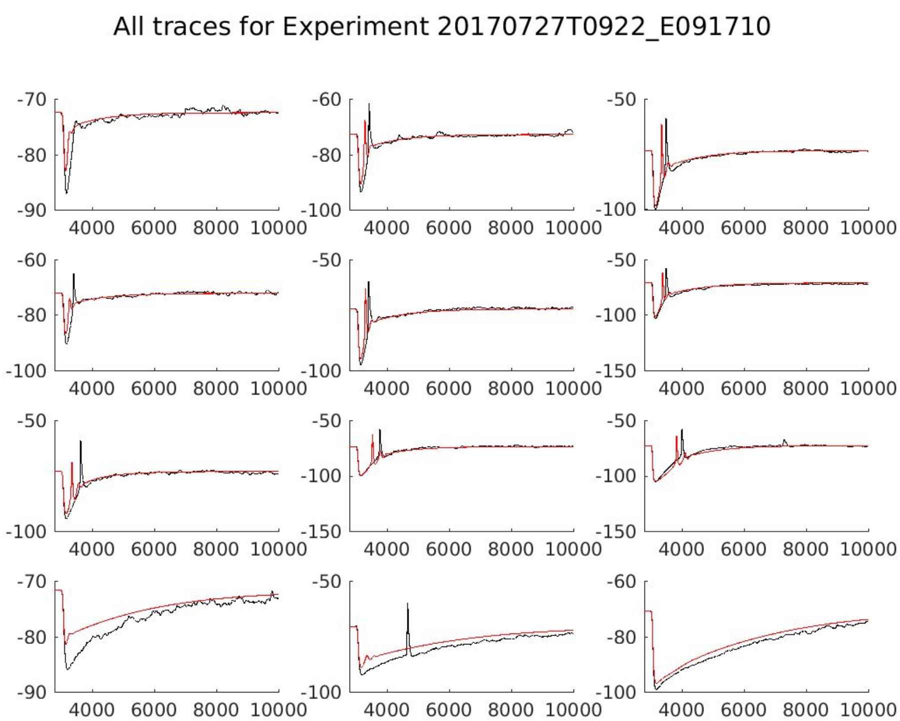
All traces for Experiment 20170727T0922_C092710



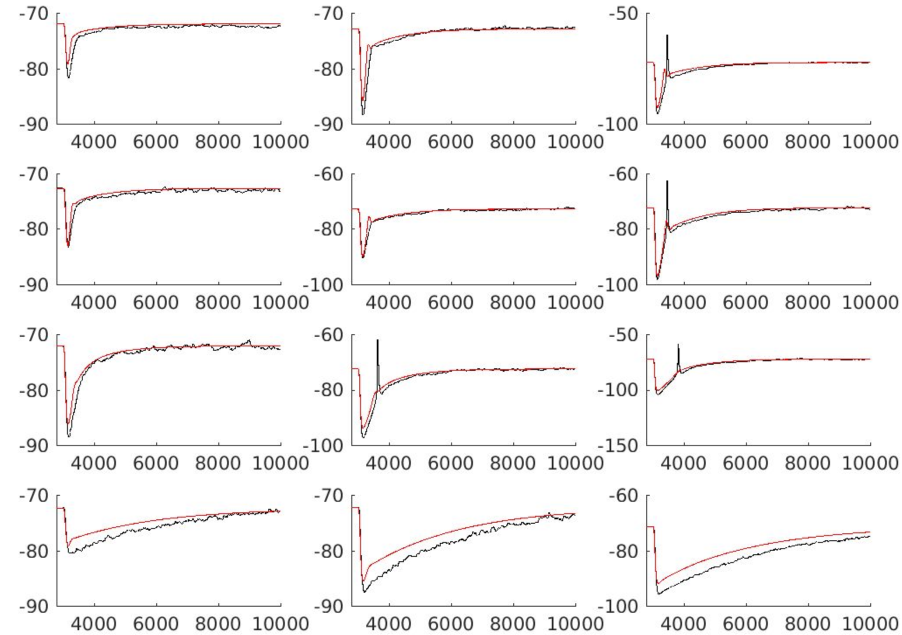
All traces for Experiment 20170727T0922_D091710



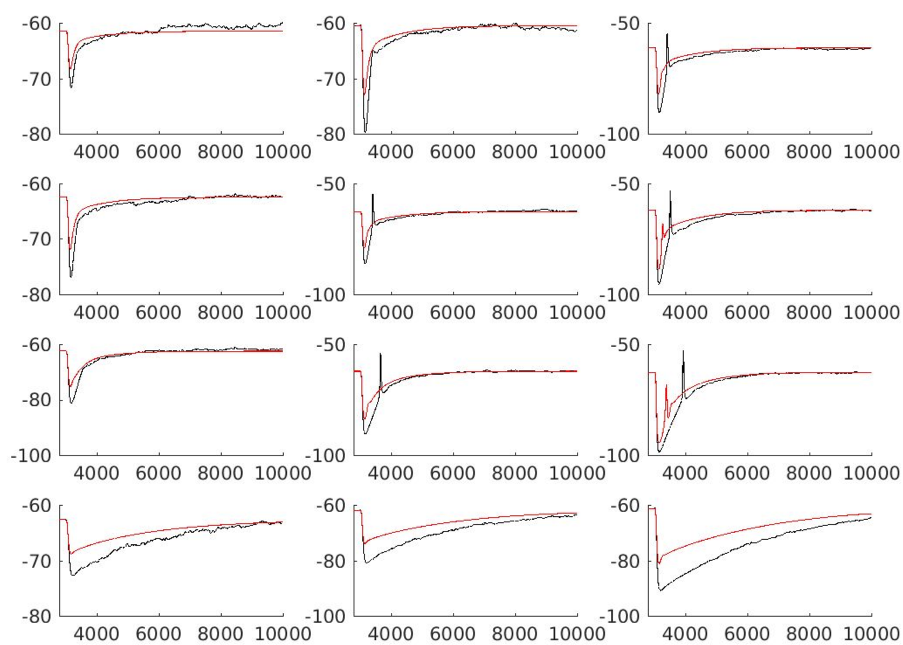

All traces for Experiment 20170727T0922_D091810
-60
-70
-80
-100
-50
-150
4000 6000 8000 10000


All traces for Experiment 20170727T0922_E091710
-50
-60
-70
-80
-90
-100
-150
4000 6000 8000 10000

All traces for Experiment 20170727T0922_E091810

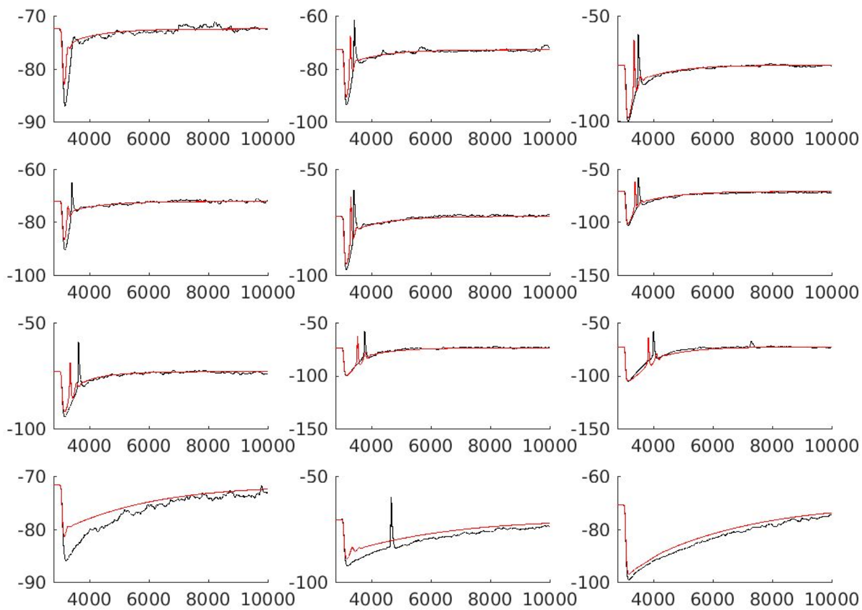


All traces for Experiment 20170727T0922_F091810



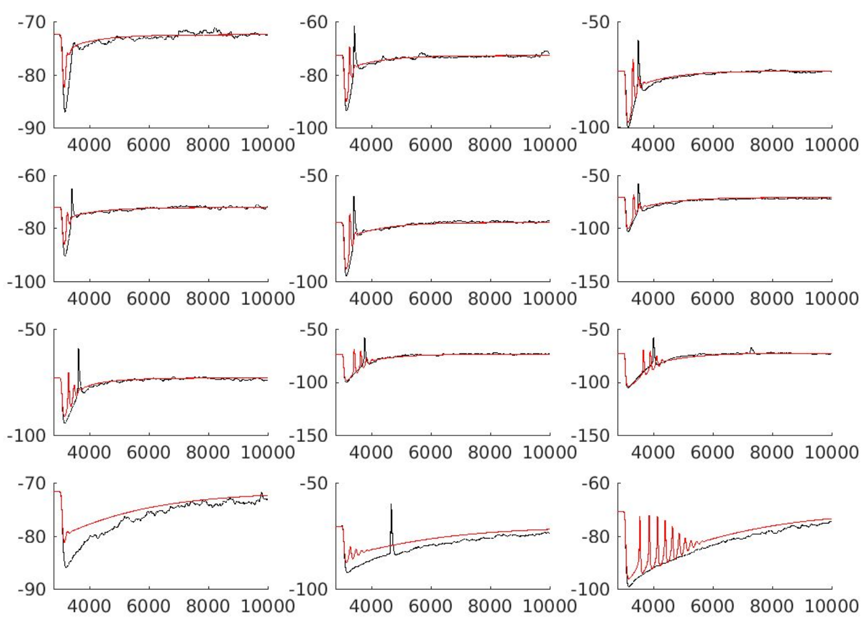
- **singleneuronfitting7_manual**: After reorganizing mod files and changing **ek** to **-97 mV**:
  - Before:

All traces for Experiment 20170727T0922_E091710



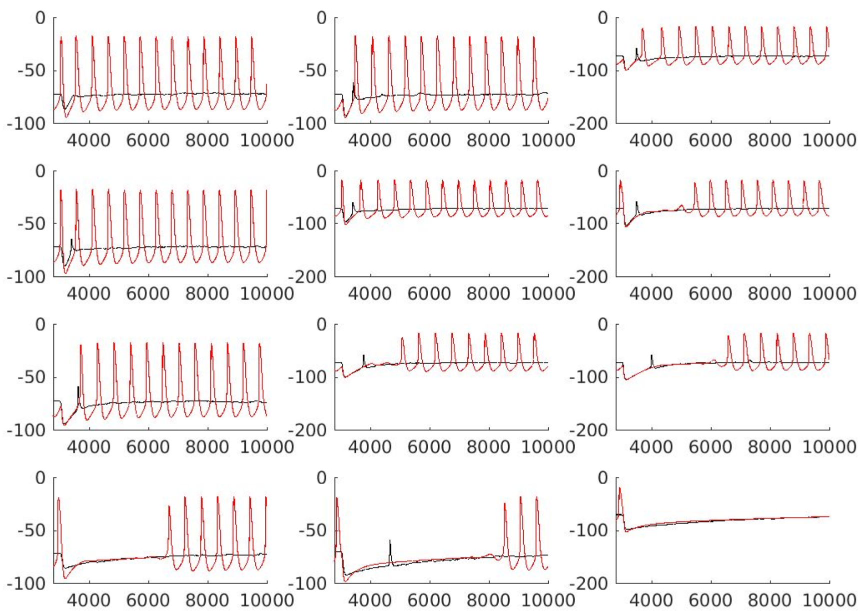
  - After:

All traces for Experiment 20170728T1317_E091710

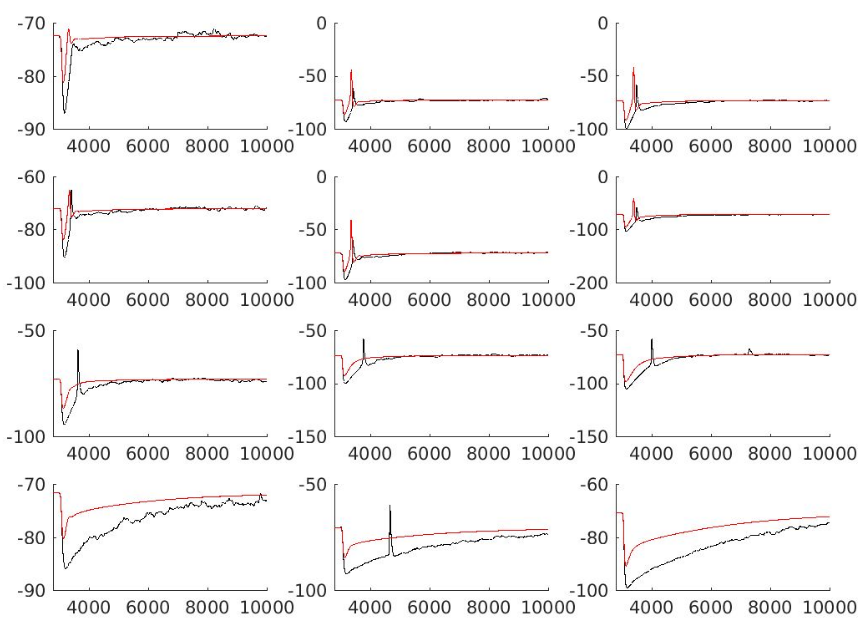


- **singleneuronfitting8**: Re-optimized with just these 12 traces. Started with default parameters from the Destexhe model (**Destexhe default**). Fitted **conductances of all channels**. Normalized **sweep error** by **holding potential**:

All traces for Experiment 20170728T1839_E091710_bef

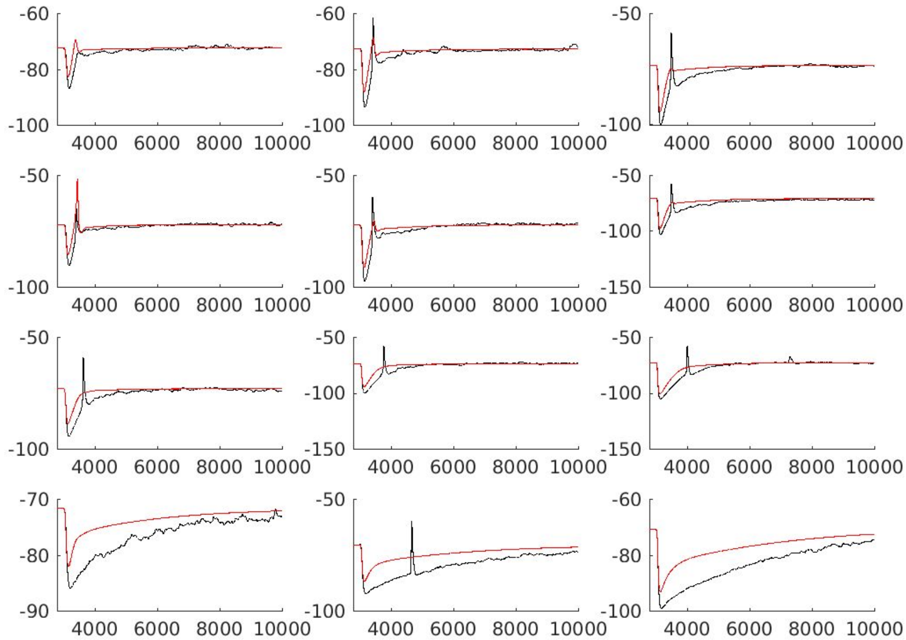


All traces for Experiment 20170728T1839_E091710_aft



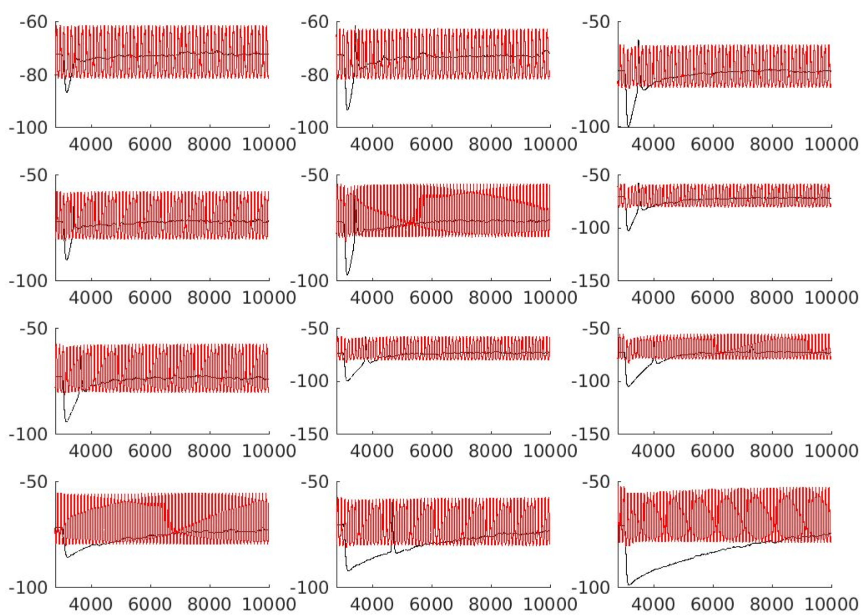
- Normalized **sweep error** by **maximum noise**:

All traces for Experiment 20170728T1925_E091710_aft



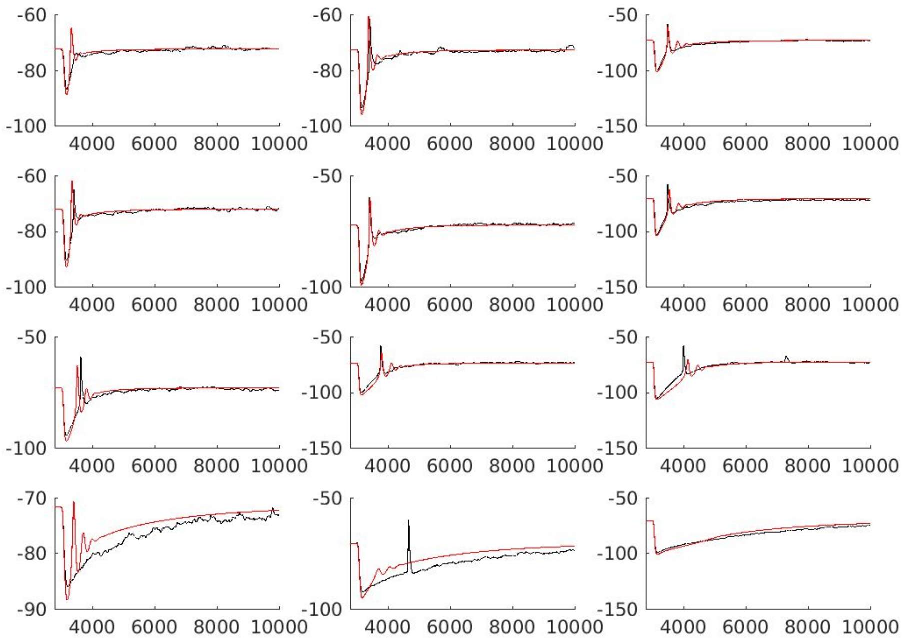
- Normalized all errors to **initial error.** Compared across initializing to **Destexhe default**, **Christine's best values** and **best values from singleneuronfitting5**.

All traces for Experiment 20170728T2233_E091710_aft

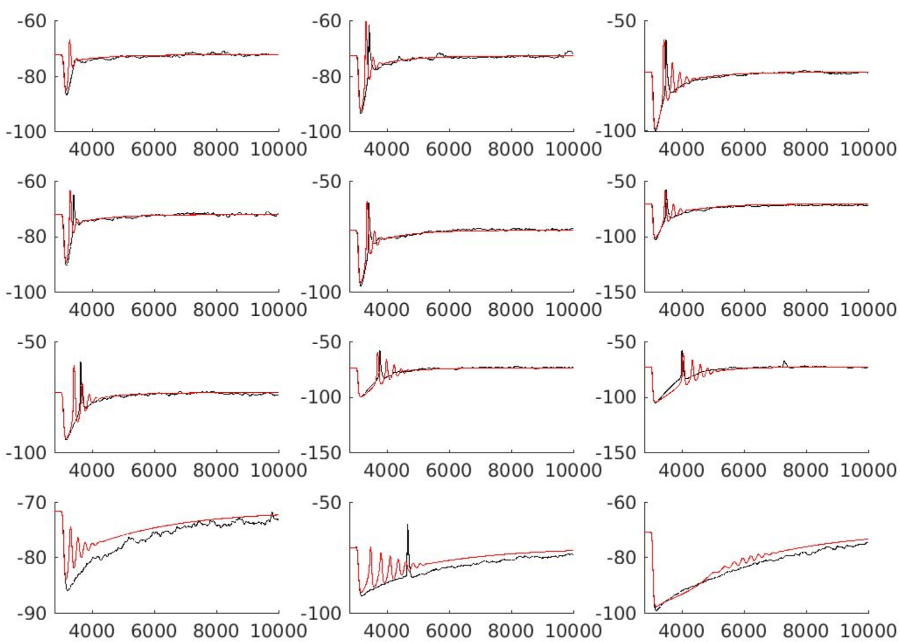


- Initialized to **Christine's best values**

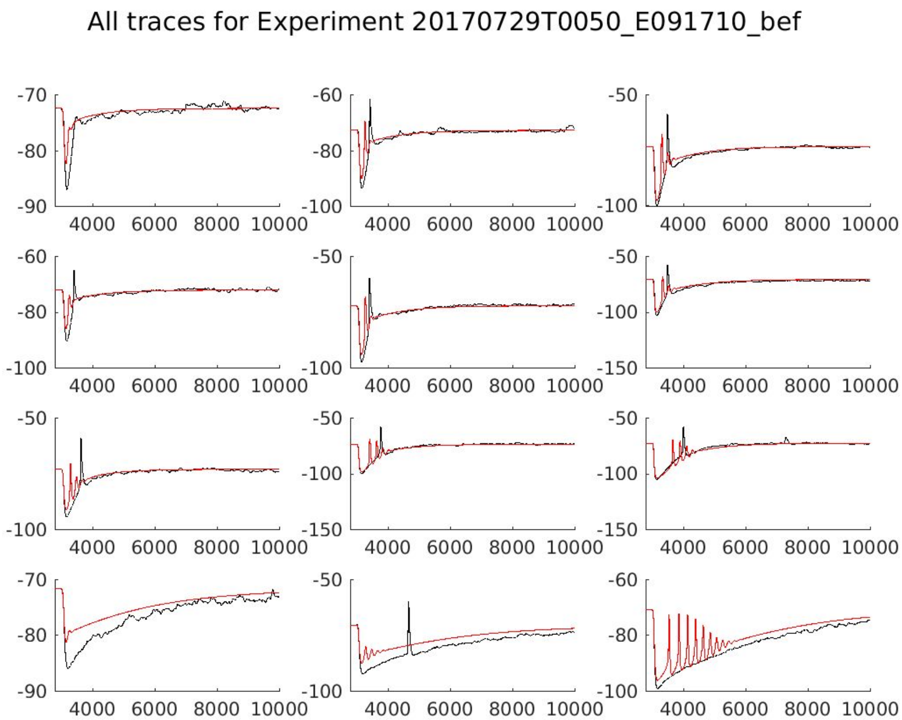
All traces for Experiment 20170729T0016_E091710_bef

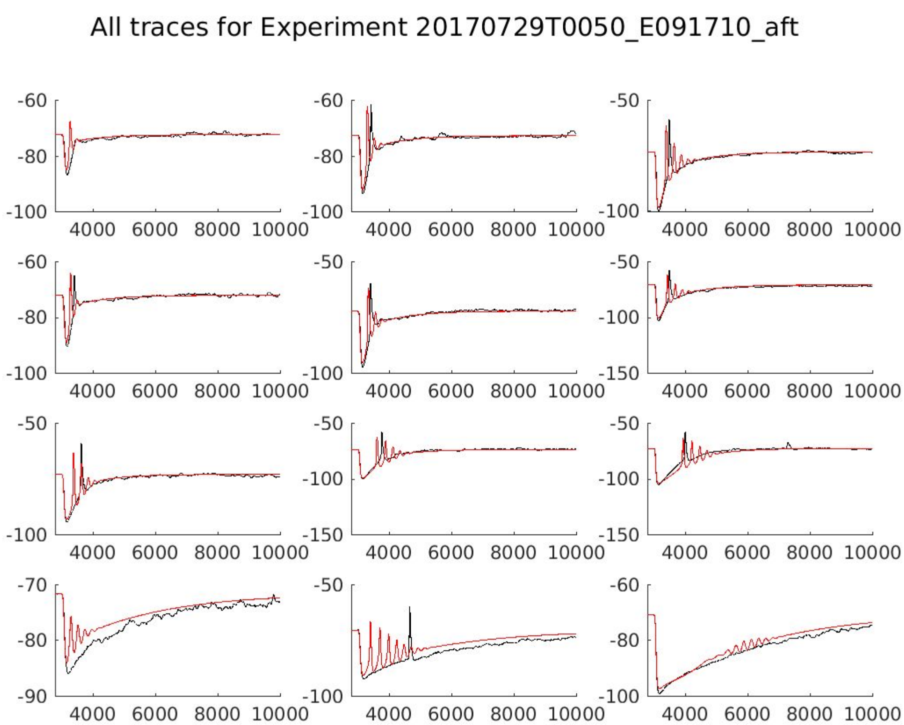


All traces for Experiment 20170729T0016_E091710_aft



- Initialized to **best values from singleneuronfitting5**





- Errors/Parameters comparison:

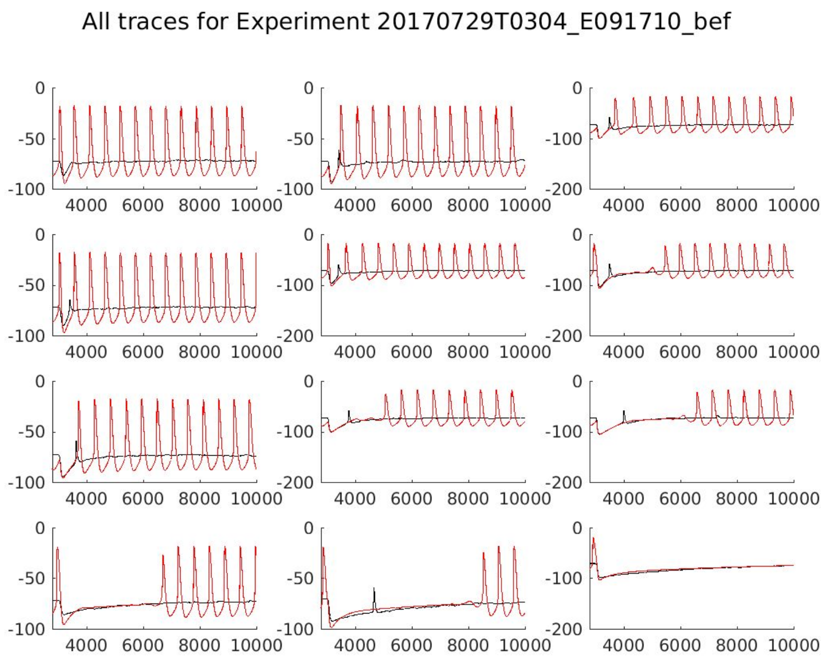
	Initialize to **Destexhe - before**	Initialize to **Destexhe - after**	Initialize to **Christine - before**	Initialize to **Christine - after**	Initialize to **singleneuronfitting5 - before**	Initialize to **singleneuronfitting5 - after**
Total error	1	0.4822	1	0.7665	1	0.8293
Sweep error	1	0.6341	1	1.341	1	1.118
LTS amp error	1	0.7521	1	0.5806	1	0.8741
LTS time error	1	0.4572	1	0.7618	1	0.898
LTS slope error	1	0.1613	1	0.6697	1	0.5716
Average LTS error	1	0.4569	1	0.6707	1	0.7813
diamSoma	38.42	**38.96**	38.42	**38.79**	36.24	**37.97**
LDend1	12.49	**58.45**	12.49	**65.9**	120	**106.3**
diamDend1ToSoma	0.2676	**0.1**	0.2676	**0.1136**	0.1	**0.1**
LDend2	84.67	**113.2**	84.67	**104.4**	117.2	**102.6**
diamDend2To1	0.8268	**1**	0.8268	**1**	0.7088	**0.8071**
distDendPercent	50	**50**	68.6	**68.6**	50	**50**
cm	0.88	**0.88**	0.789	**0.789**	0.88	**0.88**
Ra	173	173	173	173	173	173
corrD	7.954	7.954	7.954	7.954	7.954	7.954
gpas	1.00E-05	**3.04E-05**	8.21E-06	**2.82E-05**	3.26E-05	**2.93E-05**
epas	-80	**-72.24**	-80.4	**-77.86**	-70.19	**-90**

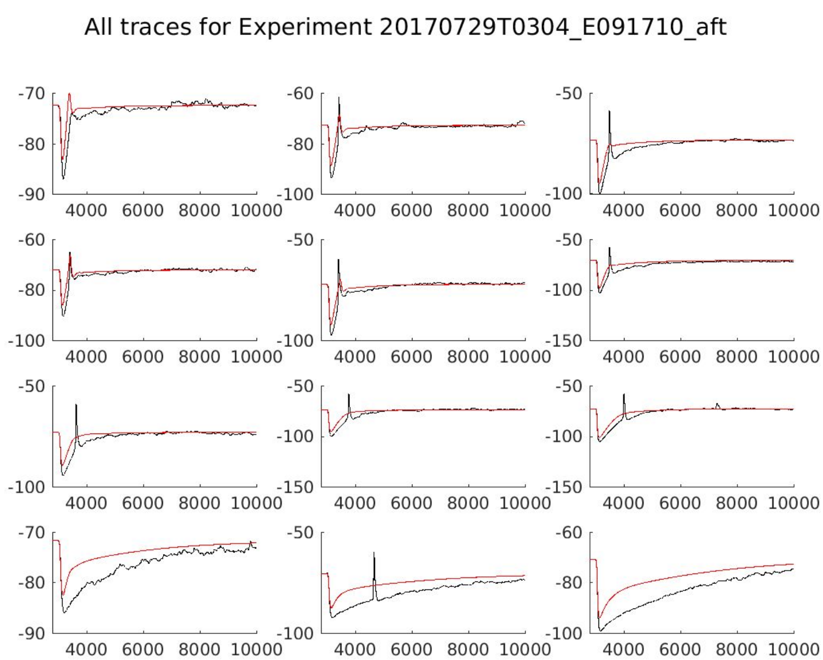
pcabarITSoma	0.0002	**4.29E-05**	5.00E-06	**1.40E-05**	2.82E-07	**7.32E-08**
pcabarITDend0	0.0002	**2.42E-05**	5.00E-06	**2.03E-06**	2.82E-07	**1.40E-07**
pcabarITDend1	0.0002	**5.65E-05**	8.91E-06	**1.52E-05**	1.84E-06	**6.17E-07**
pcabarITDend2	0.0002	**0.01**	3.98E-06	**9.70E-06**	5.66E-05	**4.98E-05**
shiftmIT	2	2	-13.8	-13.8	-13.8	-13.8
shifthIT	0	0	-4.8	-4.8	-4.8	-4.8
slopemIT	1	1	1.4	1.4	1.4	1.4
slopehIT	1	1	1	1	1	1
ghbarSoma	2.20E-05	**0.01**	1.10E-05	**2.60E-06**	3.02E-07	**9.04E-07**
ghbarDend0	2.20E-05	**0.00041**	1.10E-05	**1.40E-06**	3.02E-07	**4.72E-06**
ghbarDend1	2.20E-05	**0.000156**	1.10E-05	**2.47E-06**	2.81E-06	**1.05E-06**
ghbarDend2	2.20E-05	**7.76E-05**	1.10E-05	**1.00E-08**	1.02E-06	**1.53E-06**
eh	-43	-43	-43	-43	-43	-43
shiftmIh	0	**0**	11.4	**11.4**	11.4	**11.4**
gkbarIKirSoma	2.00E-05	**3.51E-08**	2.00E-05	**2.43E-05**	2.00E-05	**6.13E-05**
gkbarIKirDend0	2.00E-05	**2.68E-05**	2.00E-05	**1.17E-05**	2.00E-05	**3.11E-05**
gkbarIKirDend1	2.00E-05	**8.03E-06**	2.00E-05	**9.10E-05**	2.00E-05	**4.50E-05**
gkbarIKirDend2	2.00E-05	**7.67E-05**	2.00E-05	**1.33E-05**	2.00E-05	**7.63E-06**
gkbarIASoma	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.000674**

gkbarIADend0	0.0055	**0.01**	0.0055	**0.003254**	0.0055	**0.01**
gkbarIADend1	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.001752**
gkbarIADend2	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.005429**
gnabarINaPSoma	5.50E-06	**1.80E-06**	5.50E-06	**2.65E-06**	5.50E-06	**7.37E-06**
gnabarINaPDend0	5.50E-06	**1.65E-06**	5.50E-06	**6.11E-06**	5.50E-06	**1.00E-08**
gnabarINaPDend1	5.50E-06	**8.62E-05**	5.50E-06	**5.72E-06**	5.50E-06	**4.94E-05**
gnabarINaPDend2	5.50E-06	**3.53E-05**	5.50E-06	**2.53E-05**	5.50E-06	**9.13E-07**

- Problem:
    - If error is relative, there is no way to **compare across optimization runs**
    - If error is absolute, must find a way to make the errors dimensionless so that different types of errors could be **weighted and combined meaningfully**.
- Solution: normalizing by some sort of **uncertainty of measurement**
    - This also has the benefit of *weighting noisier traces less*.

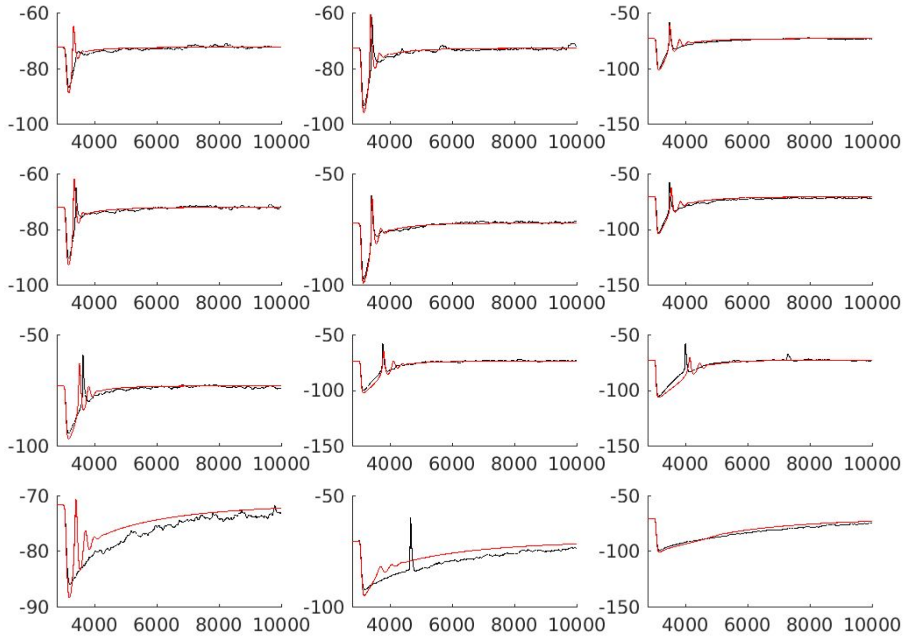
- **singleneuronfitting9**: Made errors **absolute** (do not normalize to initial error). Normalized **LTS errors** to its own **uncertainty** (LTS **amplitude** is normalized by **maximum noise**, LTS **time** is normalized by **peakwidth**, LTS **slope** is normalized by **slope*(2*maximum noise/peakprom + 2*ioffset/peakwidth)**. Changed **LTS existence error** from 1 to **10**. Changed error ratios to Sweep:LTSamp:LTStime:LTSslope = **1:1:1:1**
    - Initialized to **Destexhe default**



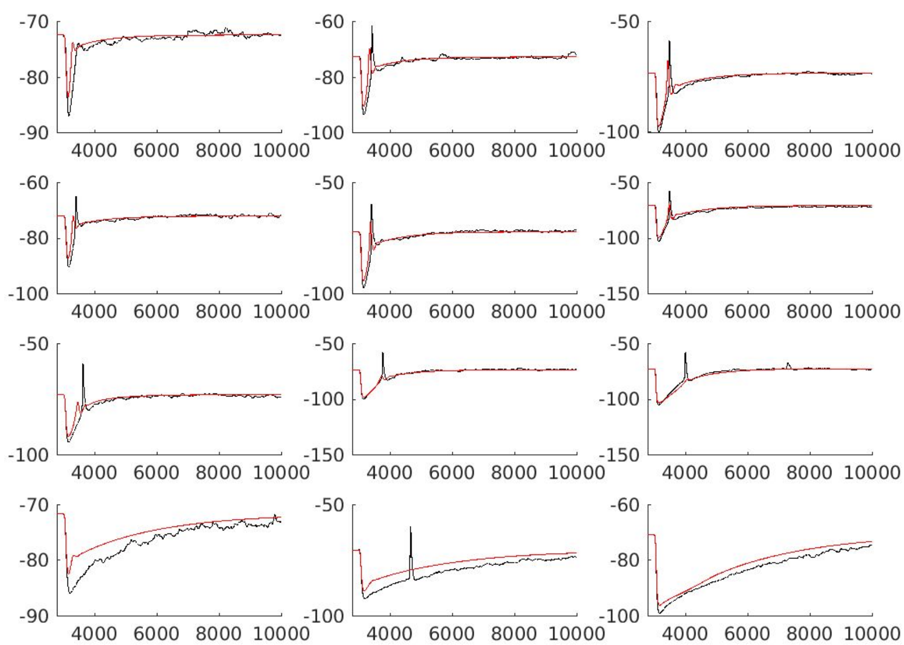


- Initialized to **Christine's best values**

All traces for Experiment 20170729T1838_E091710_bef

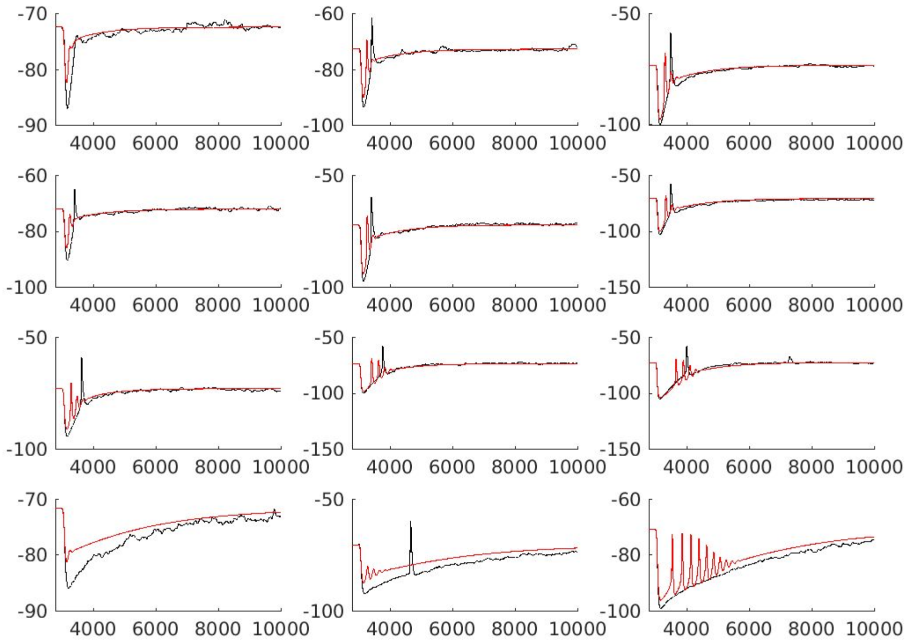


All traces for Experiment 20170729T1838_E091710_aft

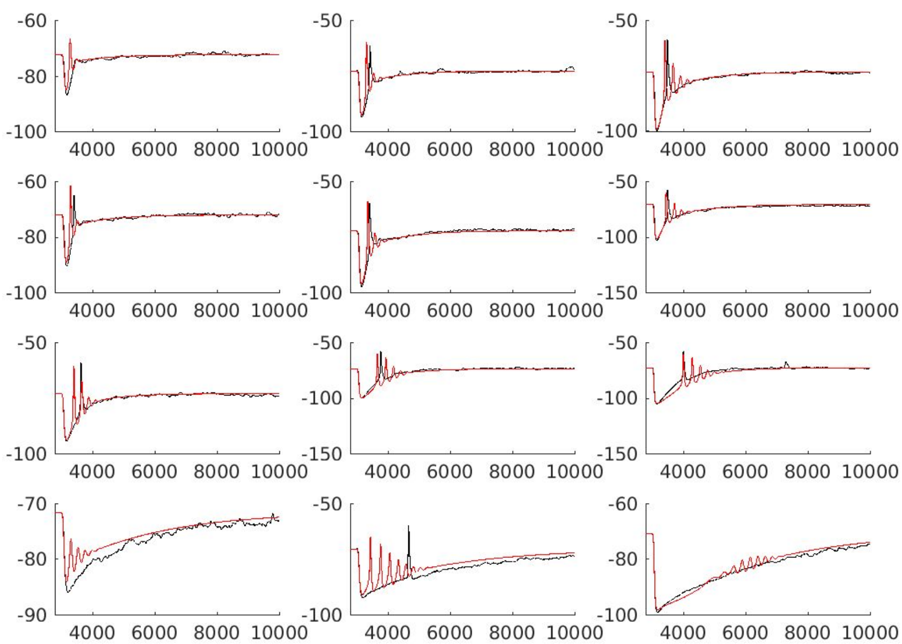


- Initialized to **best values from singleneuronfitting5**

All traces for Experiment 20170729T1910_E091710_bef



All traces for Experiment 20170729T1910_E091710_aft



- Errors/Parameters comparison:

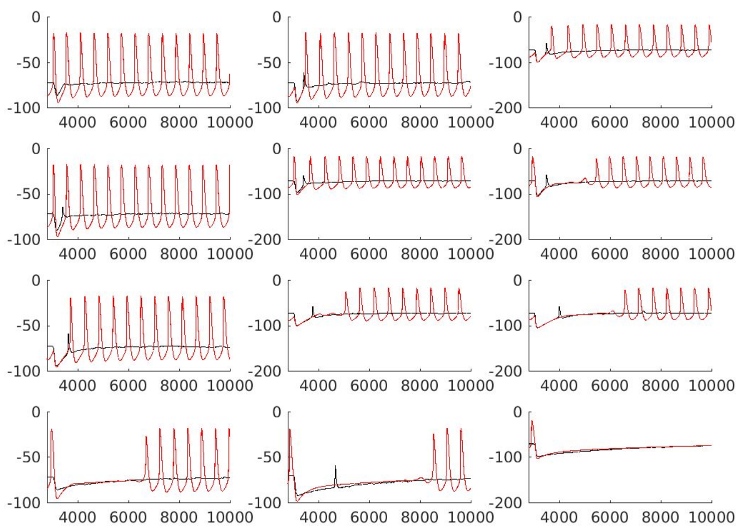
	Initialize to **Destexhe - before**	Initialize to **Destexhe - after**	Initialize to **Christine - before**	Initialize to **Christine - after**	Initialize to **singleneuronfitting5 - before**	Initialize to **singleneuronfitting5 - after**
Total error	23.18	**6.984**	7.624	**5.736**	7.288	**5.128**
Sweep error	14.46	**2.509**	1.758	**1.791**	2.133	**2.324**
LTS amp error	27.06	**8.971**	6.221	**8.389**	9.988	**3.747**
LTS time error	33.39	**8.179**	5.394	**5.986**	9.471	**8.962**
LTS slope error	17.82	**8.276**	17.12	**6.777**	7.559	**5.479**
Average LTS error	26.09	**8.476**	9.58	**7.051**	9.006	**6.063**
diamSoma	38.42	**38.96**	38.42	**38.79**	36.24	**37.97**
LDend1	12.49	**58.45**	12.49	**65.9**	120	**106.3**
diamDend1ToSoma	0.2676	**0.1**	0.2676	**0.1136**	0.1	**0.1**
LDend2	84.67	**113.2**	84.67	**104.4**	117.2	**102.6**
diamDend2To1	0.8268	**1**	0.8268	**1**	0.7088	**0.8071**
distDendPercent	50	**50**	68.6	**68.6**	50	**50**
cm	0.88	**0.88**	0.789	**0.789**	0.88	**0.88**
Ra	173	173	173	173	173	173
corrD	7.954	7.954	7.954	7.954	7.954	7.954
gpas	1.00E-05	**3.04E-05**	8.21E-06	**2.82E-05**	3.26E-05	**2.93E-05**
epas	-80	**-72.24**	-80.4	**-77.86**	-70.19	**-90**
pcabarITS	0.0002	**1.00E-08**	5.00E-06	**2.99E-06**	2.82E-07	**2.43E-07**

oma						
pcabarITDend0	0.0002	**0.000116**	5.00E-06	**5.91E-06**	2.82E-07	**3.00E-07**
pcabarITDend1	0.0002	**0.000507**	8.91E-06	**9.83E-06**	1.84E-06	**2.70E-06**
pcabarITDend2	0.0002	**5.70E-05**	3.98E-06	**5.92E-06**	5.66E-05	**4.56E-05**
shiftmIT	2	2	-13.8	-13.8	-13.8	-13.8
shifthIT	0	0	-4.8	-4.8	-4.8	-4.8
slopemIT	1	1	1.4	1.4	1.4	1.4
slopehIT	1	1	1	1	1	1
ghbarSoma	2.20E-05	**8.93E-05**	1.10E-05	**4.14E-06**	3.02E-07	**2.72E-07**
ghbarDend0	2.20E-05	**2.56E-05**	1.10E-05	**4.44E-06**	3.02E-07	**1.00E-08**
ghbarDend1	2.20E-05	**3.46E-05**	1.10E-05	**5.64E-06**	2.81E-06	**3.23E-06**
ghbarDend2	2.20E-05	**2.93E-05**	1.10E-05	**1.00E-08**	1.02E-06	**9.17E-07**
eh	-43	-43	-43	-43	-43	-43
shiftmIh	0	**0**	11.4	**11.4**	11.4	**11.4**
gkbarIKirSoma	2.00E-05	**1.86E-05**	2.00E-05	**1.42E-05**	2.00E-05	**1.61E-05**
gkbarIKirDend0	2.00E-05	**1.96E-05**	2.00E-05	**2.11E-05**	2.00E-05	**2.42E-05**
gkbarIKirDend1	2.00E-05	**2.92E-05**	2.00E-05	**8.79E-05**	2.00E-05	**1.28E-05**
gkbarIKirDend2	2.00E-05	**2.95E-05**	2.00E-05	**2.35E-05**	2.00E-05	**1.55E-05**
gkbarIASoma	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.003194**

gkbarIADend0	0.0055	**0.01**	0.0055	**0.001619**	0.0055	**0.004427**
gkbarIADend1	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.002416**
gkbarIADend2	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.001537**
gnabarINaPSoma	5.50E-06	**7.81E-06**	5.50E-06	**5.08E-06**	5.50E-06	**9.13E-06**
gnabarINaPDend0	5.50E-06	**3.52E-06**	5.50E-06	**7.50E-06**	5.50E-06	**4.70E-06**
gnabarINaPDend1	5.50E-06	**2.98E-06**	5.50E-06	**5.84E-06**	5.50E-06	**7.88E-06**
gnabarINaPDend2	5.50E-06	**7.31E-06**	5.50E-06	**7.70E-06**	5.50E-06	**1.65E-05**

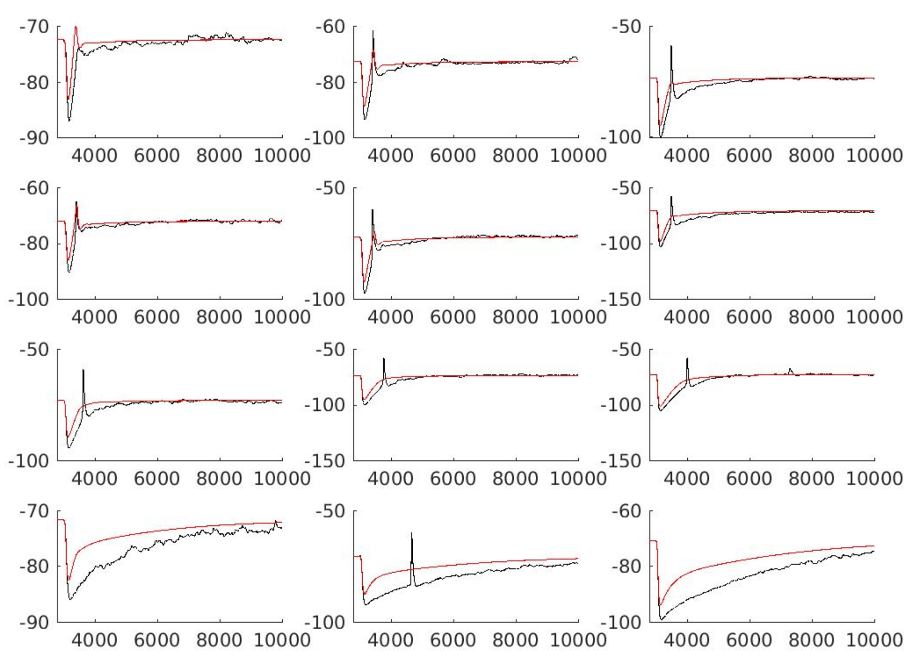
- Ran optimization **3 times consecutively**, each time using the previous best result as initial value.
  - Initialized to **Destexhe default**.

All traces for Experiment 20170729T0304_E091710_bef



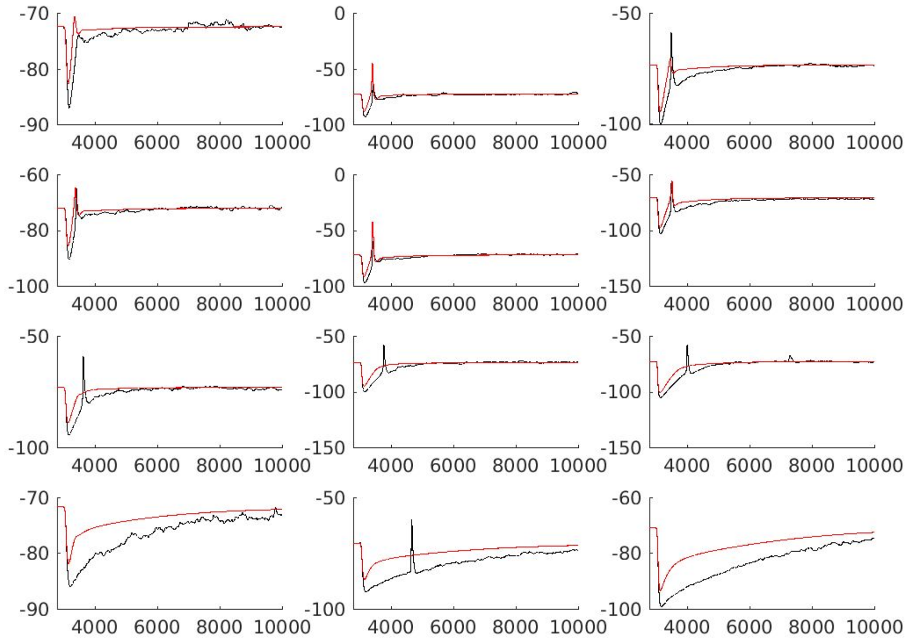
  - Iteration #1:

All traces for Experiment 20170729T0304_E091710_aft



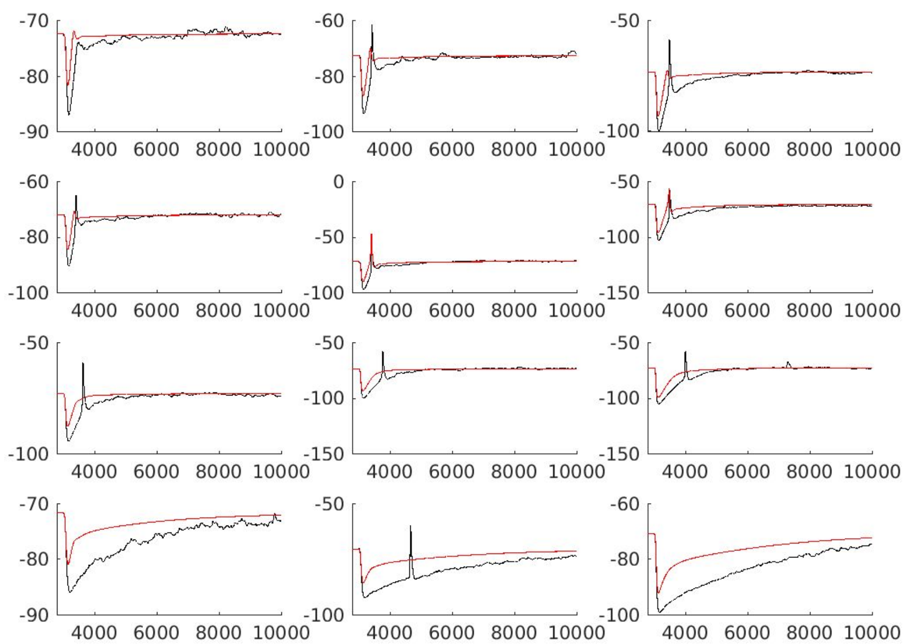
- Iteration #2:

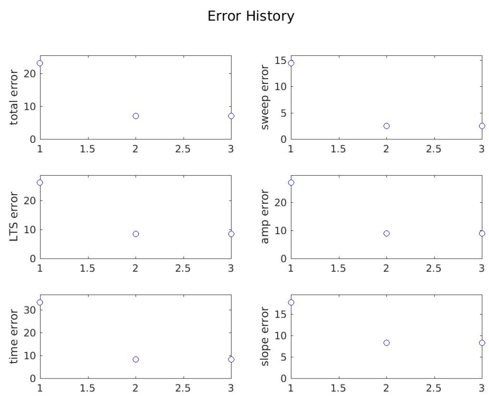
All traces for Experiment 20170729T0947_E091710_aft

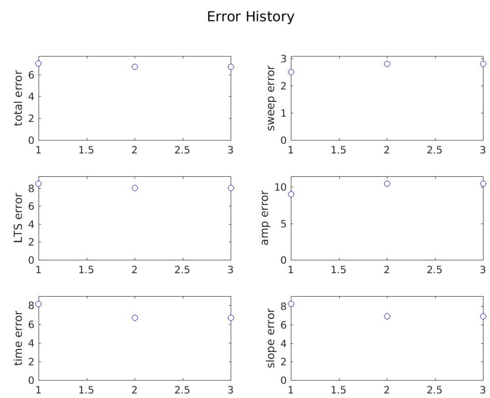


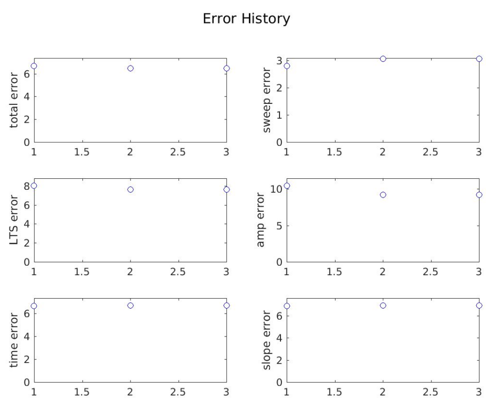
- Iteration #3:

All traces for Experiment 20170729T1044_E091710_aft









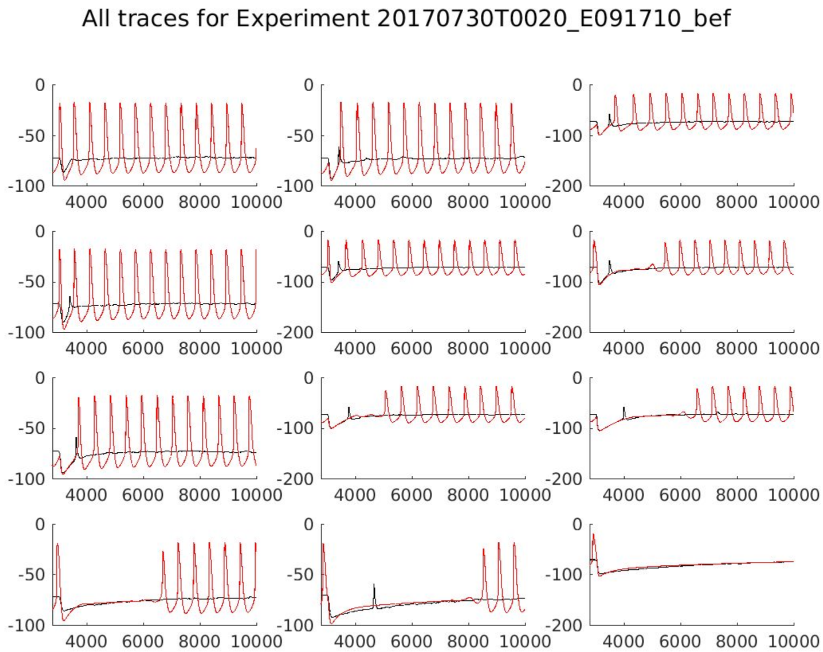
- Errors/Parameters comparison:

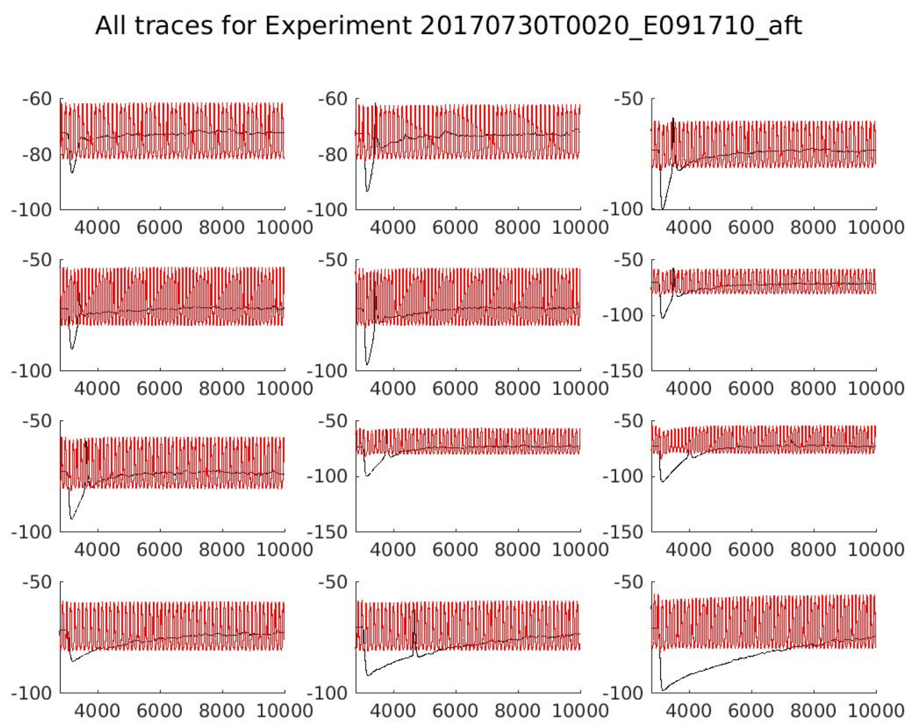
	Initialize to **Destexhe**	**Iteration 1**	**Iteration 2**	**Iteration 3**
Total error	23.18	**6.984**	**6.698**	**6.469**
Sweep error	14.46	**2.509**	**2.813**	**3.071**
LTS amp error	27.06	**8.971**	**10.41**	**9.17**
LTS time error	33.39	**8.179**	**6.674**	**6.704**
LTS slope error	17.82	**8.276**	**6.896**	**6.931**
Average LTS error	26.09	**8.476**	**7.993**	**7.602**
diamSoma	38.42	**38.96**	**36.61**	**37.13**
LDend1	12.49	**58.45**	**87.69**	**86.94**
diamDend1ToS	0.2676	**0.1**	**0.1**	**0.1**

oma				
LDend2	84.67	**113.2**	**109**	**111.1**
diamDend2To1	0.8268	**1**	**1**	**0.971**
distDendPercent	50	**50**	**50**	**50**
cm	0.88	0.88	0.88	0.88
Ra	173	173	173	173
corrD	7.954	7.954	7.954	7.954
gpas	1.00E-05	**3.04E-05**	**2.97E-05**	**2.98E-05**
epas	-80	**-72.24**	**-50**	**-50**
pcabarITSoma	0.0002	**1.00E-08**	**7.94E-08**	**7.76E-08**
pcabarITDend0	0.0002	**0.000116**	**3.94E-05**	**2.49E-05**
pcabarITDend1	0.0002	**0.000507**	**0.000657**	**0.00066**
pcabarITDend2	0.0002	**5.70E-05**	**1.00E-08**	**1.00E-08**
shiftmIT	2	2	2	2
shifthIT	0	0	0	0
slopemIT	1	1	1	1
slopehIT	1	1	1	1
ghbarSoma	2.20E-05	**8.93E-05**	**8.02E-05**	**8.62E-05**
ghbarDend0	2.20E-05	**2.56E-05**	**6.58E-05**	**7.78E-05**
ghbarDend1	2.20E-05	**3.46E-05**	**2.82E-05**	**4.35E-05**
ghbarDend2	2.20E-05	**2.93E-05**	**5.65E-05**	**8.71E-05**
eh	-43	-43	-43	-43
shiftmIh	0	0	0	0
gkbarIKirSoma	2.00E-05	**1.86E-05**	**3.15E-05**	**6.13E-05**
gkbarIKirDend0	2.00E-05	**1.96E-05**	**2.02E-05**	**3.70E-05**

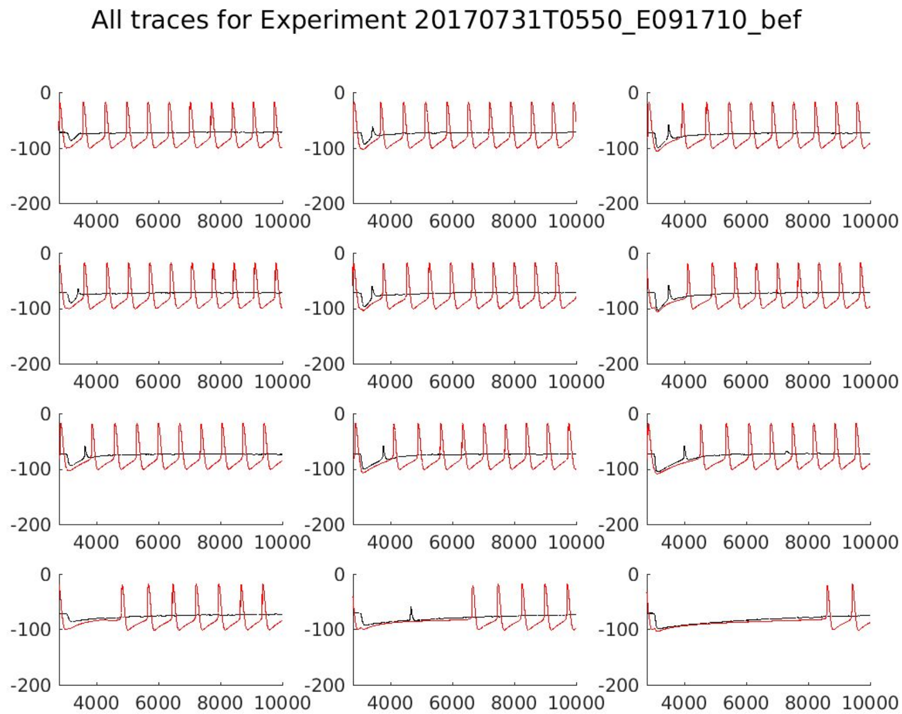
gkbarIKirDend1	2.00E-05	**2.92E-05**	**3.08E-05**	**4.18E-05**
gkbarIKirDend2	2.00E-05	**2.95E-05**	**3.24E-05**	**4.47E-05**
gkbarIASoma	0.0055	**0.01**	**0.01**	**0.008243**
gkbarIADend0	0.0055	**0.01**	**0.01**	**0.01**
gkbarIADend1	0.0055	**0.01**	**0.01**	**0.008574**
gkbarIADend2	0.0055	**0.01**	**0.01**	**0.009322**
gnabarINaPSoma	5.50E-06	**7.81E-06**	**1.01E-05**	**1.00E-08**
gnabarINaPDend0	5.50E-06	**3.52E-06**	**3.09E-06**	**1.82E-06**
gnabarINaPDend1	5.50E-06	**2.98E-06**	**4.43E-06**	**3.80E-06**
gnabarINaPDend2	5.50E-06	**7.31E-06**	**9.97E-06**	**4.82E-06**

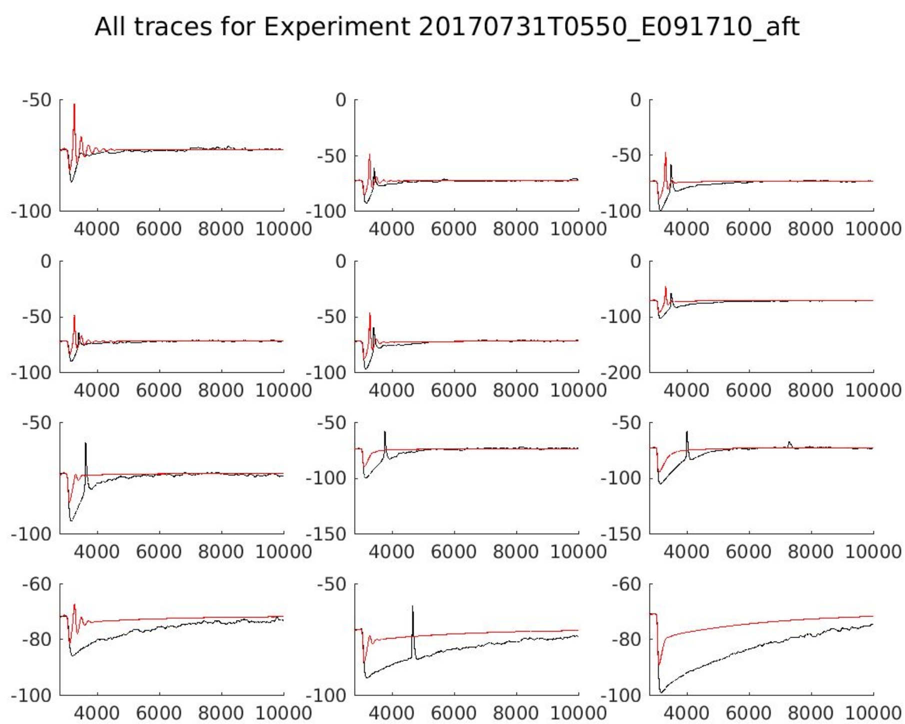
- Increased maximum number of iterations to **400**. Increased maximum number of function evaluations to **2000**. Changed **LTS existence error** from 10 to **20**. Changed error ratios to Sweep:LTSamp:LTStime:LTSslope = **2:1:2:3**
    - Initialized to **Destexhe default**

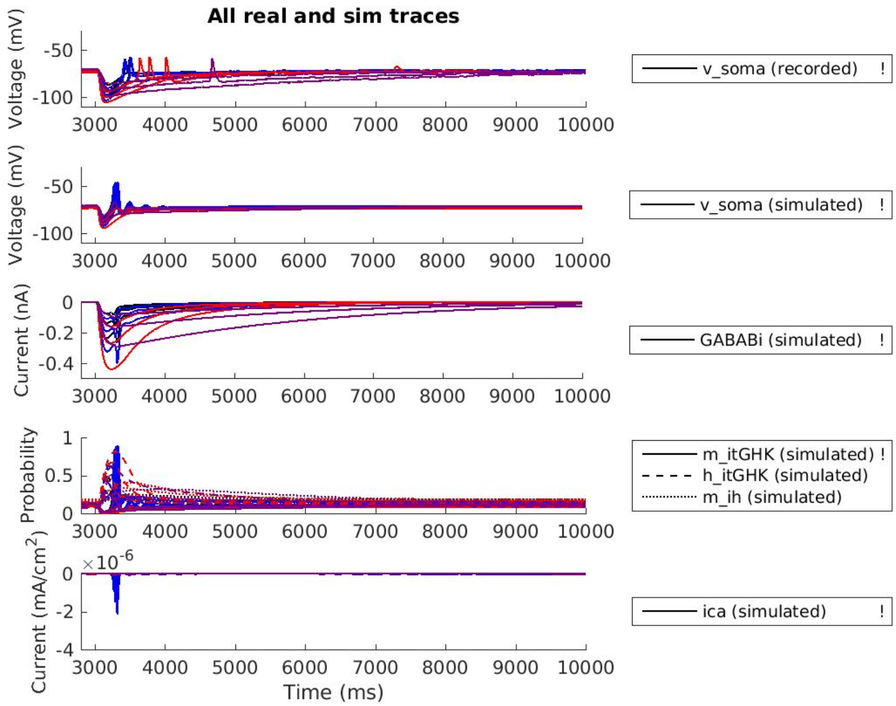


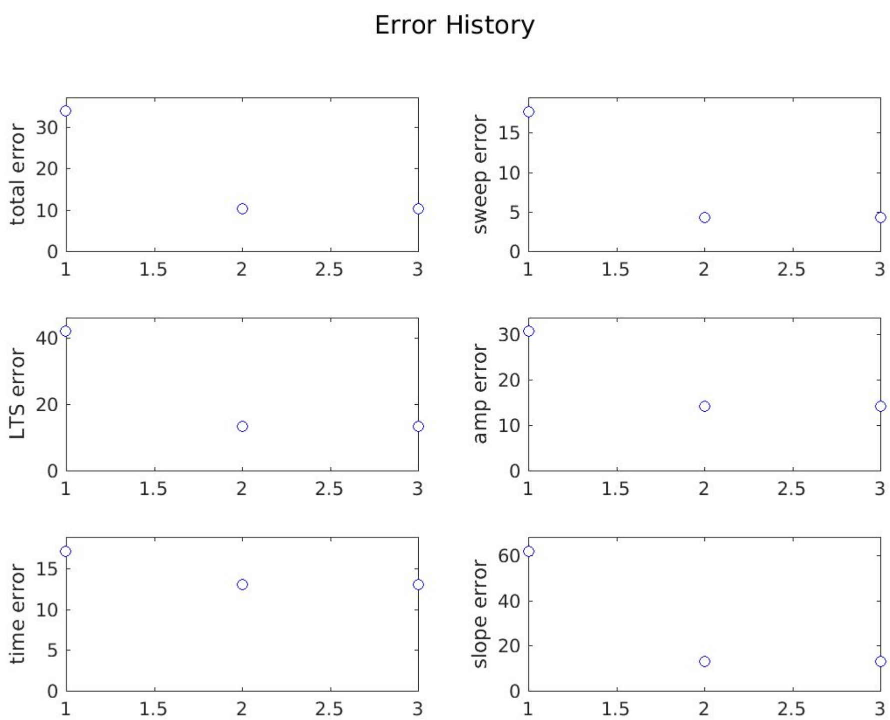


- Changed error ratios to Sweep:LTSamp:LTStime:LTSslope = **3:1:2:3**
  - Initialized to **Destexhe default**

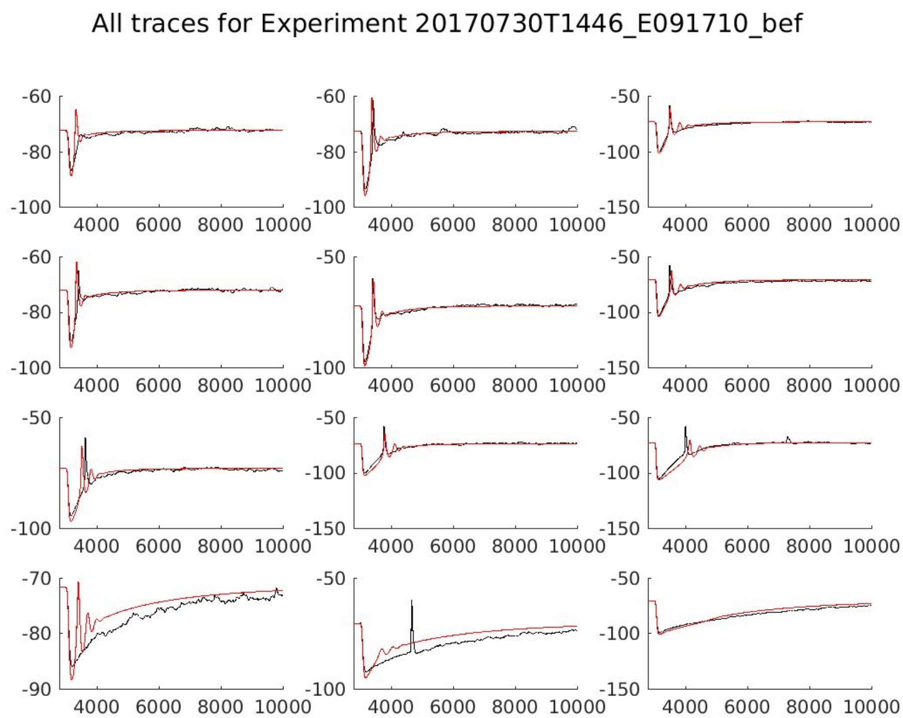


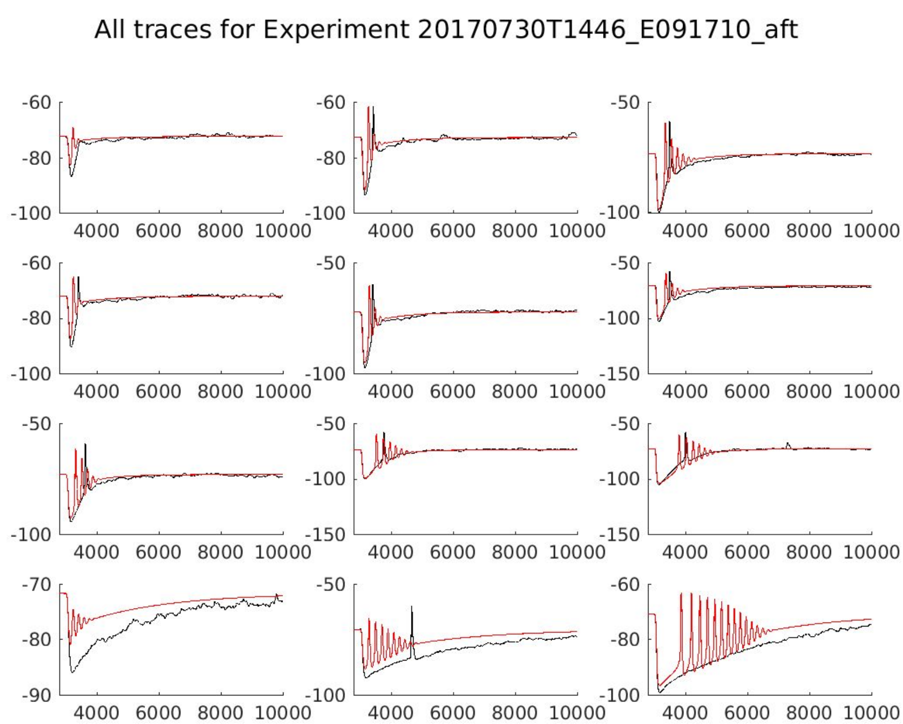


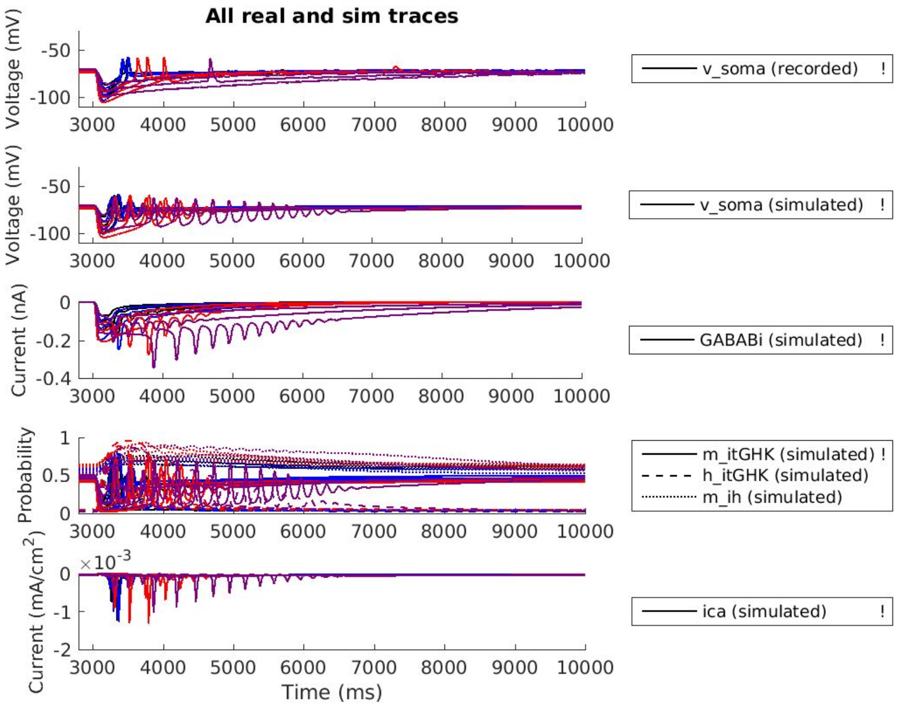

All real and sim traces
Voltage (mV)
v_soma (recorded) !
v_soma (simulated) !
Current (nA)
GABABi (simulated) !
Probability
m_itGHK (simulated) !
h_itGHK (simulated)
m_ih (simulated)
Current (mA/cm2)
×10-6
ica (simulated) !
Time (ms)

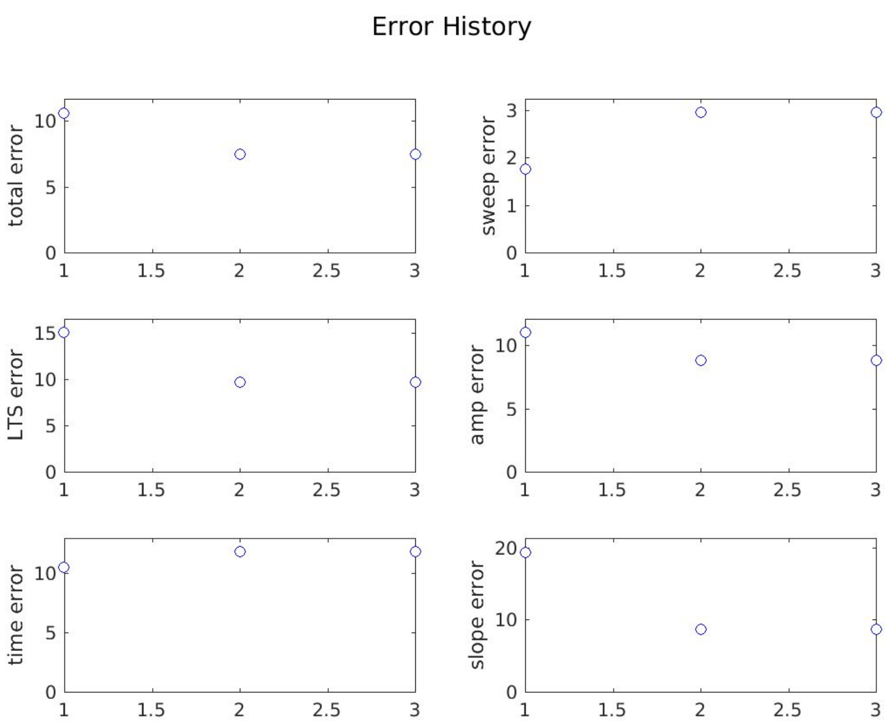

Error History
total error
sweep error
LTS error
amp error
time error
slope error

- Initialized to **Christine's best values**



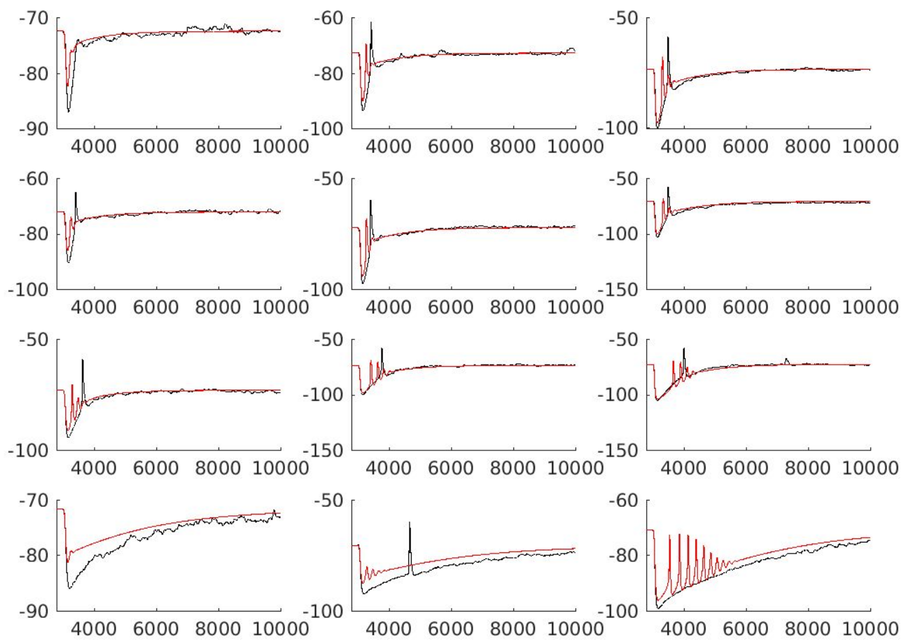



All real and sim traces
Voltage (mV)
-50
-100
3000 4000 5000 6000 7000 8000 9000 10000
v_soma (recorded) !
v_soma (simulated) !
Current (nA)
0
-0.2
-0.4
GABABi (simulated) !
Probability
1
0.5
0
m_itGHK (simulated) !
h_itGHK (simulated)
m_ih (simulated)
Current (mA/cm2)
×10-3
-1
-2
ica (simulated) !
Time (ms)

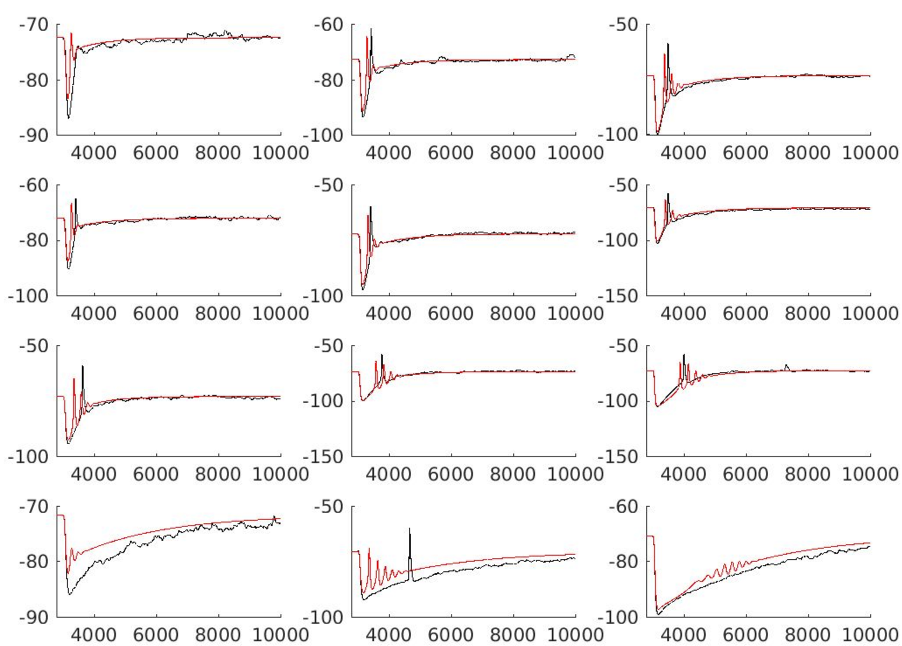

Error History
total error
sweep error
LTS error
amp error
time error
slope error
1 1.5 2 2.5 3

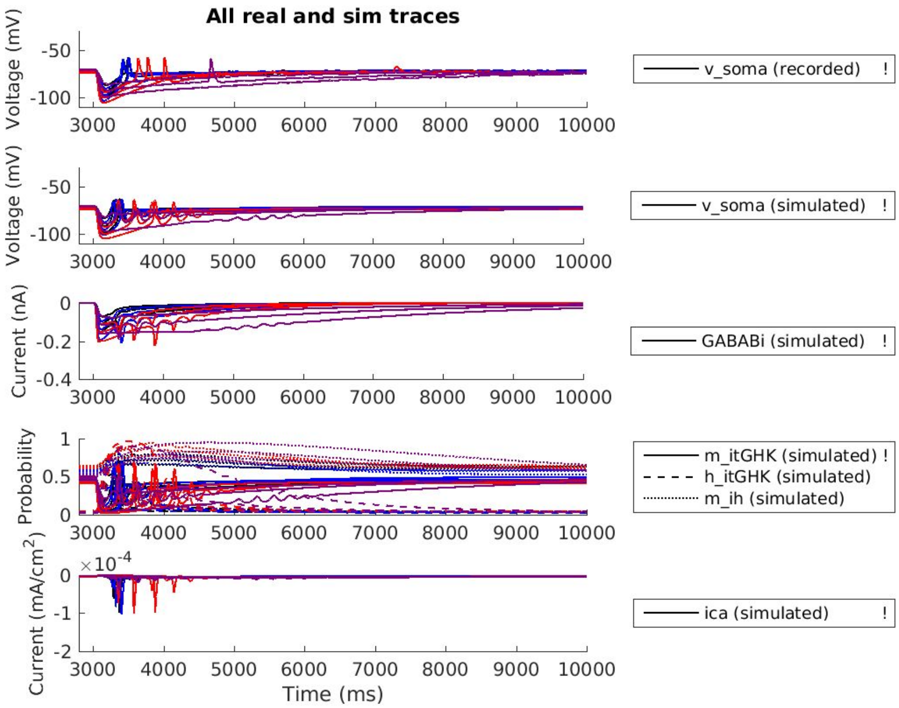
- Initialized to **best values from singleneuronfitting5**

All traces for Experiment 20170730T1841_E091710_bef

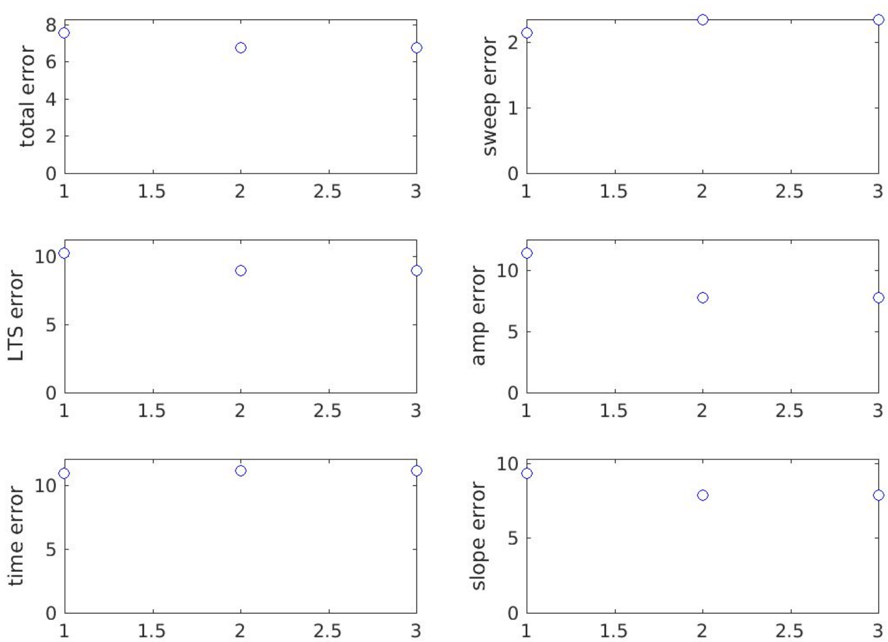


All traces for Experiment 20170730T1841_E091710_aft





Error History



- Errors/Parameters comparison:

	Initialize to **Destexhe - before**	Initialize to **Destexhe - after**	Initialize to **Christine - before**	Initialize to **Christine - after**	Initialize to **singleneuronfitting5 - before**	Initialize to **singleneuronfitting5 - after**
Total error	33.82	**10.22**	10.6	**7.457**	7.519	**6.73**
Sweep error	17.7	**4.24**	1.758	**2.938**	2.133	**2.338**
LTS amp error	30.62	**14.1**	10.98	**8.813**	11.39	**7.747**
LTS time error	17.18	**13**	10.53	**11.8**	10.94	**11.1**
LTS slope error	62.11	**13.05**	19.37	**8.632**	9.334	**7.87**
Average LTS error	41.89	**13.21**	15.02	**9.717**	10.21	**8.925**
diamSoma	38.42	**38.96**	38.42	**38.79**	36.24	**37.97**
LDend1	12.49	**58.45**	12.49	**65.9**	120	**106.3**
diamDend1ToSoma	0.2676	**0.1**	0.2676	**0.1136**	0.1	**0.1**
LDend2	84.67	**113.2**	84.67	**104.4**	117.2	**102.6**
diamDend2To1	0.8268	**1**	0.8268	**1**	0.7088	**0.8071**
distDendPercent	50	**50**	68.6	**68.6**	50	**50**
cm	0.88	**0.88**	0.789	**0.789**	0.88	**0.88**
Ra	173	173	173	173	173	173
corrD	7.954	7.954	7.954	7.954	7.954	7.954
gpas	1.00E-05	**3.04E-05**	8.21E-06	**2.82E-05**	3.26E-05	**2.93E-05**
epas	-80	**-72.24**	-80.4	**-77.86**	-70.19	**-90**
pcabarITS	0.0002	**1.00E-08**	5.00E-06	**2.58E-06**	2.82E-07	**2.32E-07**

oma						
pcabarITDend0	0.0002	**7.20E-05**	5.00E-06	**3.32E-06**	2.82E-07	**3.37E-07**
pcabarITDend1	0.0002	**0.000115**	8.91E-06	**5.83E-06**	1.84E-06	**1.08E-06**
pcabarITDend2	0.0002	**9.16E-05**	3.98E-06	**3.47E-05**	5.66E-05	**5.05E-05**
shiftmIT	-2	-2	-13.8	-13.8	-13.8	-13.8
shifthIT	0	0	-4.8	-4.8	-4.8	-4.8
slopemIT	1	1	1.4	1.4	1.4	1.4
slopehIT	1	1	1	1	1	1
ghbarSoma	2.20E-05	**1.73E-05**	1.10E-05	**3.84E-06**	3.02E-07	**6.33E-07**
ghbarDend0	2.20E-05	**6.41E-06**	1.10E-05	**3.74E-06**	3.02E-07	**4.98E-07**
ghbarDend1	2.20E-05	**0.001241**	1.10E-05	**3.64E-06**	2.81E-06	**8.37E-06**
ghbarDend2	2.20E-05	**1.47E-05**	1.10E-05	**1.00E-08**	1.02E-06	**1.22E-06**
eh	-43	-43	-43	-43	-43	-43
shiftmIh	0	**0**	11.4	**11.4**	11.4	**11.4**
gkbarIKirSoma	2.00E-05	**0.000135**	2.00E-05	**2.23E-05**	2.00E-05	**8.84E-06**
gkbarIKirDend0	2.00E-05	**0.000131**	2.00E-05	**1.86E-05**	2.00E-05	**1.75E-05**
gkbarIKirDend1	2.00E-05	**0.001417**	2.00E-05	**5.08E-05**	2.00E-05	**1.00E-08**
gkbarIKirDend2	2.00E-05	**0.000127**	2.00E-05	**3.61E-05**	2.00E-05	**2.80E-05**
gkbarIASoma	0.0055	**0.001049**	0.0055	**0.01**	0.0055	**0.01**

gkbarIADend0	0.0055	**0.009727**	0.0055	**0.01**	0.0055	**0.01**
gkbarIADend1	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.003335**
gkbarIADend2	0.0055	**0.01**	0.0055	**0.01**	0.0055	**0.001926**
gnabarINaPSoma	5.50E-06	**1.40E-06**	5.50E-06	**3.21E-06**	5.50E-06	**4.13E-06**
gnabarINaPDend0	5.50E-06	**1.18E-06**	5.50E-06	**5.63E-06**	5.50E-06	**5.68E-06**
gnabarINaPDend1	5.50E-06	**1.78E-06**	5.50E-06	**5.84E-06**	5.50E-06	**5.92E-06**
gnabarINaPDend2	5.50E-06	**1.98E-05**	5.50E-06	**6.53E-06**	5.50E-06	**8.69E-06**

<u>Plan for next week</u>

- minEASE:
  - Skip to **unchecked events** when using keyboard
  - Allow **.mat** files to be imported too
  - Recompute **IEIs, ISIs, decay times, etc.** after adding/deleting/changing events

- Single Neuron Model:
  - List all the equations used and try writing out an **explicit objective function**
  - Write code for **fitting across cells** (pick a **“stereotyped trace”** from all trials, Change parameters for each cell)

- Area paper:
  - Start writing background information for area paper
  - Decide on committee members, defense date and send emails

- Knowledge buildup:
  - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)
  - Cohen (*Analyzing Neural Time Series Data*)

<u>Plan for next week</u>

- Single Neuron Model:
  - Organize all mechanisms in the model
  - Place all range parameters in GUI and fit again
  - Explore Ed’s way of parallelizing Matlab without using a toolbox license.
  - List all the equations used and write out objective function explicitly
  - Figure out a way to fit across cells
- Area paper:
  - Browse recent literature on GABA B receptors
  - Decide on topic for area paper
- Knowledge buildup:
  - Sterratt et al (*Principles of Computational Modelling in Neuroscience*)

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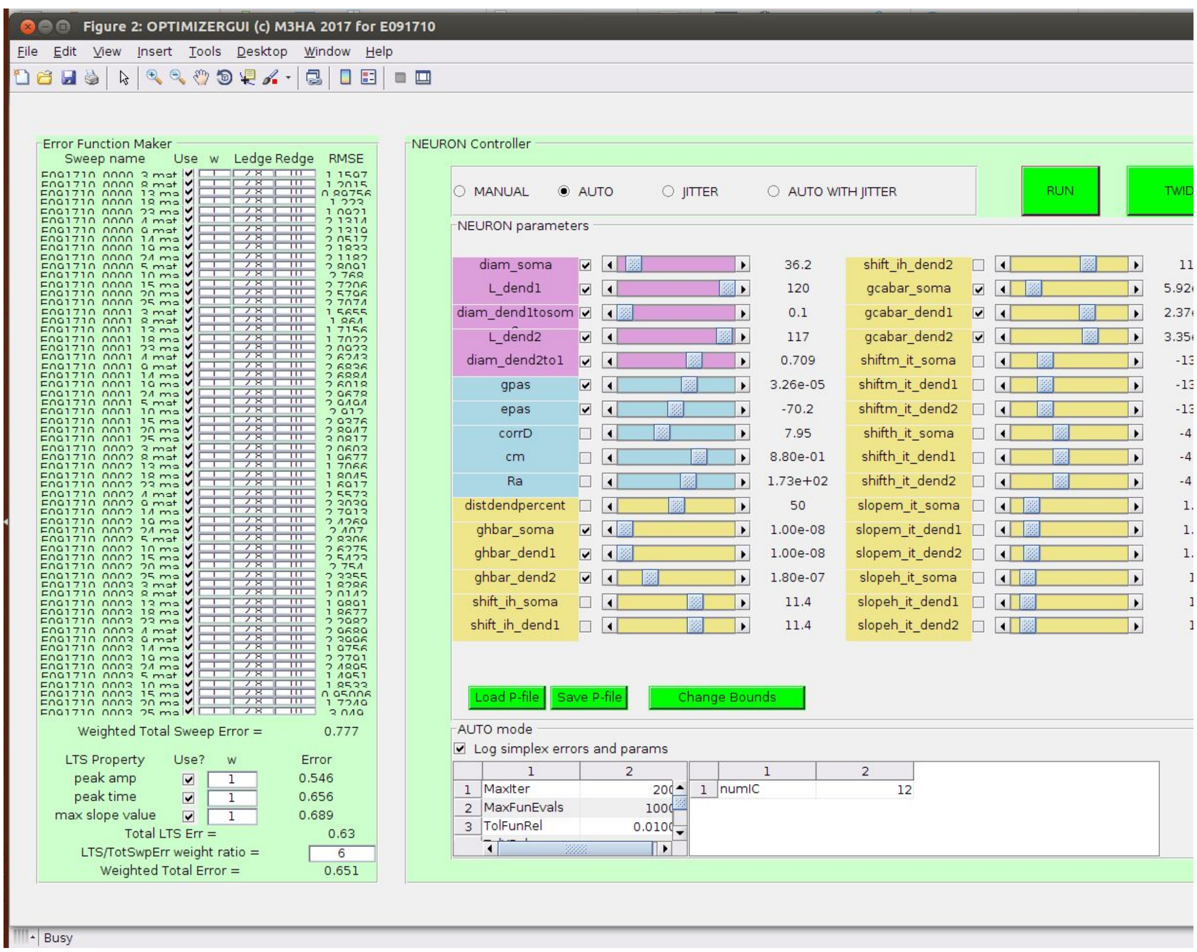
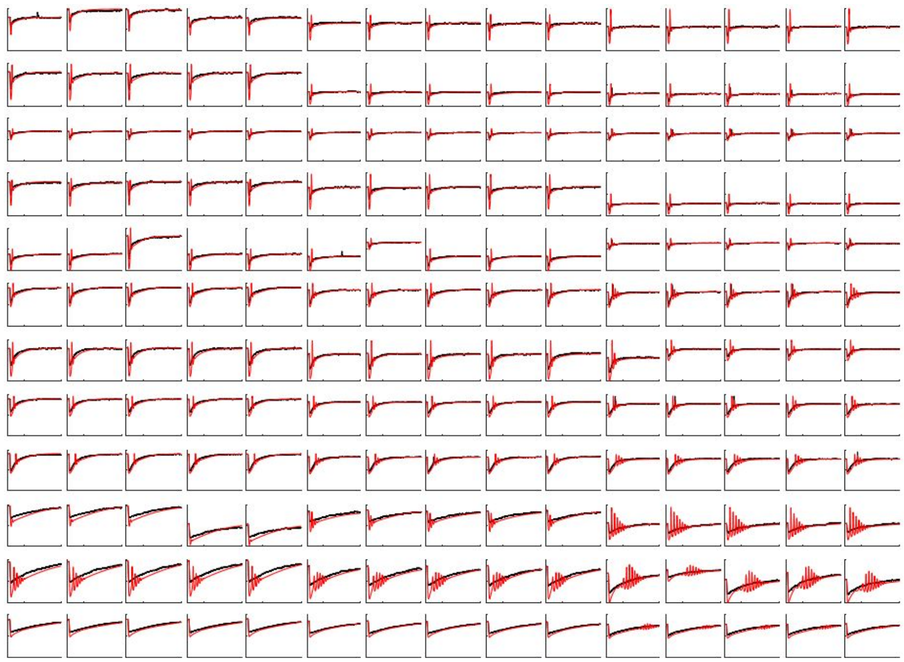
Single Neuron Fitting (cont'd)

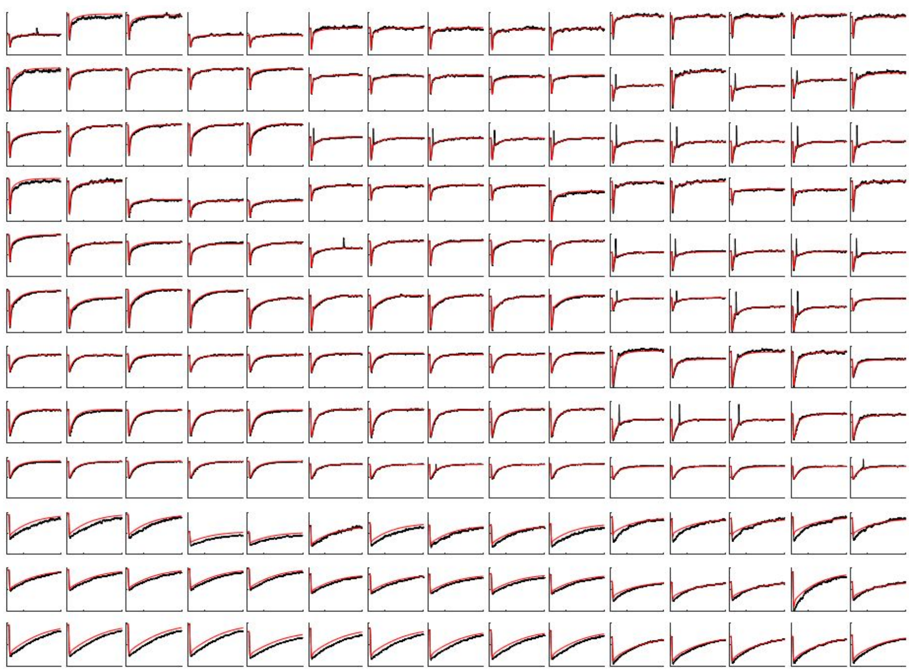
- **singleneuronfitting5.slurm**:
  - Fitted **10** cells with LTS amp:LTS time:LTS slope:sweep error ratio = **2:2:2:1**
  - **20** initial conditions on Rivanna
  - Passive parameters fitted:
    - **diam_soma**, **diam_dend1tosoma**, **diam_dend2to1**
    - **L_dend1**, **L_dend2**
    - **gpas**, **epas**
  - Active parameters fitted:
    - **ghbar_soma**, **ghbar_dend1**, **ghbar_dend2**
    - **gcabar_soma**, **gcabar_dend1**, **gcabar_dend2**

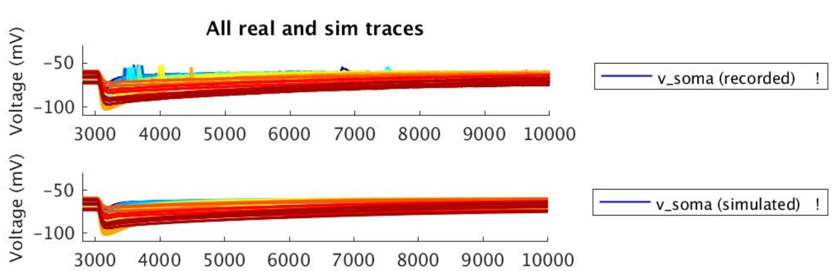


- **D091710**, before optimization

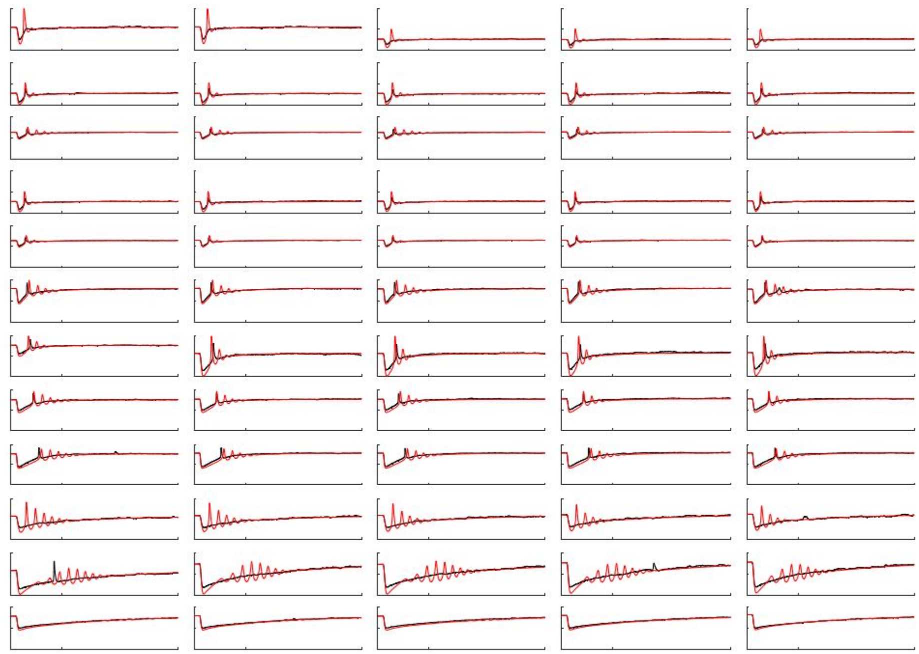


- **D091710**, after optimization

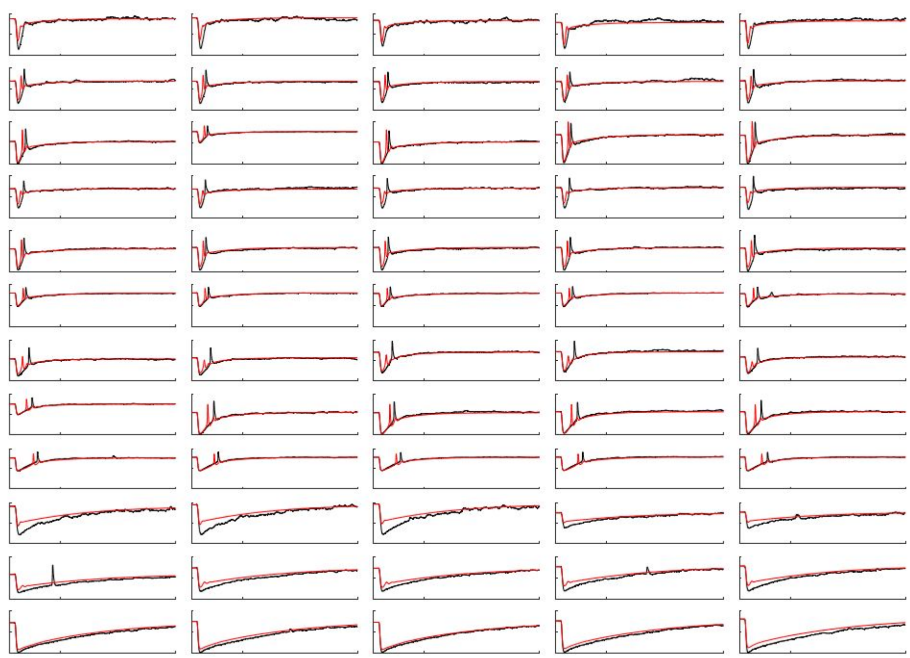


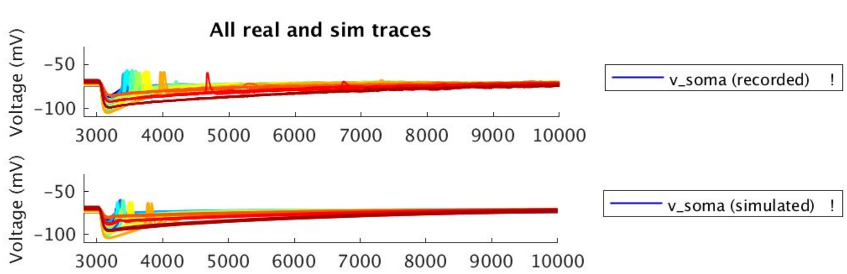


- **E091710**, before optimization

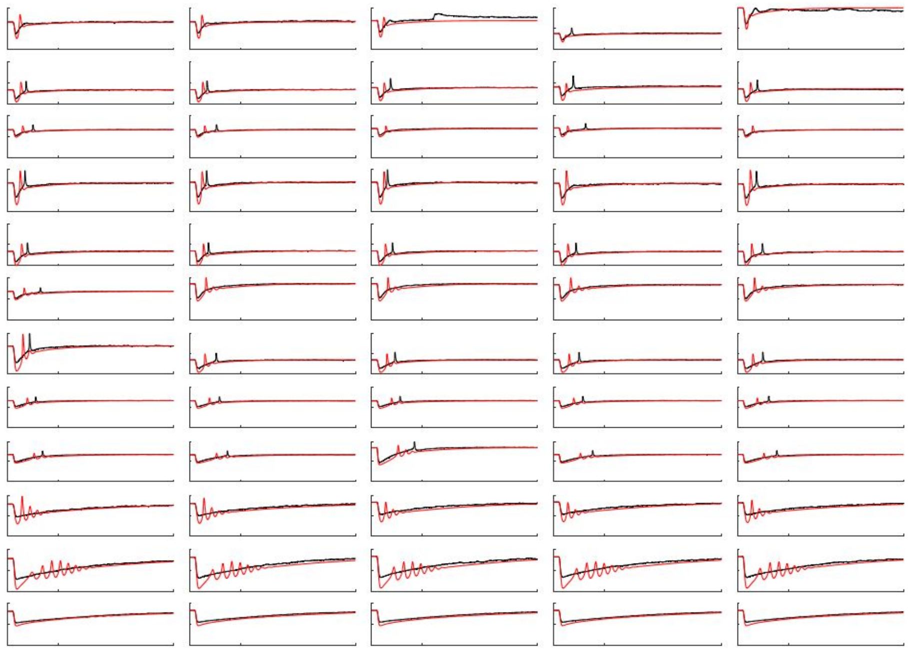


- **E091710**, after optimization

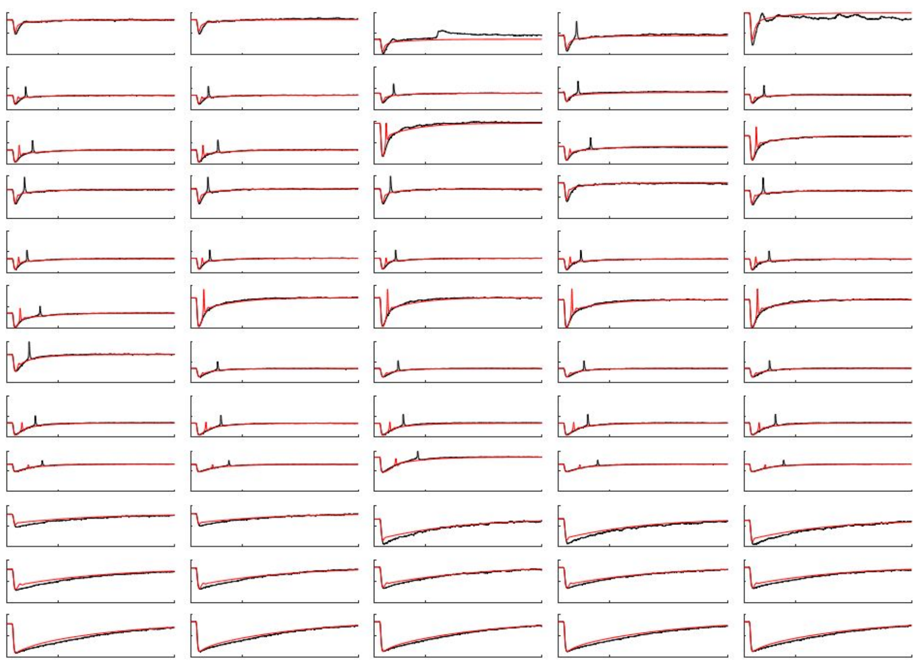


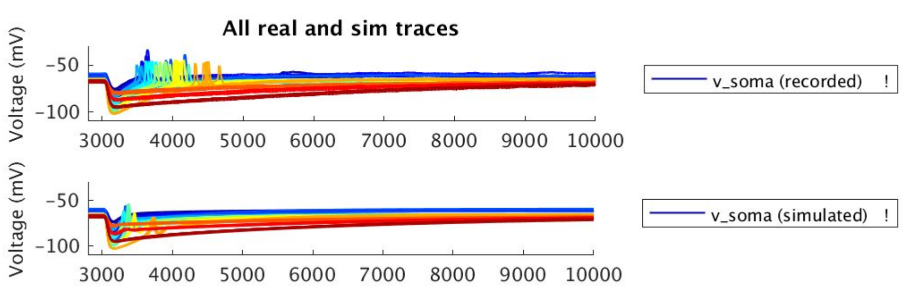


- **B091810**, before optimization

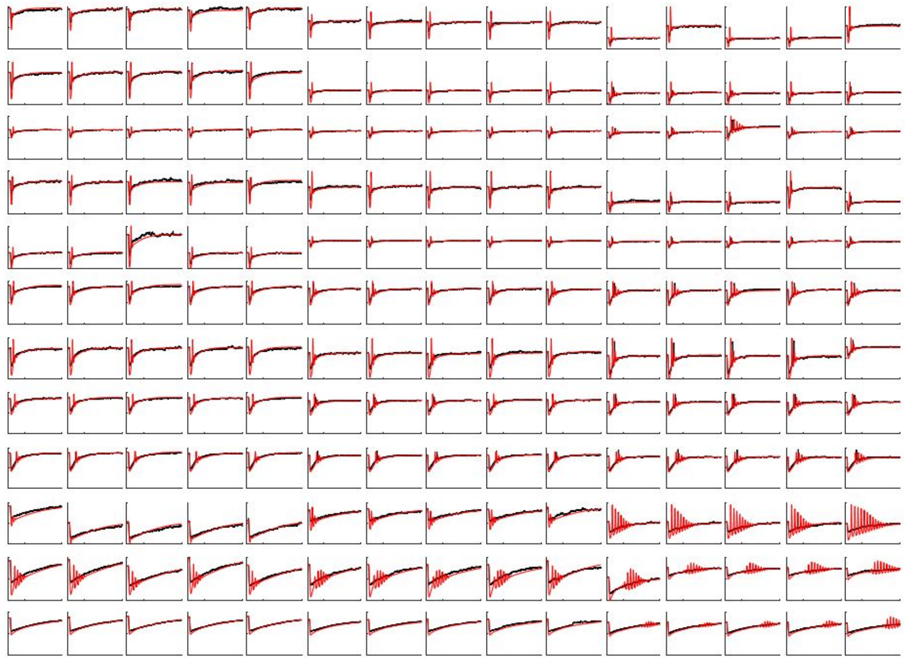


- **B091810**, after optimization

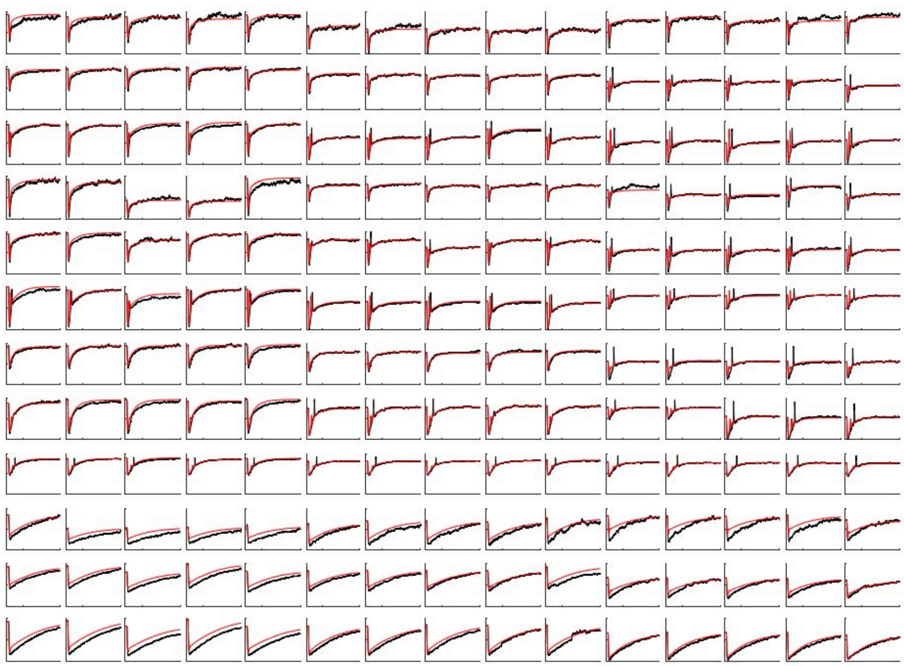


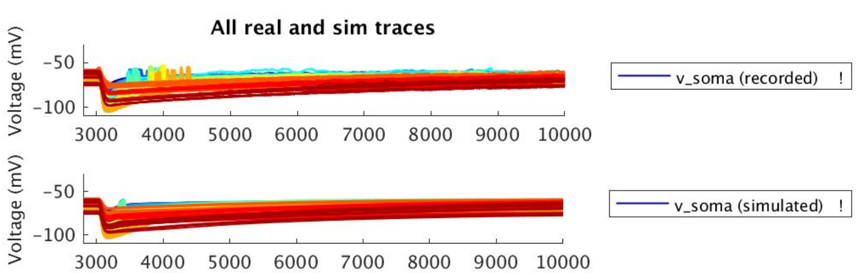


- **D091810**, before optimization

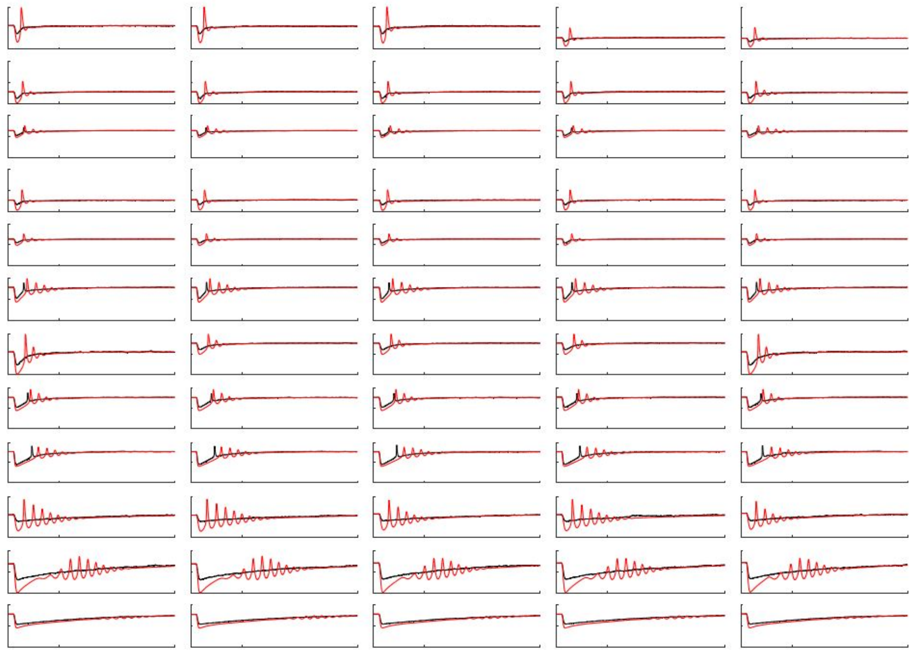


- **D091810**, after optimization

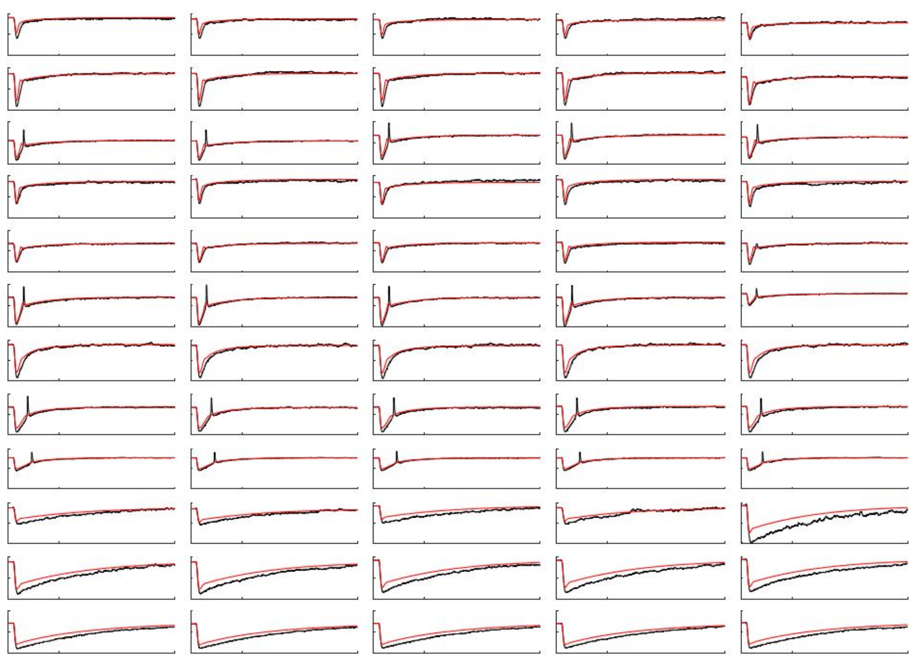


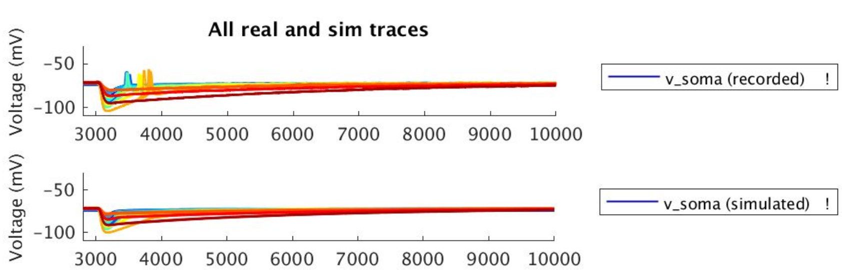


- **E091810**, before optimization

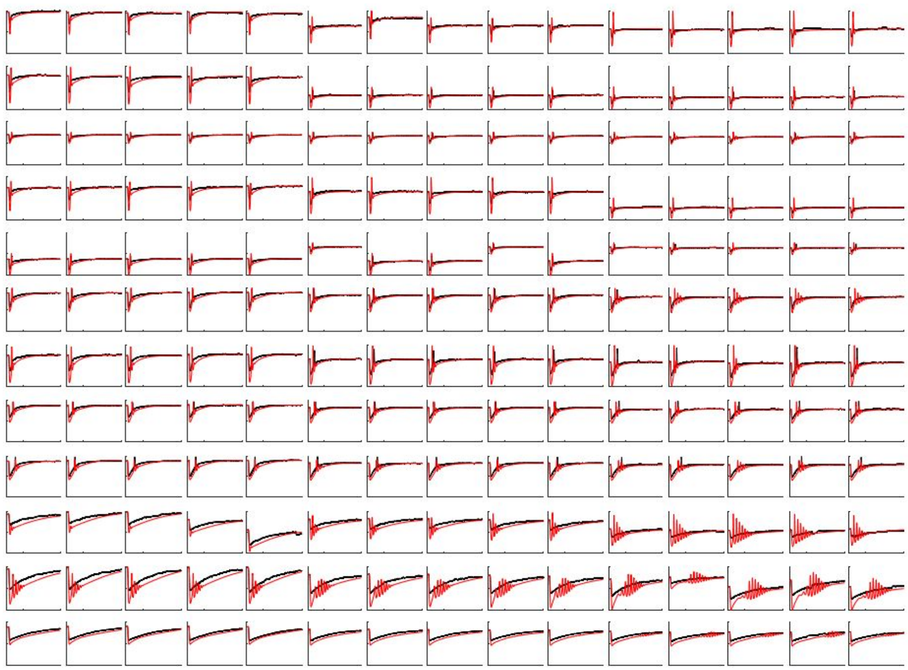


- **E091810**, after optimization

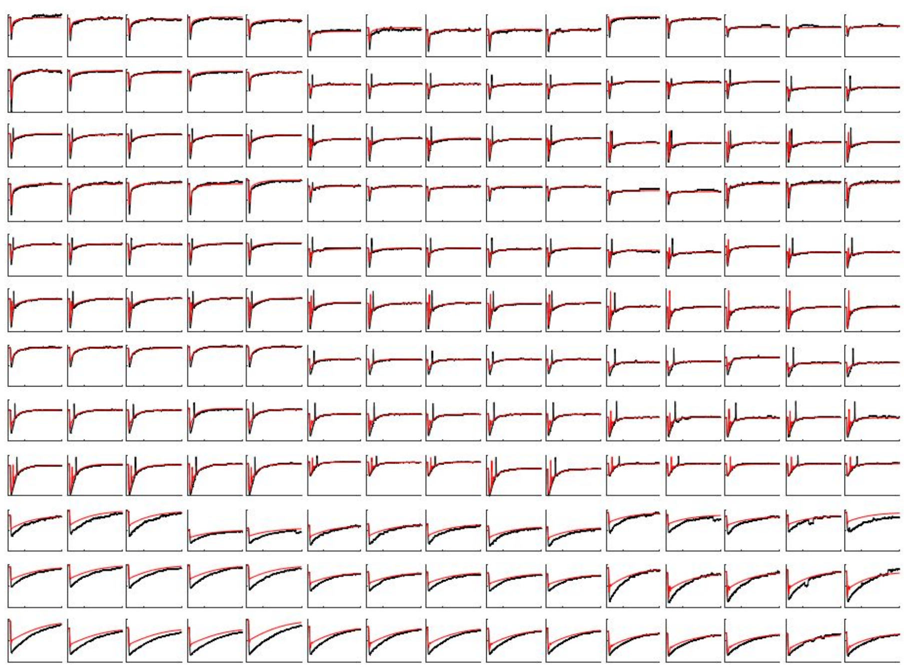


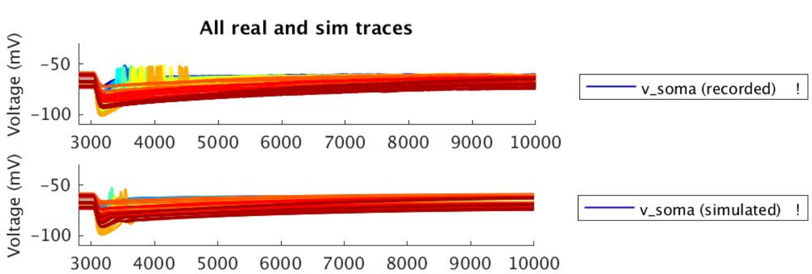


- **F091810**, before optimization

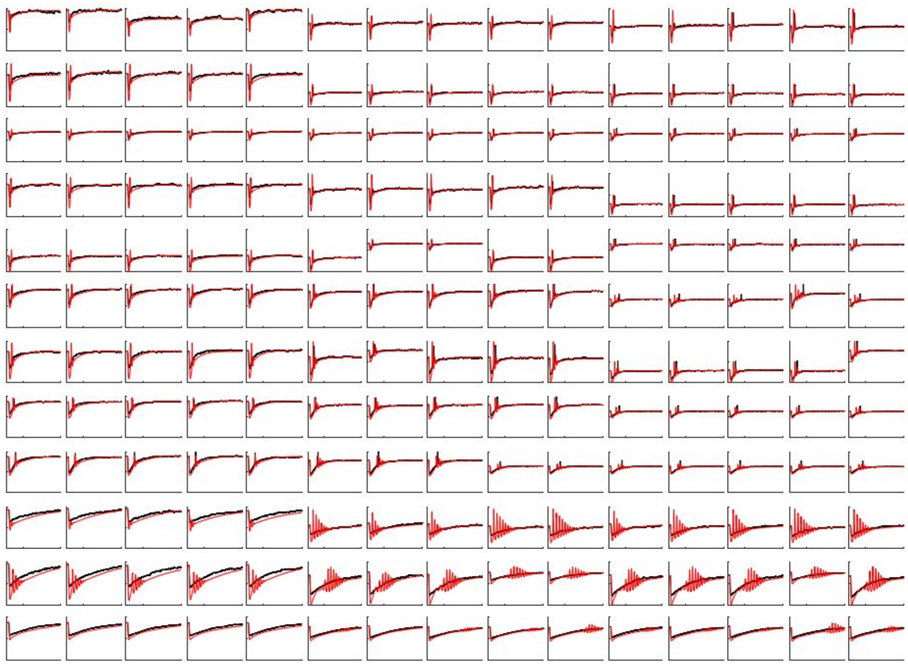


- **F091810**, after optimization

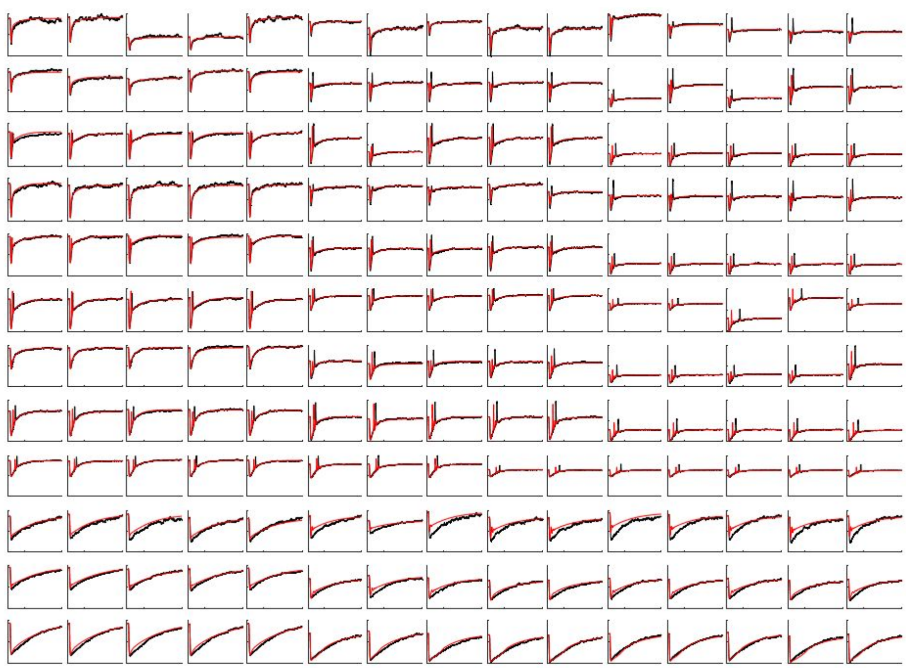


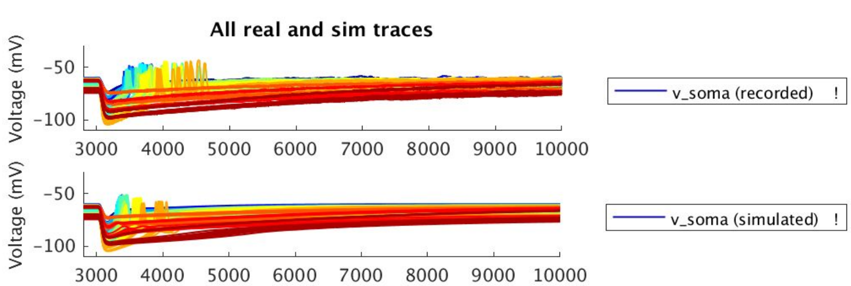


- **A092110**, before optimization

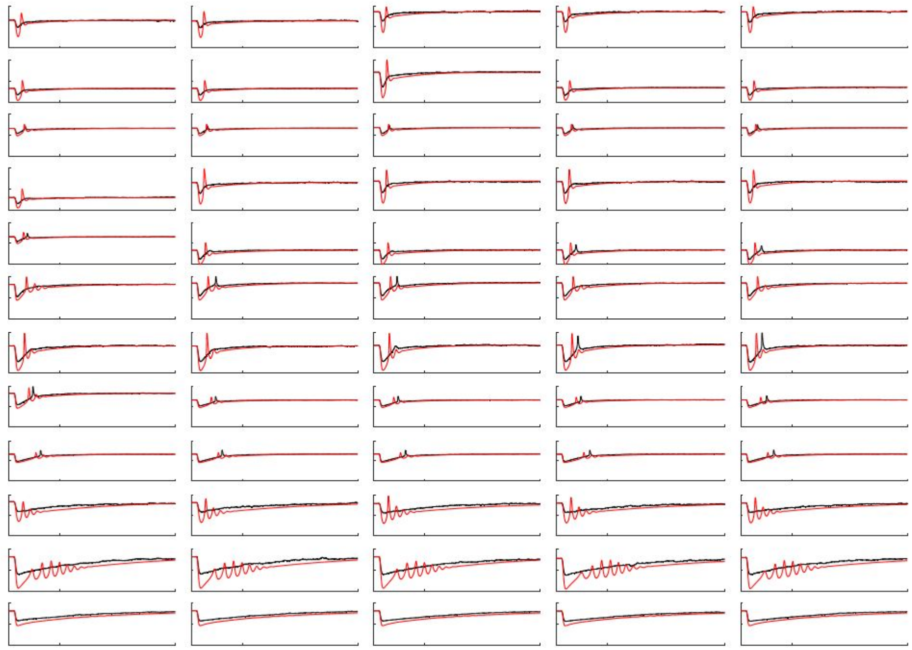


- **A092110**, after optimization

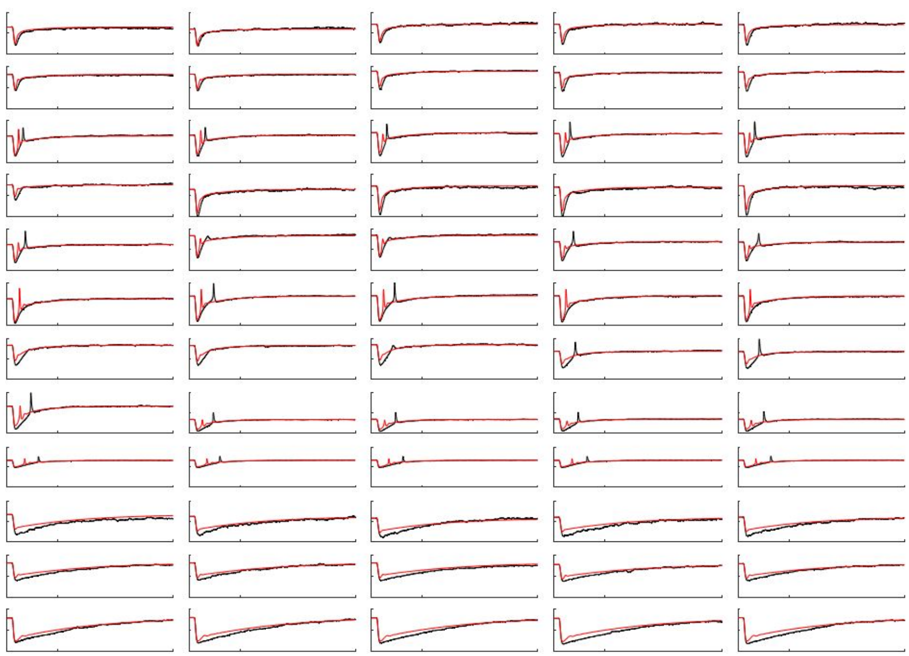


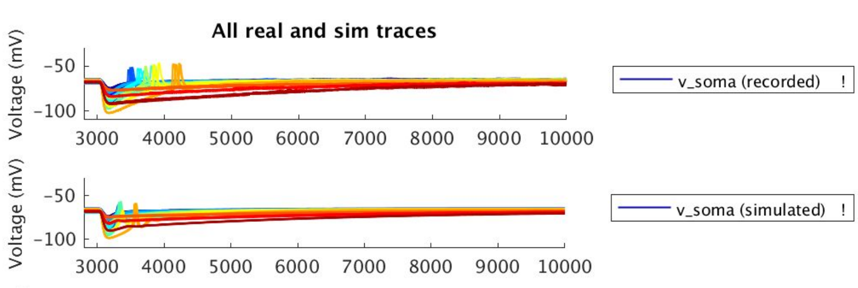


- **C092110**, before optimization

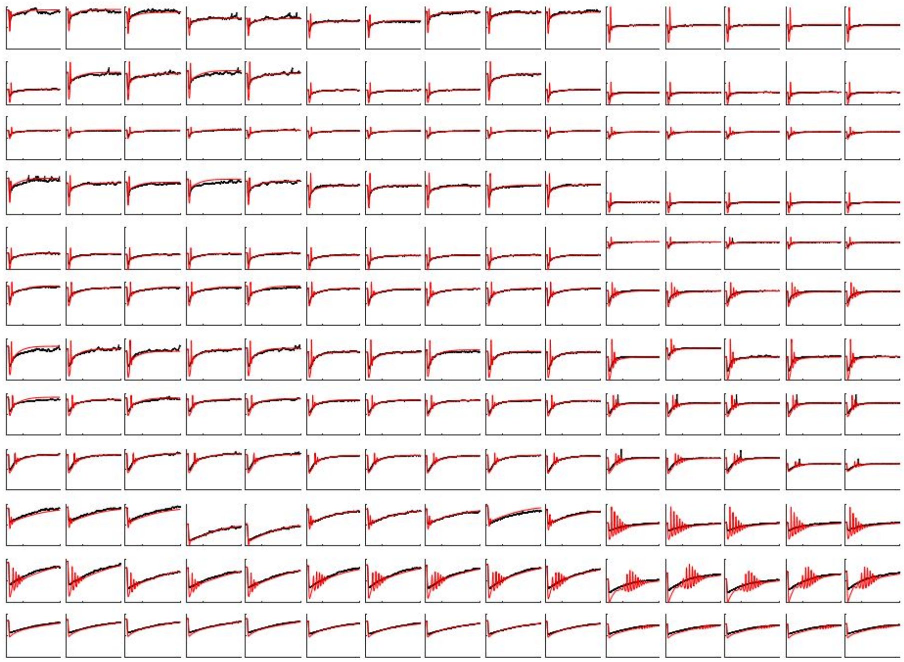


- **C092110**, after optimization

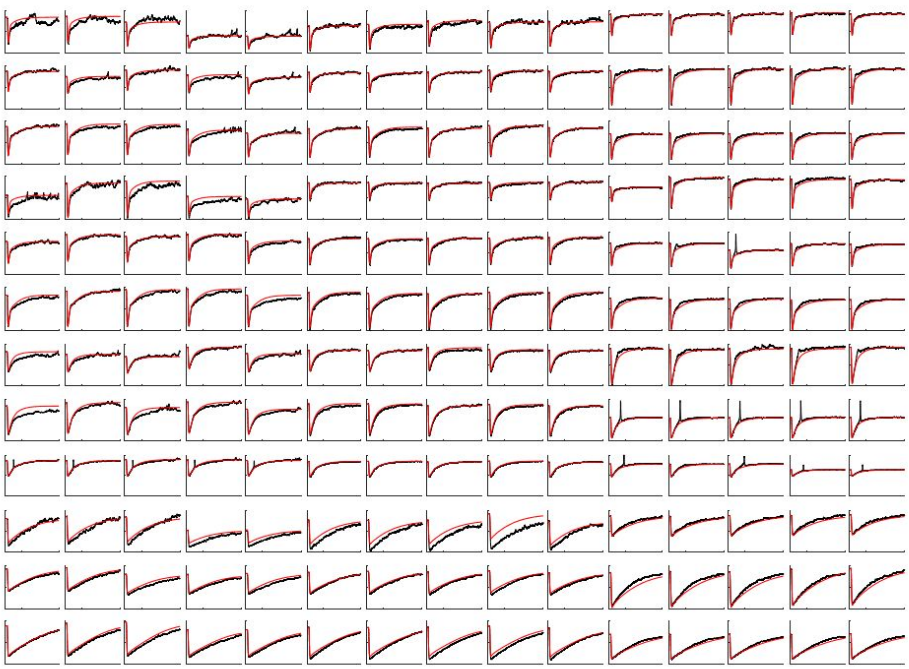


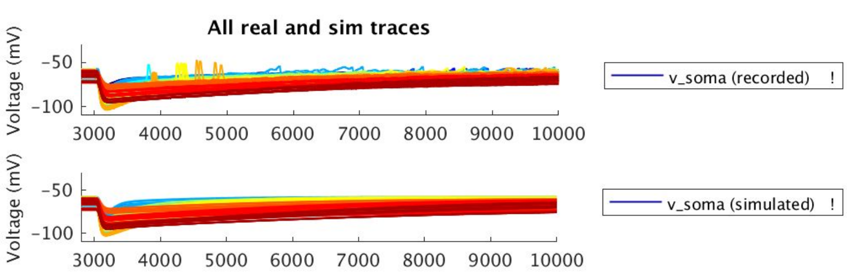


- **B092710**, before optimization

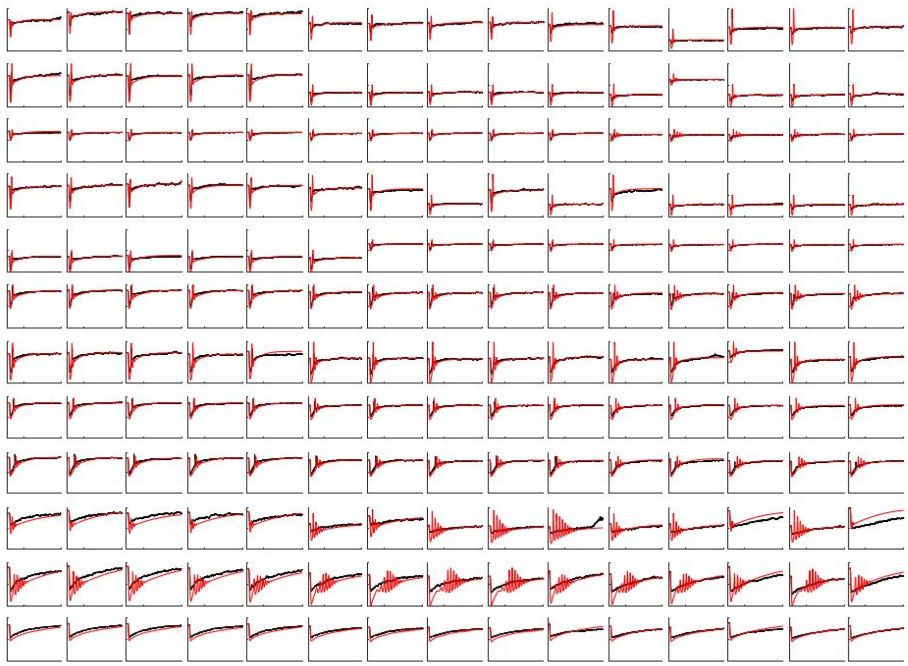


- **B092710**, after optimization

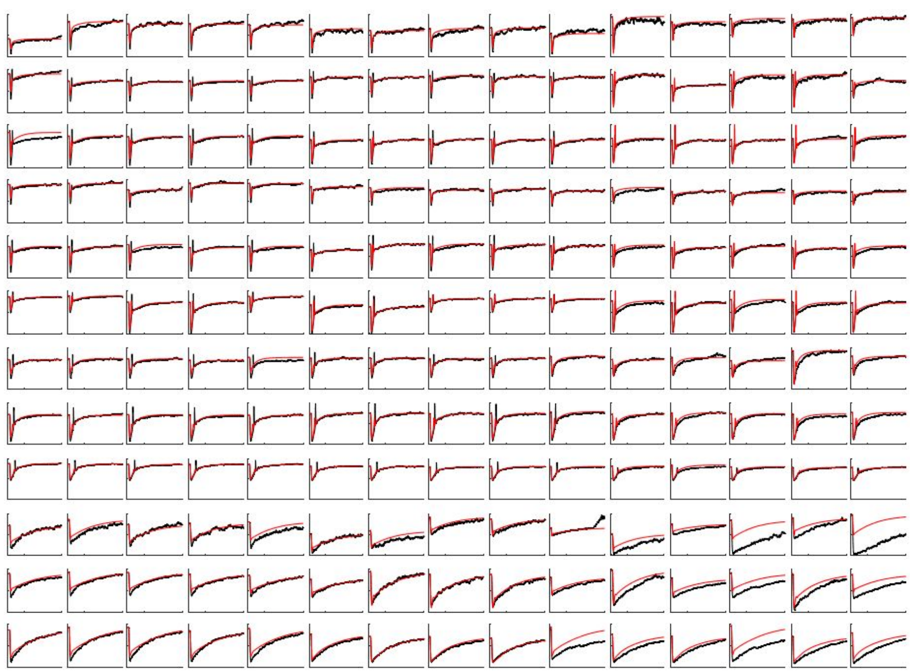


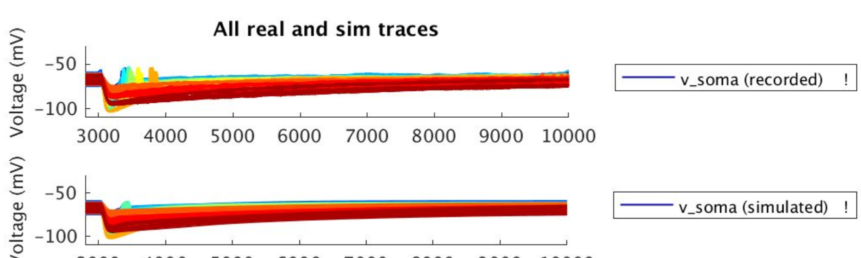


○ **C092710**, before optimization



○ **C092710**, after optimization





Plan for next week

- Single Neuron Model:
    - Organize all mechanisms in the model
    - List all the equations used and write out objective function explicitly
- Johnston & Wu:
    - Read Ch 7~15, Appendix A & B
- Area paper:
    - Browse recent literature
    - Think about topic for area paper

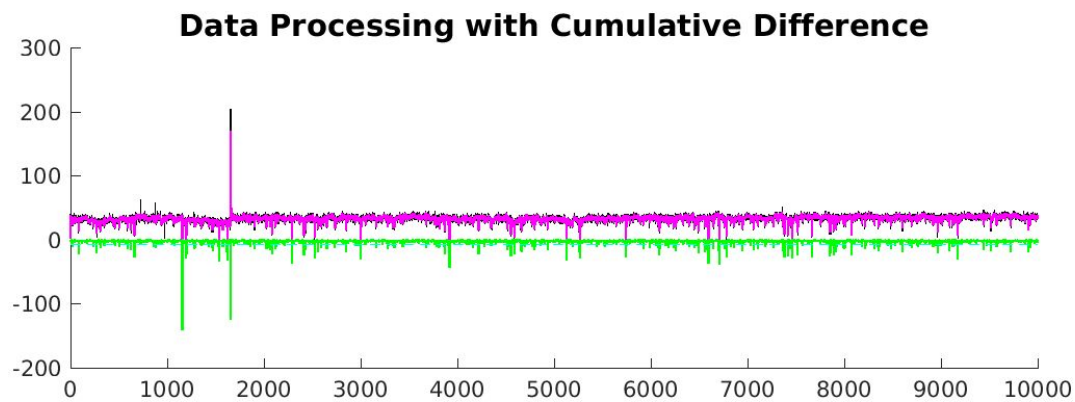
5/20/2017~6/5/2017

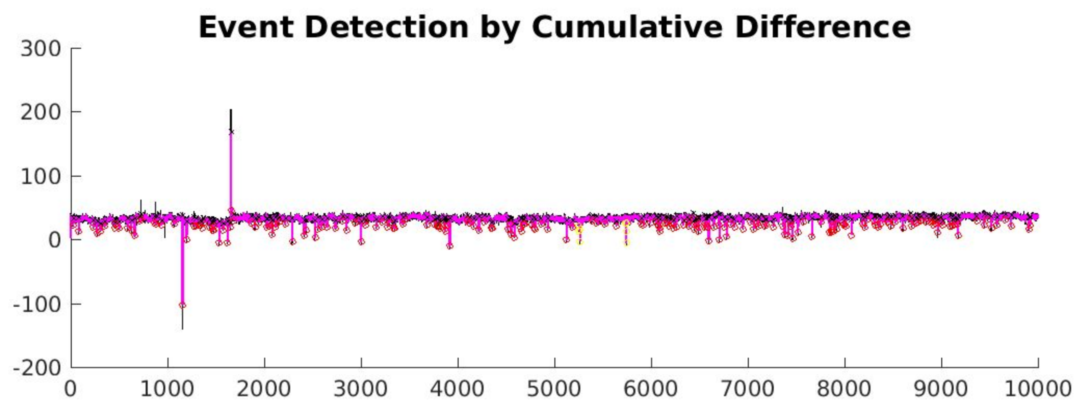
minEASE

- Default parameters:

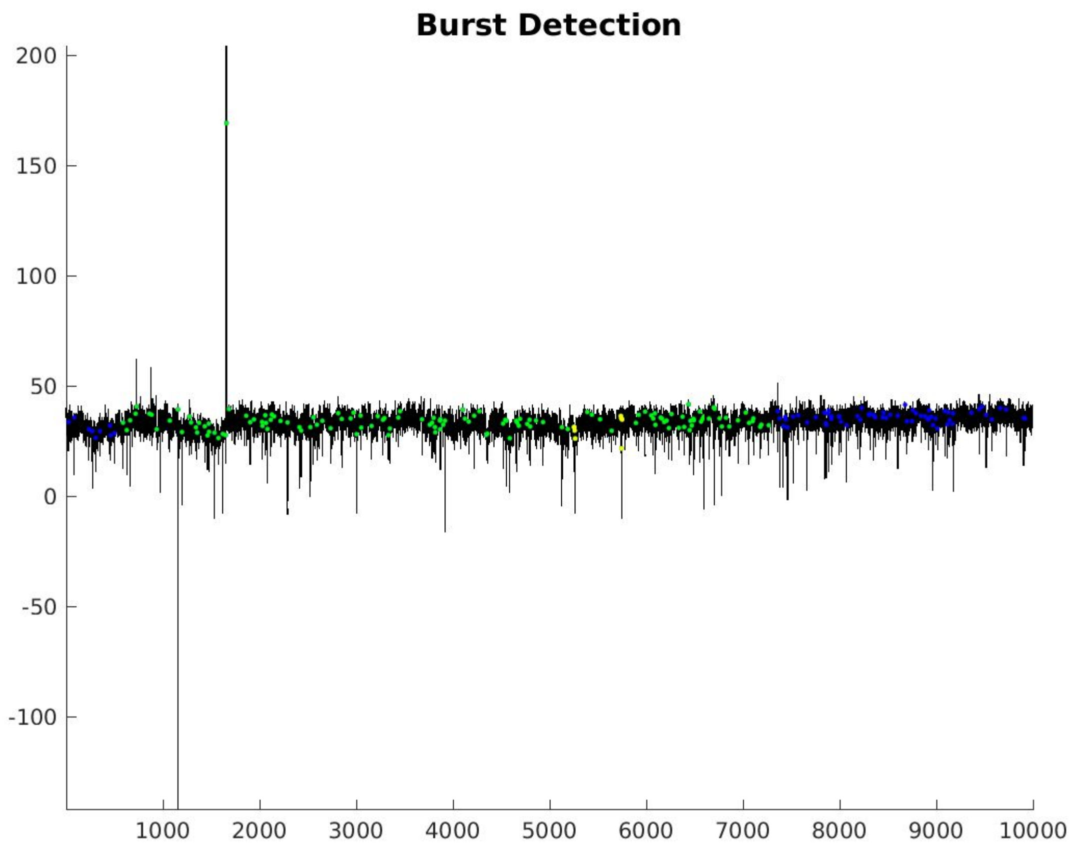
Direction of PSC ("E" or "I")	E
Lowpass Filter Cutoff Frequency (Hz)	3000
Lowpass Butterworth Filter Order	8
Noise Window Size (samples)	100
Noise Skewness Cutoff	0.2
Noise Excess Kurtosis Cutoff	0.2
Signal to Noise ratio for an event	2
Minimum Amplitude Threshold for an event (pA)	8
Moving Average Filter Window (ms)	0.5
Minimum Baseline Difference (pA)	8
Crude Burst Region Size (events)	50
Minimum Spikes Per Burst	3
Maximum Inter-Spike Interval (ms)	10
Minimum PSC Amplitude (pA)	10
Maximum PSC 10-90% Rise Time (ms)	8
Maximum PSC 50% Decay Time (ms)	50
Total PSC Trace Length (ms)	50
PSC Trace Length Before Breakpoint (ms)	3
Start Detection (sec)	0
End Detection (sec or "end")	end
Seal Test Window [start, end] (ms)	[1000, 1050]

- Autodetection results so far:
    - Event Detection & Classification
        - **Original current trace** is in black
        - **Moving-average-filtered current trace** is in magenta
        - **Direction-filtered current trace** is in green
        - PSCs are in red
        - Bursts are in yellow

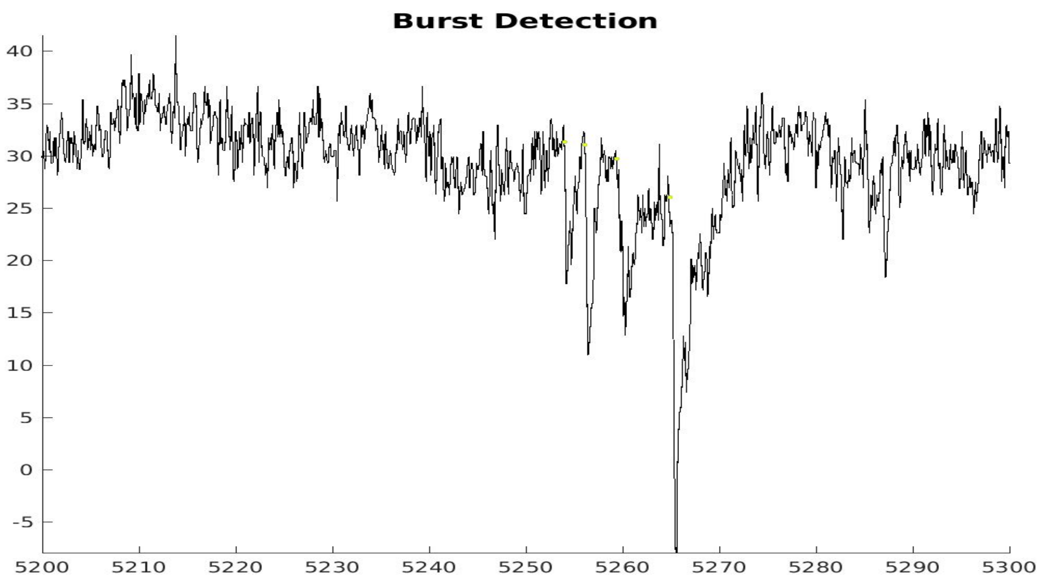


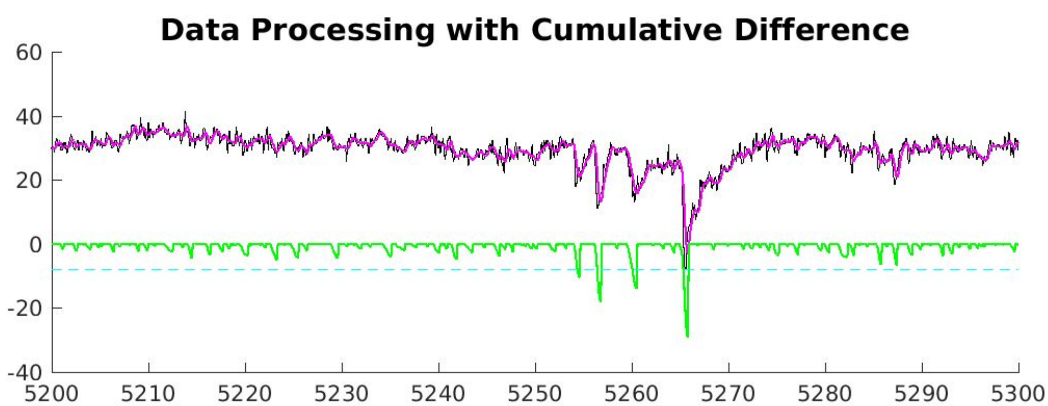


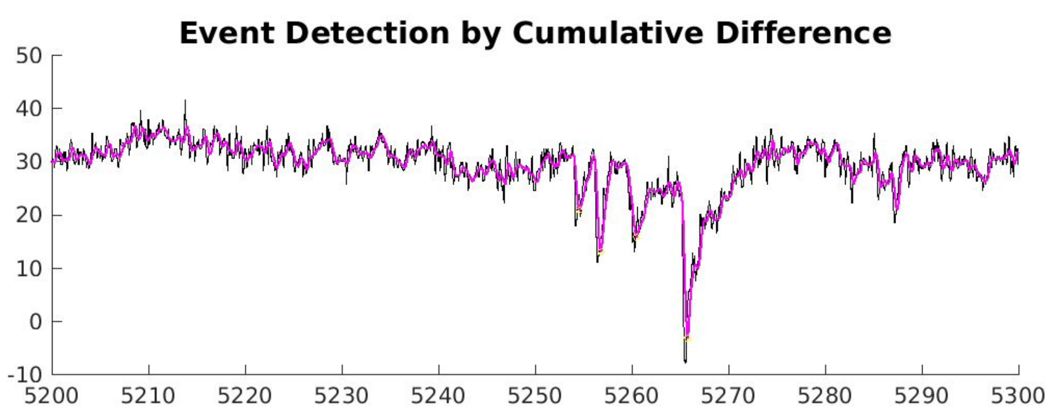
- Burst Detection
  - Maximum Inter-Spike Interval = **10 ms**
  - Minimum Spikes Per Burst = **3**
  - All **event breakpoints** are in blue
  - **“Crude burst regions”** are in green
  - “**Bursts**” are in yellow



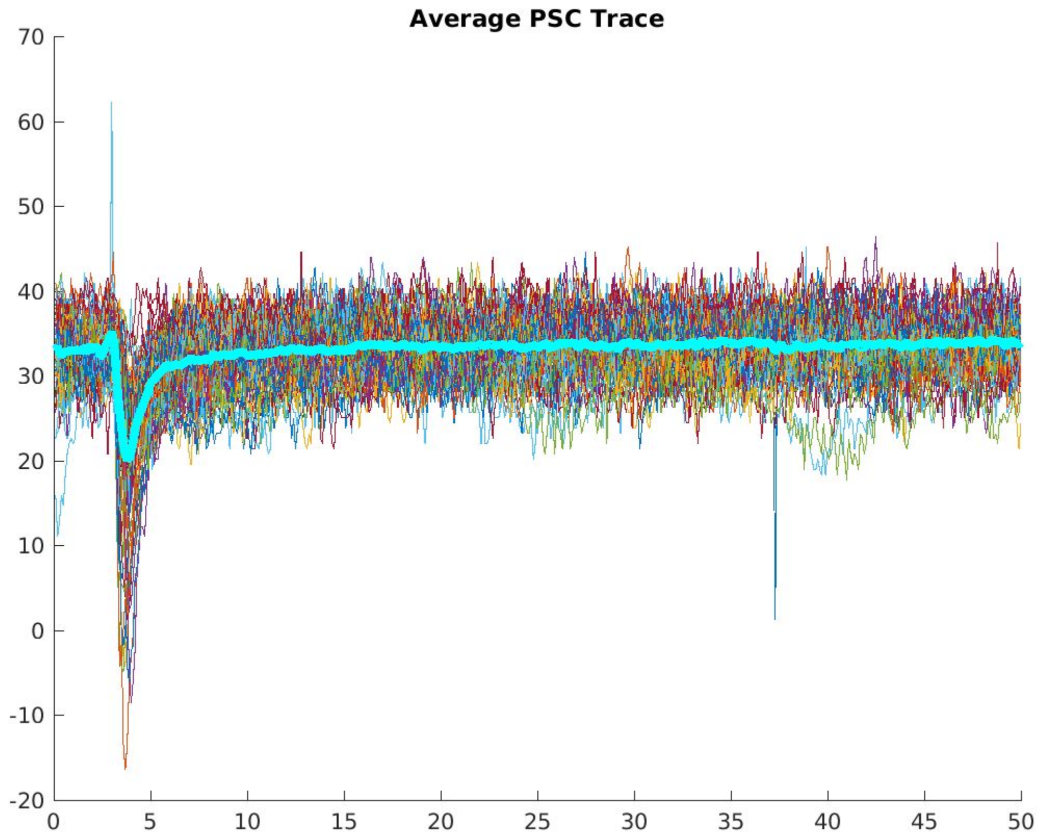
- Zoomed in to a “burst”:







- Trace Averaging
    - Averaged PSC trace is in cyan



Plan for next week

- Continue improving minEASE until Tuesday
- Resume improving fitting on Wednesday

2/10/2017

Made solutions

- **ACSF 10x**:
  - Added water to ~1800 mL and mixed in **2 L bottle**
  - Added water to 2 L in **volumetric flask** (Actual: slightly above the line)
  - Transferred back to 2 L bottle and stored in fridge

Compound	Final Conc. (mM) for 1x	MW (g/mol)	g / 2 L for 10x*
KCl	**2.5**	74.55	3.7275
Glucose	**10**	180.16	36.03
NaCl	**126**	58.44	147.27
$aH_2PO_4 \cdot H_2O$	**1.25**	137.99	3.4498
$MgSO_4 \cdot 7H_2O$	**1**	246.47	4.9294
$CaCl_2 \cdot 2H_2O$	**2**	147.01	5.8804

* Actual figures used this time was from the website

2/16/2017

- **Internal solution**:
  - **Potassium-gluconate internal** (Considered relatively physiological; aka Sun's GABAB internal)
  - Made **0.99 mL** aliquots
    - Added ~75 mL initially
    - Measured the pH while stirring, increasing the pH to **7.3~7.4** by adding KOH (First 4M, then 1M)
    - Final pH was: **7.30**
    - Osmolality was 282, 272, 277, 276 (target 293 mmol/kg)
    - Stirred a little more and wait longer: osmolality was 297, 297, 278, 279, 275 (target 293 mmol/kg)
    - Total solution was ~88 mL (88 0.99 mL aliquots)

Compound	Final Conc. (mM)	MW (g/mol)	g / 100 mL (add < 95 mL initially though)
K-gluconate (D-gluconic acid)	**100**	234.24	2.3424
$MgCl_2 \cdot 6H_2O$	**9**	203.30	0.1830
KCl	**13**	74.55	0.0969
$CaCl_2 \cdot 2H_2O$	**0.07**	147.01	0.0010
Hepes buffer	**10**	238.3	0.2383
EGTA	**10**	380.35	0.3804

* Actual figures used this time was from the website

2/17/2017

- **10 uL ATP & GTP** aliquots to be added to internal on the day of:

Compound	Final Conc. (mM)	MW (g/mol)	g / 1 mL
Na_2ATP	**2**	551.1	0.1102
NaGTP	**0.5**	523.2	0.0262

2/13/2017~2/26/2017

Chloride-dependent RT Network

- All files are under **/media/adamX/RTCl/**
- File structure:

File name	Description	Requires	Used By
neuronlaunch.m	Launches NEURON with simulation commands and plot output figures	run2.hoc run.hoc (obsolete) show_RTnet.m raster_plot.m single_neuron.m	
run.hoc	Runs network simulation (obsolete)	net.hoc dummy.mod	neuronlaunch.m (potentially)
run2.hoc	Define global parameters (**ncells** & **celsius**) and load procedures	net.hoc	neuronlaunch.m
net.hoc	Procedures for network simulations: buildnet(), randleak(), vinit(), REsinglecp(), REsingleact(), RErandact(), sim()	RE.tem gabaA_Cl.mod gabaa.mod (potentially)	run.hoc run2.hoc
RE.tem	Template file for defining reticular thalamic neurons	HH2.mod ITs.mod IKCa.mod cadecay.mod cldif2.mod	net.hoc
show_RTnet.m	Shows network topology for each RT network	/Downloaded_Functions/dirr.m	neuronlaunch.m
raster_plot.m	Shows a spike raster plot for each set of neurons	/Downloaded_Functions/dirr.m	neuronlaunch.m
single_neuron.m	Shows single neuron voltage & chloride concentration traces for each neuron	/Downloaded_Functions/dirr.m	neuronlaunch.m
HH2.mod	Fast Na+ and K+ currents responsible for action potentials (**Destexhe, 1992**)		RE.tem
ITs.mod	Low threshold calcium current (**Sohal, 1997**)		RE.tem

IKCa.mod	Linear calcium-dependent potassium current (**Sohal, 2003**)		RE.tem
cadecay.mod	Fast mechanism for submembranal Ca++ concentration (cai) (**Destexhe, 1995**)		RE.tem
cldif2.mod	Chloride accumulation and diffusion with chloride pump (Lineweaver-Burke equation) and chloride leak (**Jedlicka et al 2011**)		RE.tem
gabaA_Cl.mod	Synaptic GABAergic mechanism that's dependent on chloride concentration (**Jedlicka et al 2011**)		net.hoc
gabaA_Cl.mod	Simple GABA-A receptor		net.hoc

- Output folder: Use current date & time in the format: **YYYYMMDDThhmm**
- Output files (in output folder):

File name	Content
sim_params.csv	simulation parameters
sim_commands.txt	simulation commands
sim_output.txt	simulation standard outputs
RERE.syn	RE-RE synaptic connections
RE.spi	RE spike train output
RE.singv	RE single neuron voltage traces
RE.singcli	RE single neuron chloride concentration traces
RE.leak	RE single neuron leak properties

- Parameters (**neuronlaunch.m** & **run2.hoc**)
  - Global parameters to be defined at the start of NEURON, to be consistent with run.hoc or run2.hoc:

Name	Initial value	Description
ncells	100	# of cells
celsius	34	Temperature of experiment (celsius), Sohal & Huguenard 2003

  - Network parameters:

Name	Initial value	Description
REREradius	4	Radius of intra-RE connections, Sohal & Huguenard 2003
sp_thr	0	Action potential threshold (mV)
syn_del	1	Synaptic delay (ms)
syn_w	0.5	Synaptic weight (fraction of channels activated)

  - RE cell parameters:

Name	Initial value	Description
RErest	-77	Resting membrane potential (mV) of RE cells, Sohal & Huguenard 2003
REgpasLB	4.50E-05	Lower bound for passive leak conductance (S/cm^2) in RE cells, Sohal & Huguenard 2003
REgpasUB	5.50E-05	Upper bound for passive leak conductance (S/cm^2) in RE cells, Sohal & Huguenard 2003
REGgaba	0.04	Conductance (μS) of GABA-A synapses on RE cells Sohal & Huguenard 2003: to be varied between 40~100 nS
gaba_grel	0.2	Relative conductance of HCO3 of the GABA-A receptor

- Activation mode:

Name	Initial value	Description
actmode	1	Activation mode: 1 - Activate a single RE cell by injecting a current pulse 2 - Activate a single RE cell by changing the membrane potential instantaneously 3 - Activate RE cells with a Gaussian likelihood by changing the mp instantaneously

- Activation parameters for 'cp' mode

Name	Initial value	Description
actcellID	50	ID # of neuron to activate
cp_start	500	Current pulse delay (ms)
cp_dur	200	Current pulse duration (ms)
cp_amp	10	Current pulse amplitude (nA)

- Activation parameters for 'single' or 'random' mode:

Name	Initial value	Description
actcellv	0	Voltage (mV) to set activated neuron to
actwidth	50	Width of Gaussian distribution for randomly activating cells
actmaxp	0.5	Maximum likelihood of activation at center

- Simulation parameters:

Name	Initial value	Description
niters	1	Number of times to run simulation
tstop	2000	Total time of simulation (ms)
dt	0.1	Time step of integration (ms)

- Plot flags:

Name	Initial value	Description
plotspikes	1	Whether to plot spike data
plotsingleneurondata	1	Whether to plot single neuron data

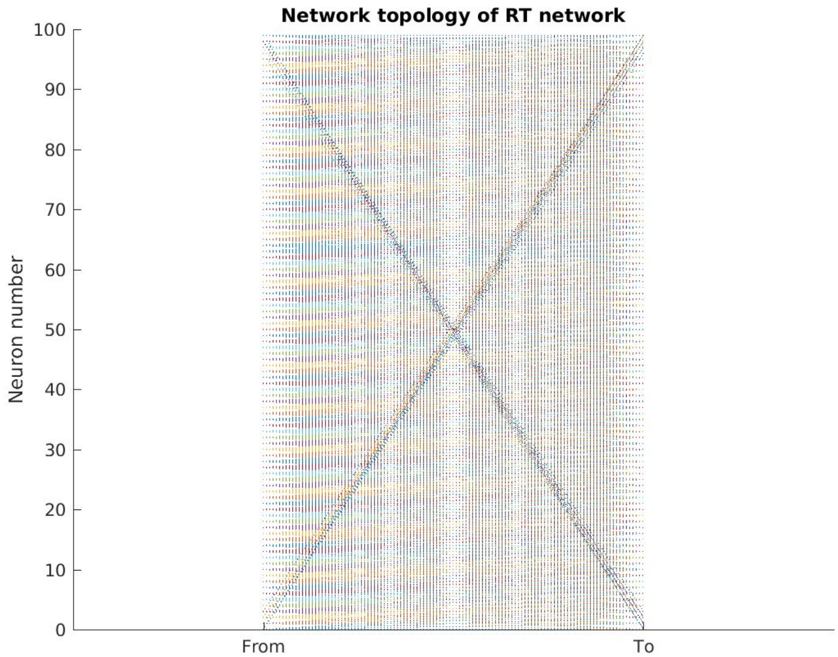
- ID #s of neurons to plot:

Name	Initial value	Description
act	50	ID # of the activated neuron
act_left1	49	ID # of the neuron one below the activated neuron
act_left2	48	ID # of the neuron 2 below the activated neuron
far	1	ID # of a far away neuron

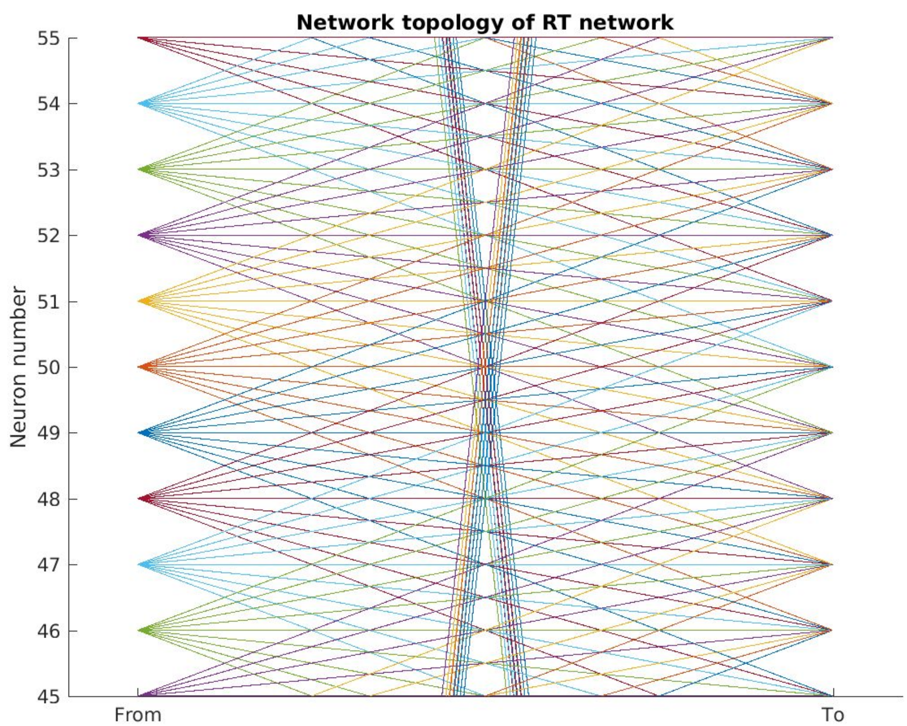
- Procedures (**net.hoc**)
  - **buildnet**(REGgaba, gaba_grel, RERERadius, sp_thr, syn_del, syn_w, sREREsynF_full)
    - Creates neurons (**ncells** of them) according to the template in **RE.tem**
    - Places **a GABA-A receptor** (**gabaA_Cl.mod**) on the soma of each neuron with **gmax** (maximum conductance in μS) & **grel** (relative conductance of HCO_3) set by **REGgaba** & **gaba_grel**, respectively.
    - Set up GABA-A synapses between RE cells:
      - Each cell projects to each of the adjacent **RERERadius** cells on either side (total # of synapses should be **2*RERERadius*ncells**)
      - There are **no autapses**
      - There are **no boundaries**; the network is **circular**
      - The threshold for an action potential to occur is **sp_thr** mV
      - The delay accounting for synaptic transmission is **syn_del** ms
      - The weight of synaptic activation is **syn_w** (fraction of channels open), i.e., gmax will be multiplied by this fraction
    - Print synaptic map to a file with name **sREREsynF_full** (currently **RERE.syn)**
    - Set up vectors to record all spike events
    - Set up vectors to record all single neuron voltage & chloride concentration traces

- **randleak**(REgpasLB, REgpasUB, sREleakF_full)
    - Randomize leak properties for each RE cell using a **uniform distribution**; currently only **gpas** is randomized (from **REgpasLB** to **REgpasUB**)
    - Print leak properties to a file with name **sREleakF_full** (currently **RE.leak**)
- **vinit**(RErest)
    - Initialize all mechanisms and point processes (**finitialize()**)
    - Set initial membrane potential of each neuron to **RErest**
- **REsinglecp**(actcellID, cp_start, cp_dur, cp_amp)
    - Place a current clamp electrode (**IClamp**) at the neuron with ID # **actcellID**
    - Current pulse delay is **cp_start** ms
    - Current pulse duration is **cp_dur** ms
    - Current pulse amplitude is **cp_amp** nA
- **REsingleact**(actcellID, actcellv)
    - Set initial membrane potential of the neuron with ID # **actcellID** to be **actcellv** mV
- **RErandact**(actcellID, actwidth, actmaxp, actcellv)
    - With a probability set by a Gaussian distribution with maximum **actmaxp** centered at **actcellID** with standard deviation **actwidth**, set initial membrane potential of a neuron to be **actcellv** mV
- **sim**(tstop, dt, plotspikes, plotsingleneurondata, sREspikeF_full, sREvF_full, sREcliF_full)
    - Using a total time of **tstop** and a time step of **dt**, simulate
    - If **plotspikes** is 1, print the spike train data to a file with name **sREspikeF_full** (currently **RE.spi**)
    - If **plotsingleneurondata** is 1, print the single neuron voltage & chloride concentration traces to a file with name **sREvF_full** (currently **RE.singv**) & **sREcliF_full** (currently **RE.singcli**), respectively

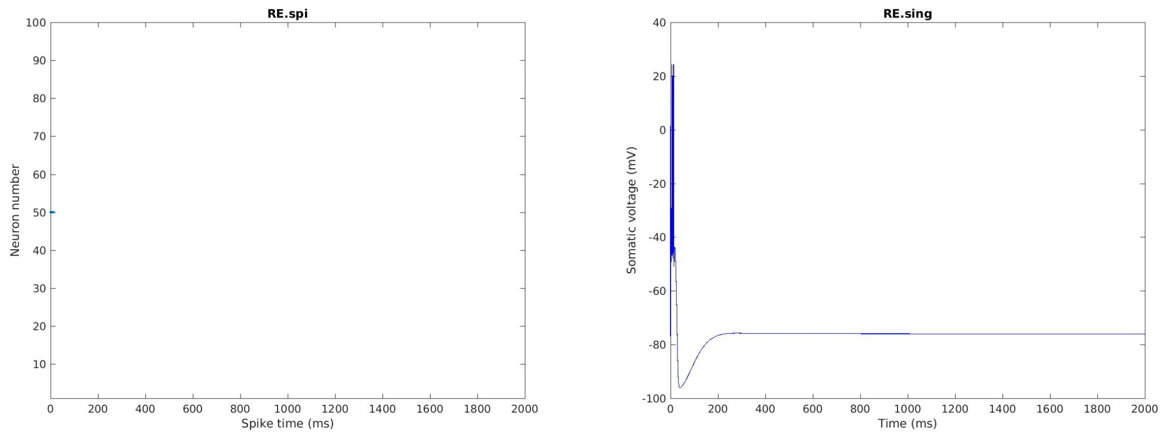
- Preliminary results
  - Network topology



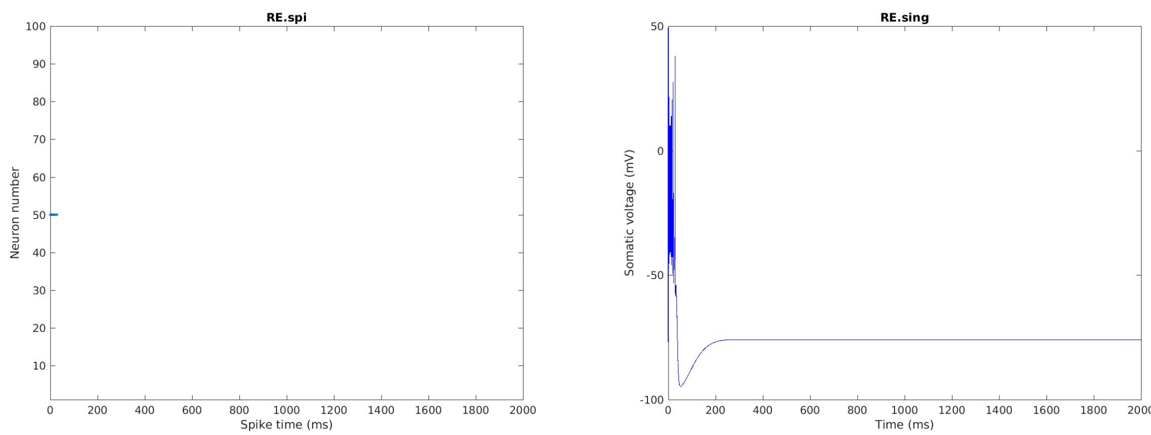
  - Network topology zoomed in



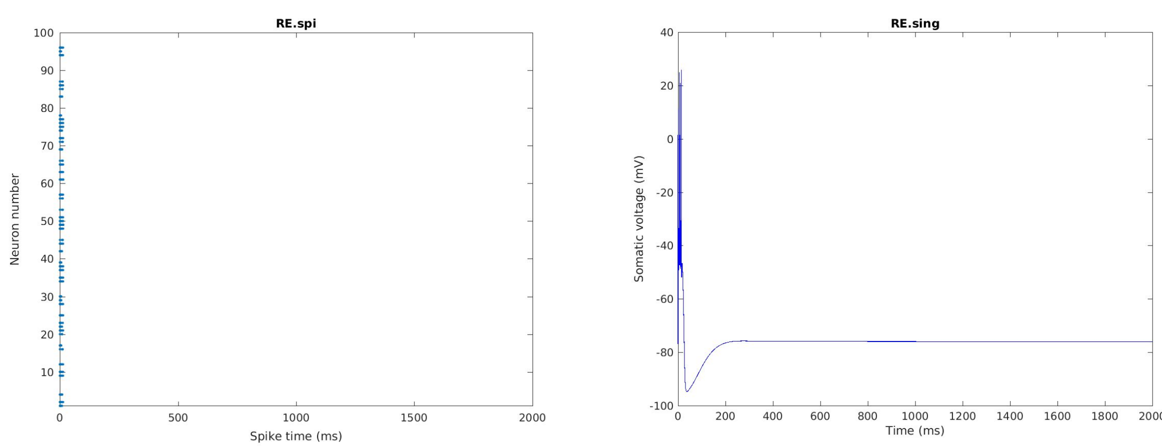
- Without chloride-dependence (**gabaa.mod**), gmax = **0.070 μS**, set single neuron to **0 mV**



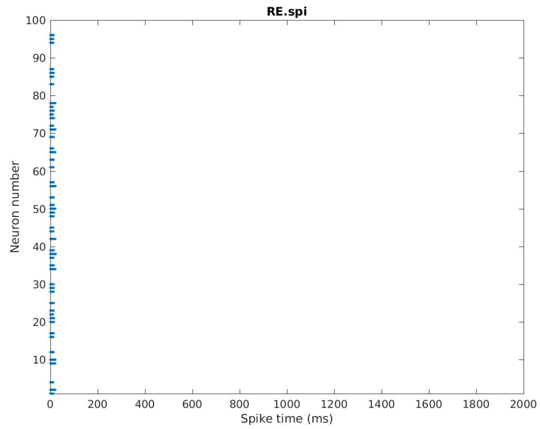
- Without chloride-dependence (**gabaa.mod**), gmax = **0.070 μS**, set single neuron to **50 mV**

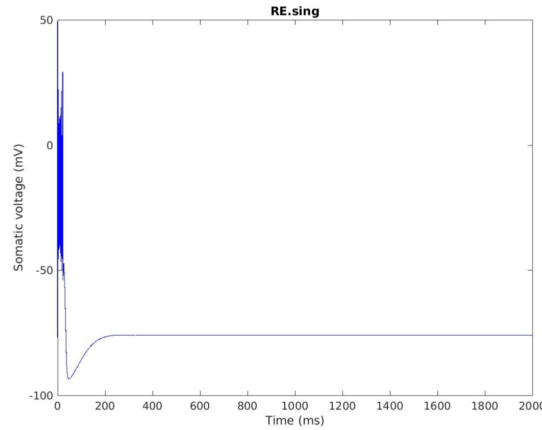


- Without chloride-dependence (**gabaa.mod**), gmax = **0.070 μS**, set random neurons to **0 mV**

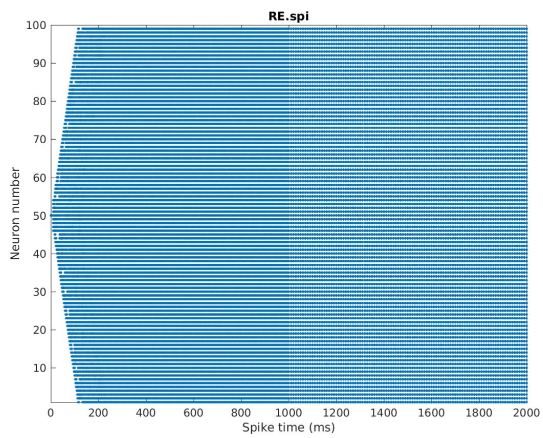


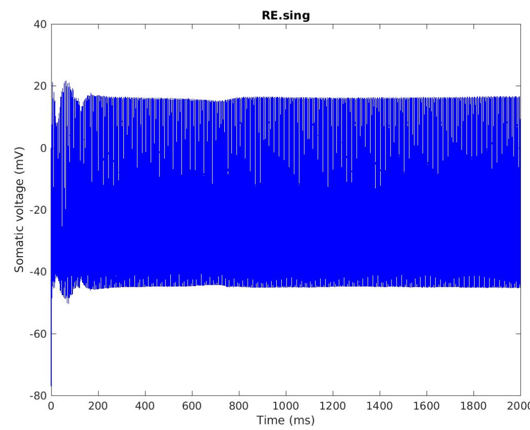
- Without chloride-dependence (**gabaa.mod**), gmax = **0.070 µS**, set random neurons to **50 mV**



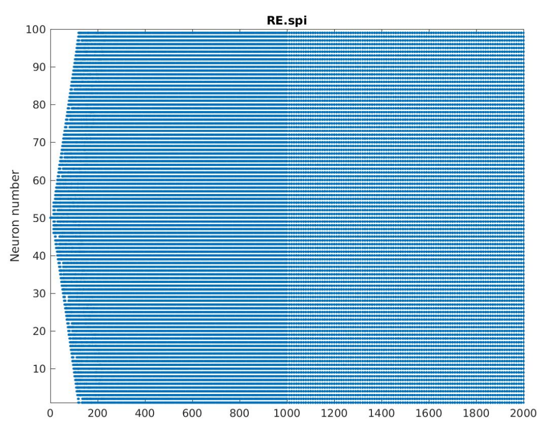


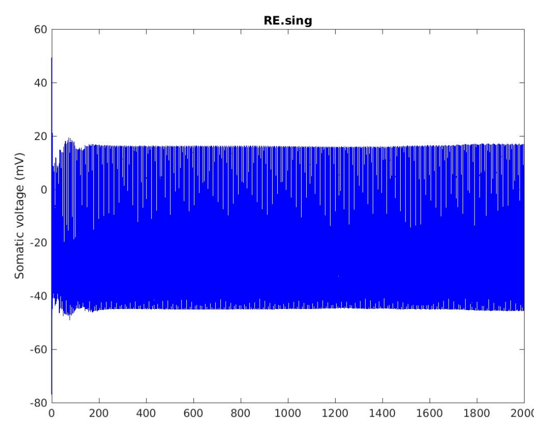
- With chloride-dependence (**gabaA_Cl.mod**), gmax = **0.070 µS**, set single neuron to **0 mV**



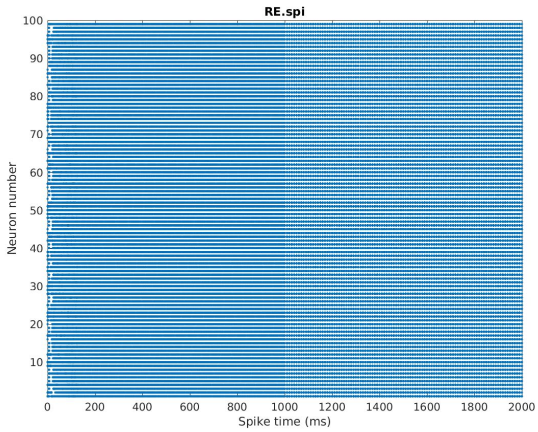


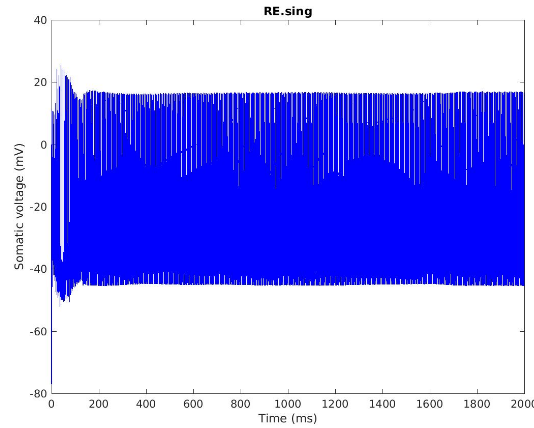
- With chloride-dependence (**gabaA_Cl.mod**), gmax = **0.070 µS**, set single neuron to **50 mV**



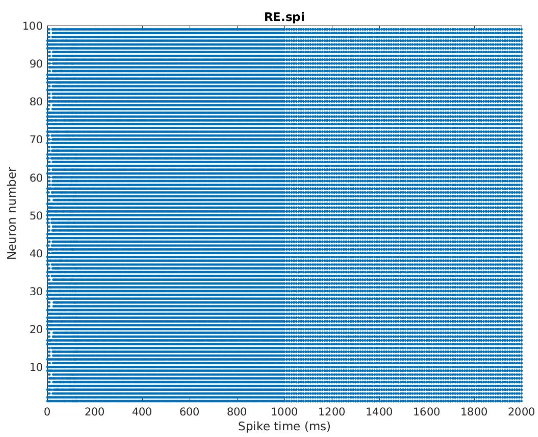


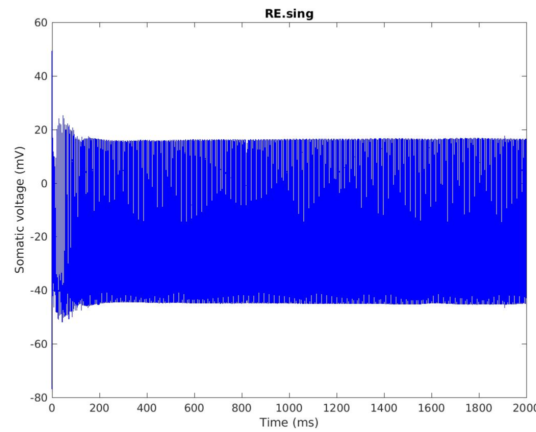
- With chloride-dependence (**gabaA_Cl.mod**), gmax = **0.070 µS**, set random neurons to **0 mV**



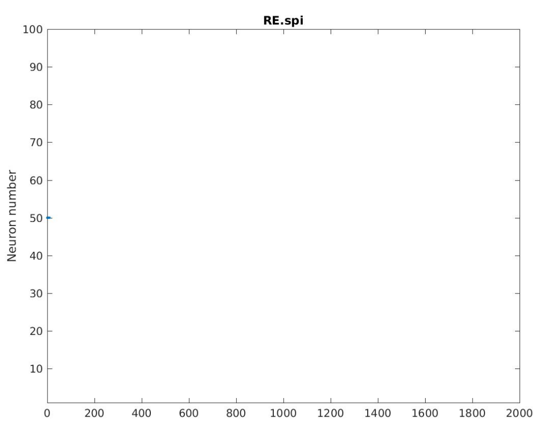


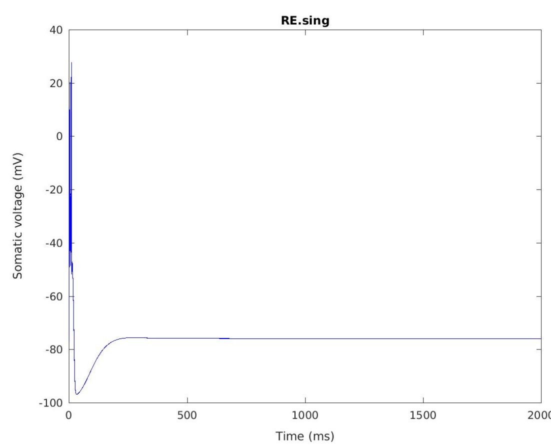
- With chloride-dependence (**gabaA_Cl.mod**), gmax = **0.070 µS**, set random neurons to **50 mV**



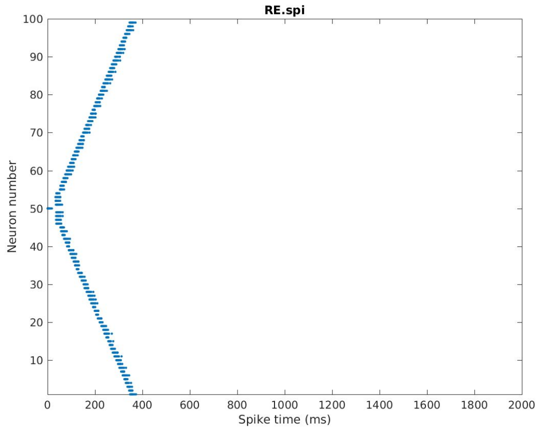


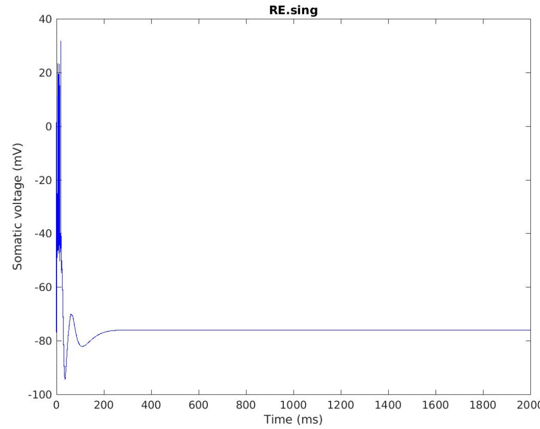
- gmax = **0.007 µS**, set single neuron to **0 mV**



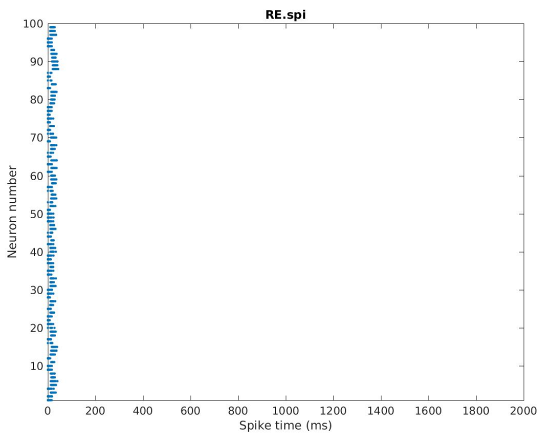


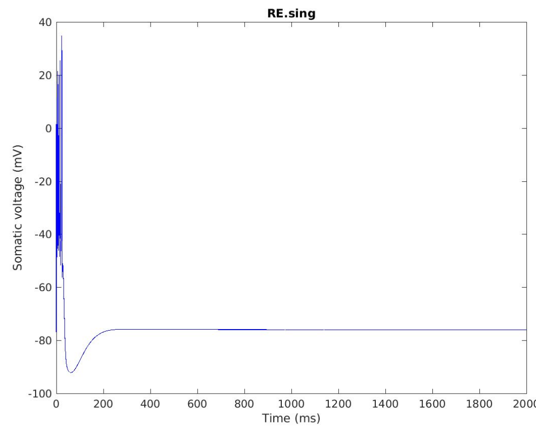
- gmax = **0.010 μS**, set single neuron to **0 mV**



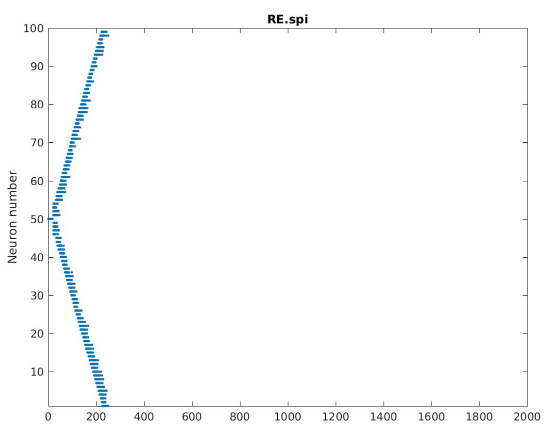


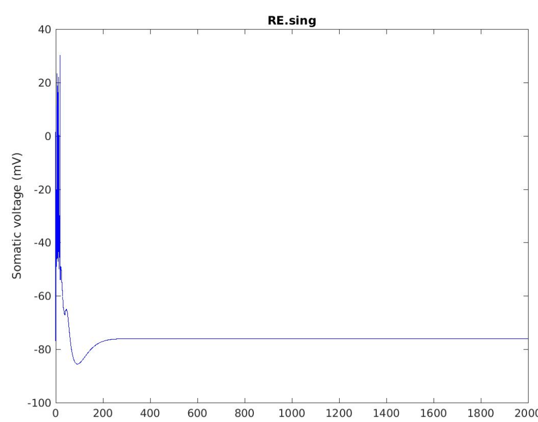
- gmax = **0.010 μS**, set random neurons to **50 mV**



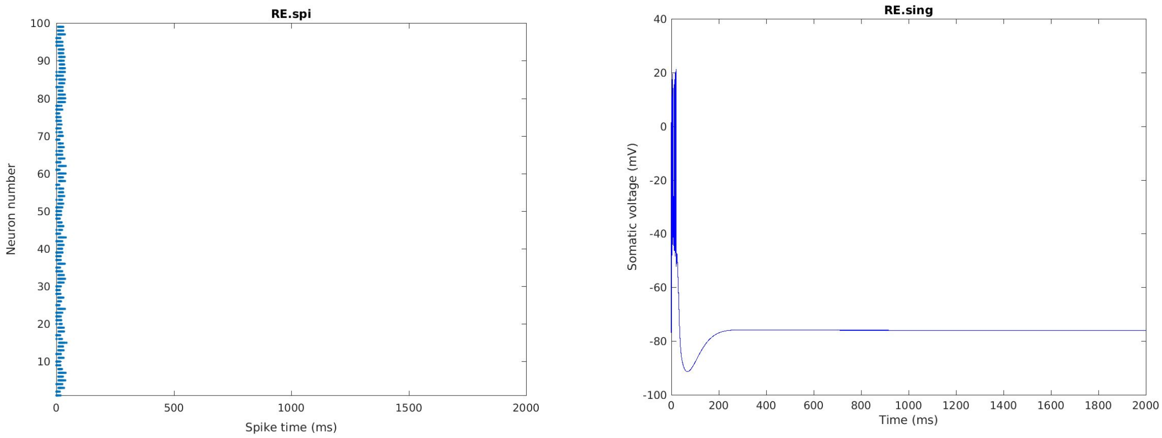


- gmax = **0.020 μS**, set single neuron to **0 mV**

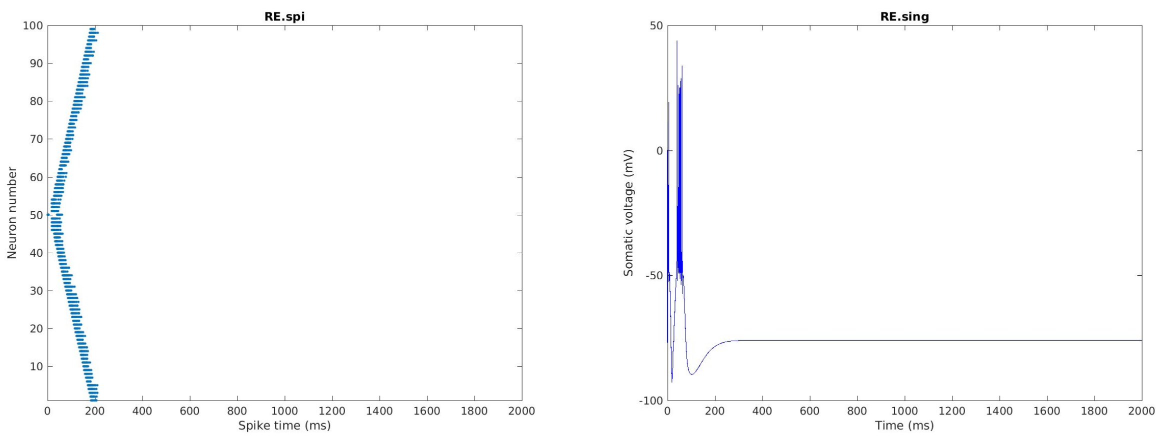




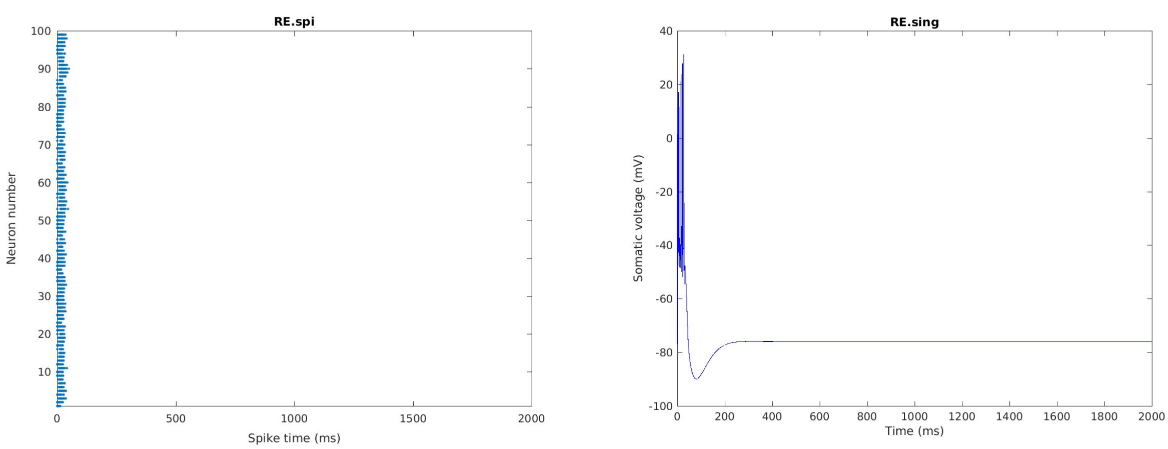
- gmax = **0.020 μS**, set random neurons to **50 mV**



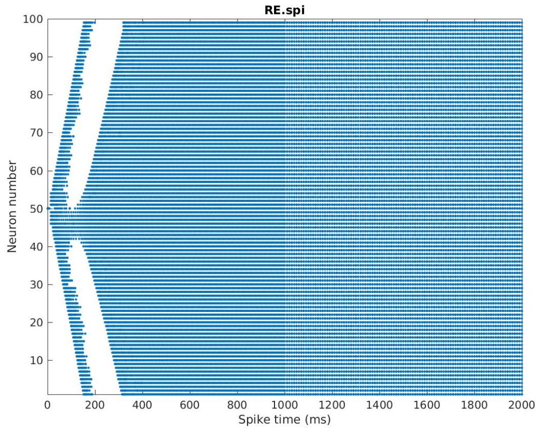
- gmax = **0.030 μS**, set single neuron to **0 mV**

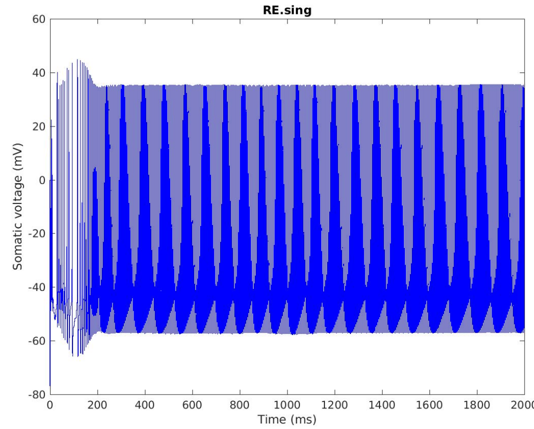


- gmax = **0.030 μS**, set random neurons to **50 mV**

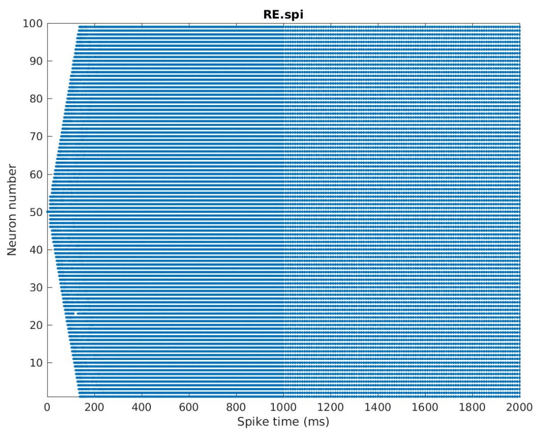


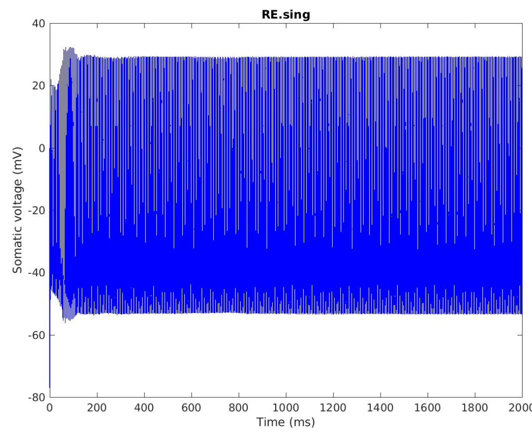
- gmax = **0.040 μS**, set single neuron to **0 mV**



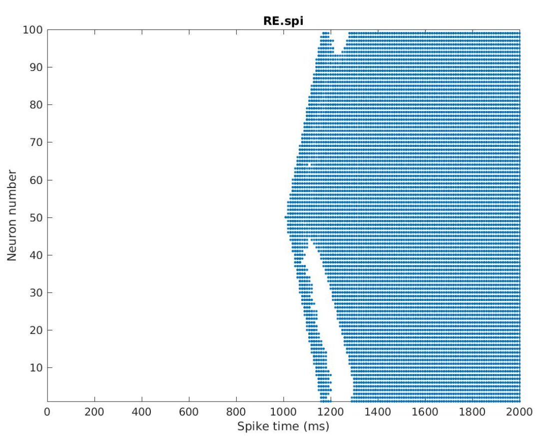


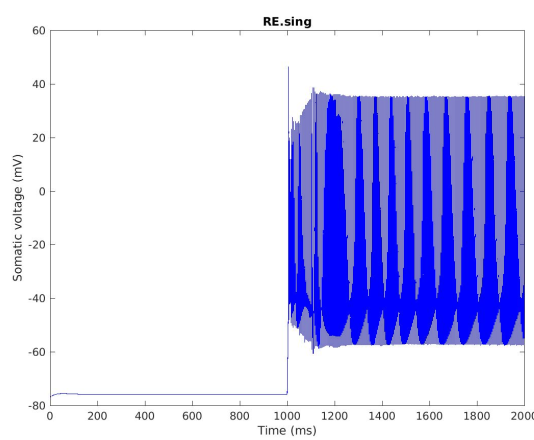
- gmax = **0.050 μS**, set single neuron to **0 mV**



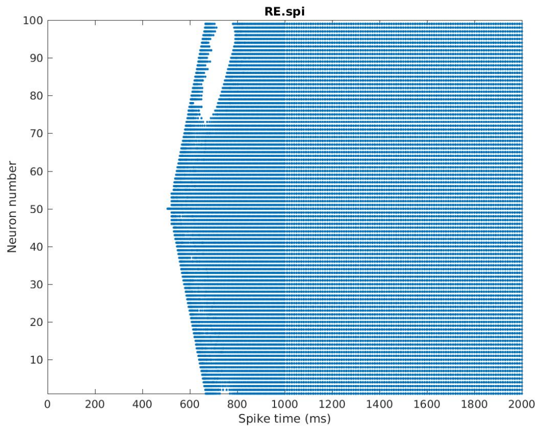


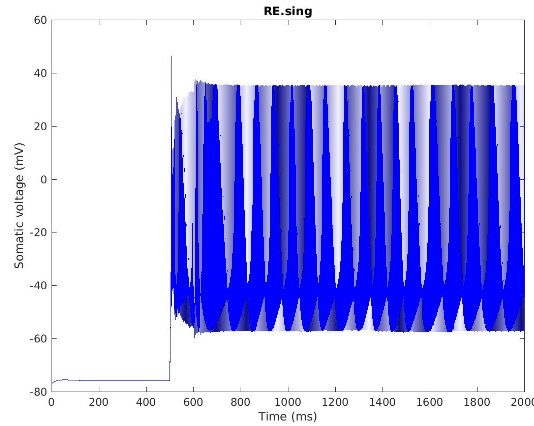
- gmax = **0.040 μS**, applied a current pulse (delay **1000 ms**, duration **100 ms**, amplitude **10 nA**) to single neuron



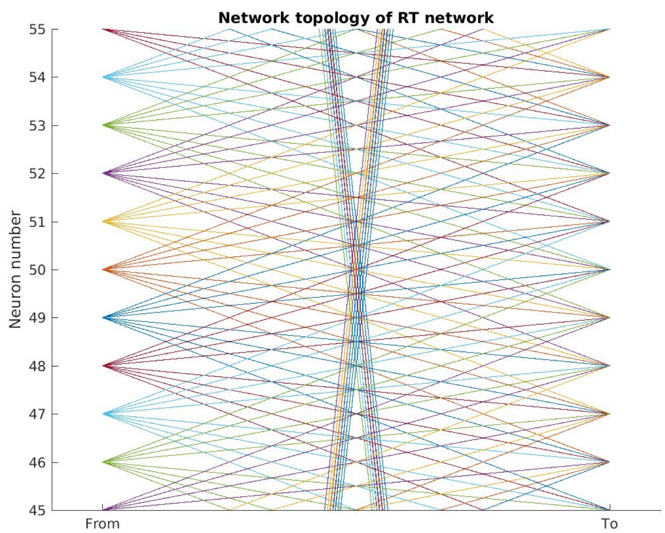


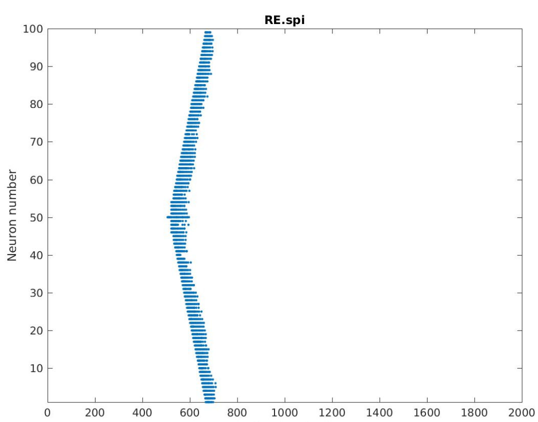
- gmax = 0.040 μS, applied a current pulse (delay **500 ms**, duration 100 ms, amplitude 10 nA) to single neuron

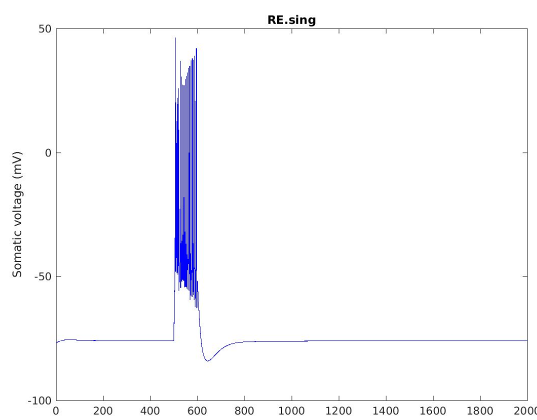




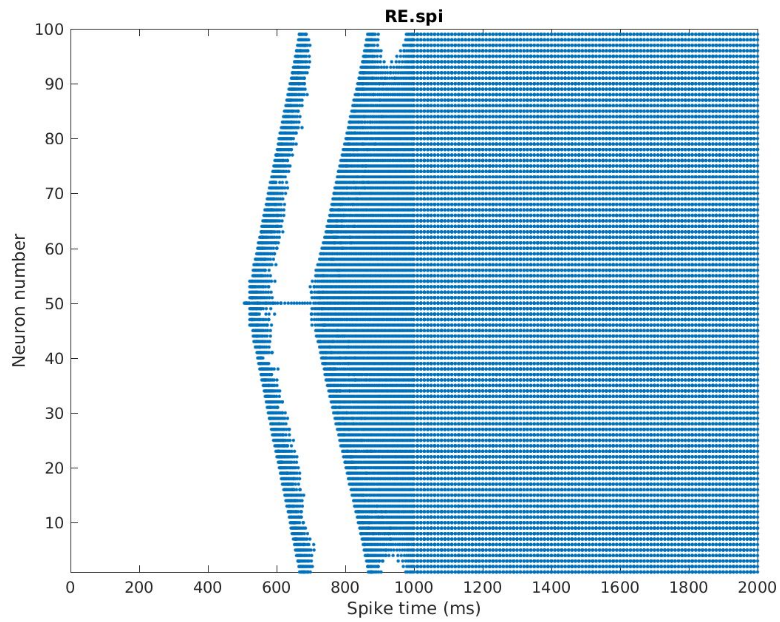
- Removed autapses

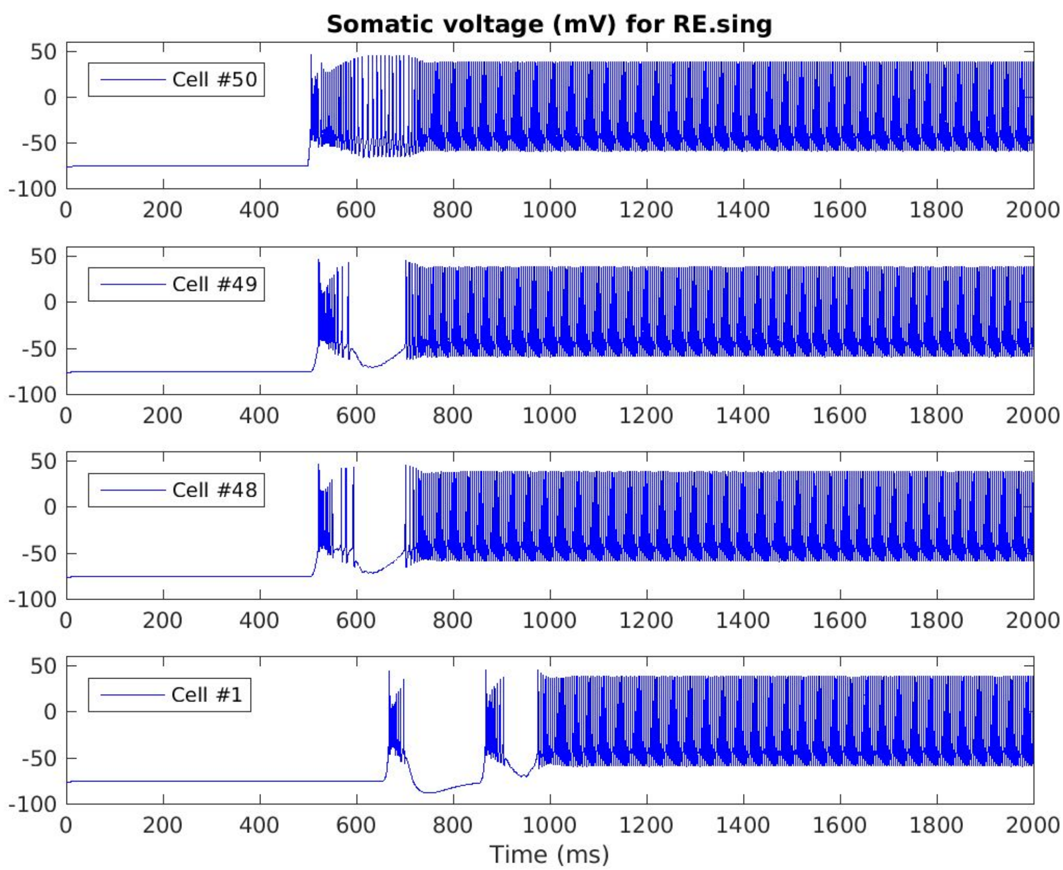




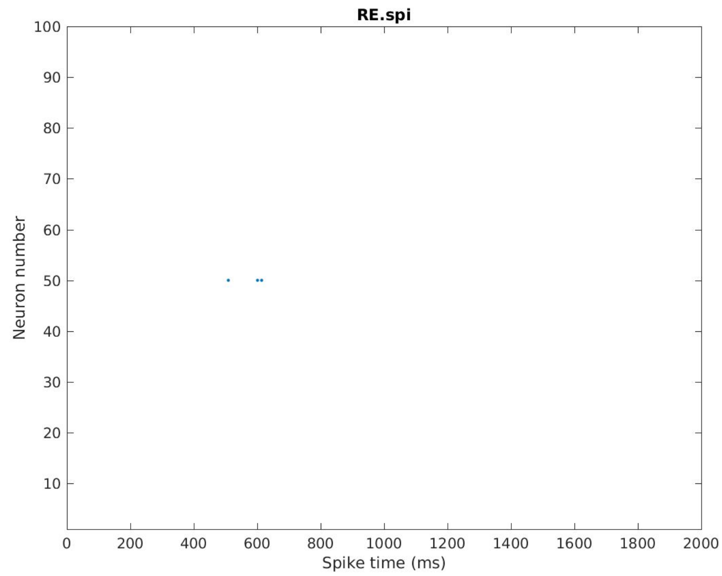


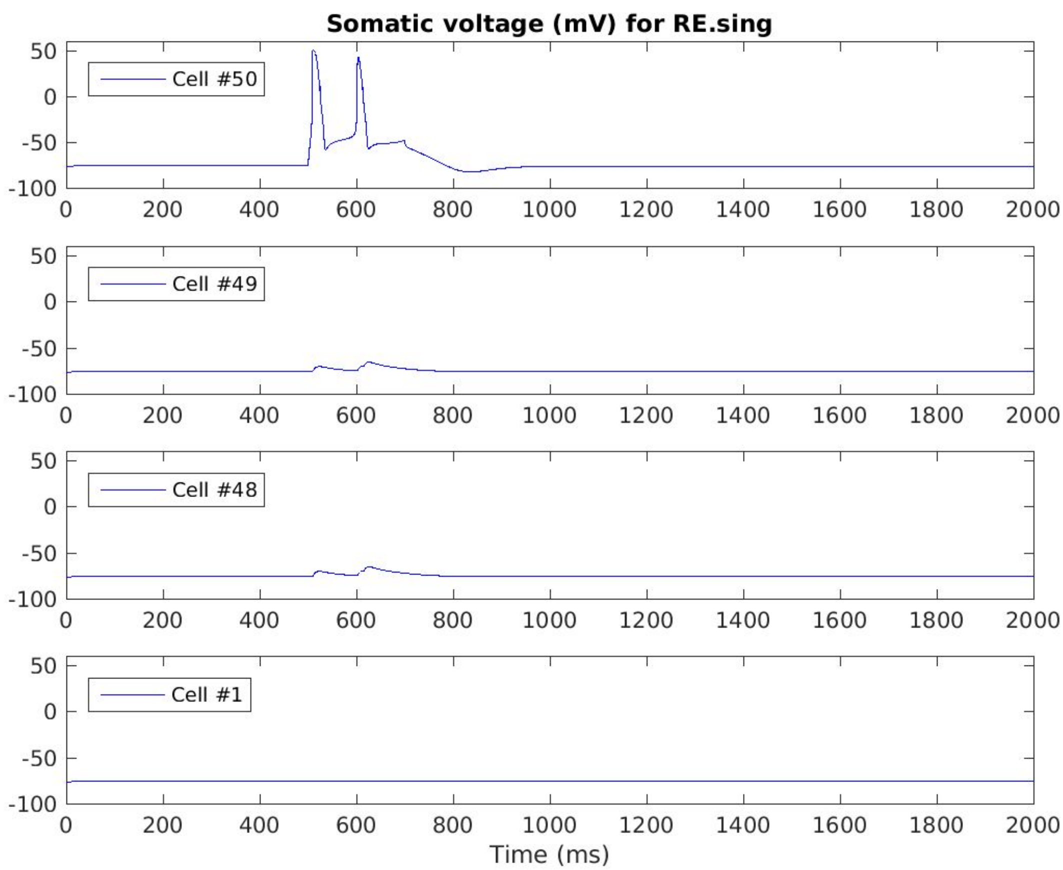
- gmax = 0.040 μS, applied a current pulse (delay 500 ms, duration **200 ms**, amplitude 10 nA) to single neuron



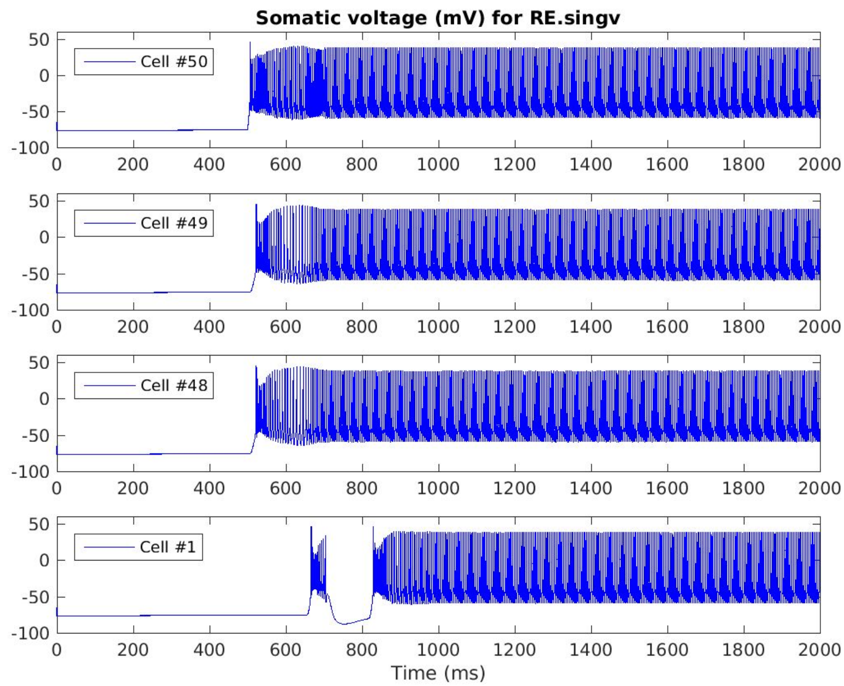


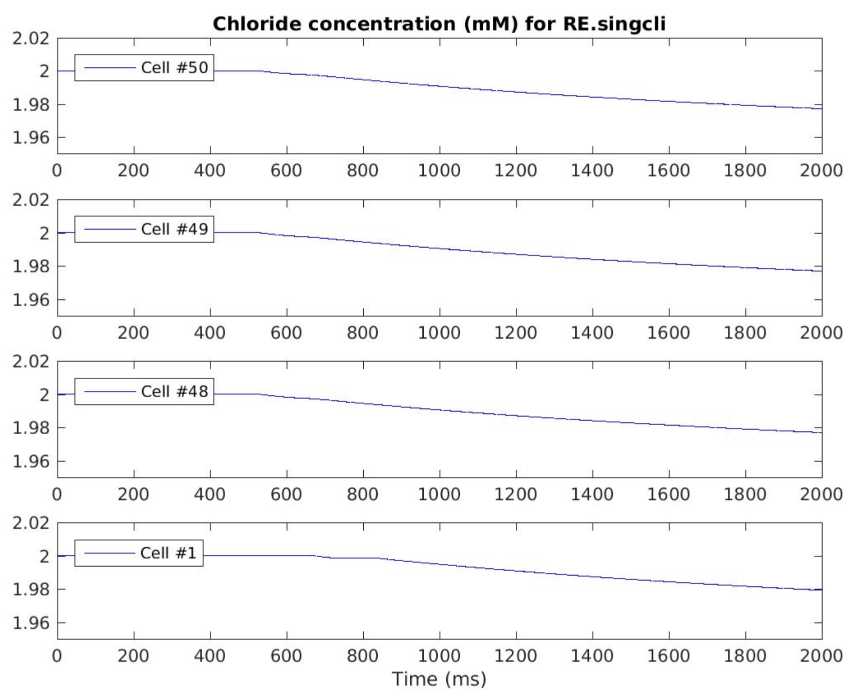
- When code was first transferred from run.hoc to neuronlaunch.m, **celsius** was not implemented correctly and was at the NEURON default **6.3 degrees Celsius**. This produced extremely slow action potentials:





- Fixed placement of **finitialize()** (should be before soma voltage is set) and plotted chloride concentration.





- **Why does chloride concentration decrease?**

Plan for next week

- LGN electrophysiology:
  - Try patching on Wed, Fri, Sat

- Chloride-dependent RT Network:
  - Understand how each **mechanism** works and potentially change synaptic weights as a function of **Ninputs**
  - Change **synaptic weights** and **chloride extrusion time constants**
  - Vary parameters such as **celsius, syn_del**, **syn_w**, **REGgaba**, **cp_dur**, **cp_amp**

- Data Analysis - voltage traces:
  - Fix **find_LTS.m** to enforce overrules.
  - Rerun dclampDataExtractor.m with all the **overrules enforced** (**dclampDataExtractor14.slurm**, giving the version **old15**)
  - Run **compare_statistics.m**: Compare with **version 13** (old13); find all traces with altered LTS onset times and reclassify; find all traces with altered spikes per peak and reclassify
  - Ran **update_figures.sh**. Examined each special cases folder and looked for any classification discrepancies
  - Run **find_special_cases.m**, reclassify. Run **copy_LTS_figures.sh**, then **backup_figures.sh**
  - Run **find_more_gray_area_traces.sh**, reclassify
  - Run **find_remaining_vtraces_scaled.m** & **check_filecounts.sh** again to make sure all **7430** voltage traces were classified both in the set **peakclass** and in the set **noisiness**.
  - Run **update_figures.sh** again. Examine each special cases folder and look for any classification discrepancies
  - Compute new histograms, thresholds, correlations, bargraphs, passive parameters under **all fitmodes**

- Brian's tasks:
  - Devise a good threshold for **"noisy recordings"**
  - Take out any trace with error greater than the threshold from the trace averaging. Compute the **mean recorded voltage change** ($\Delta\bar{V}_{rec}$), the **mean current pulse amplitude** (**cpa_mean**), the **mean pulse width** (**pw_mean**) by averaging over all traces remaining.

12/19/2016

Audio monitor

Dear Mark,

This is what I found in a forum:

"They suggested me to check on WPI for an external audio monitor."
I couldn't find it though.

"If you want the least expensive solution, just hook up an active speaker (from your mp3 player). There are connector adapters for that. You might want to mute the audio when the Axoclamp input is in open circuit condition (dedicated audio monitors may have a feature to suppress upon large amplitude oscillations / amp saturation) or, if possible, ground the input with a clip (does not work with modern pipette holders). "

"If you solder a BNC cable with a Audio 3.5mm Cable, it is possible to connect directly the BNC output (Monitor) to the Mic jack in the PC, and in windows 7, there is a mode were all sounds received via the Mic are re-directed to the system speakers, that worked for me. "

https://www.researchgate.net/post/is_there_a_way_to_audio_monitor_an_electrophysiology_signal_using_Clampex_10 [accessed Dec 19, 2016].

I also found this page, which shows you how to build a voltage-controlled oscillator:
http://www.instructables.com/id/How-to-Make-a-Voltage-Controlled-Oscillator/

Which one will be best?

Thanks,
Adam

1/9/2017

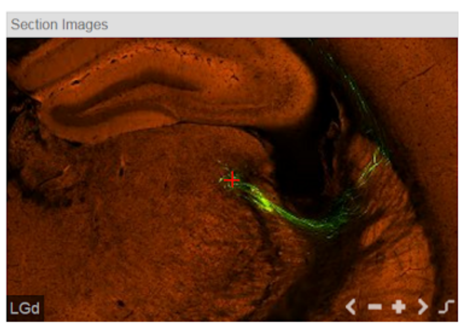
<u>Literature search on LGN slice recordings</u>

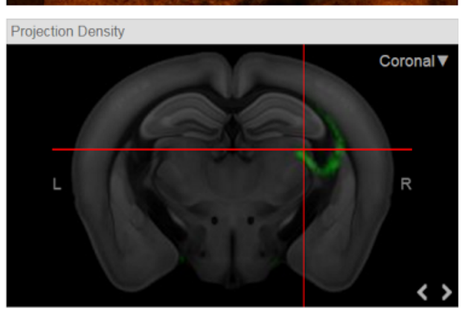
- Geoff:
  - Thalamic Relay Functions and Their Role in Corticocortical Communication: Generalizations from the Visual System
    http://www.sciencedirect.com/science/article/pii/S0896627301005827
  - Tonic and burst firing: dual modes of thalamocortical relay
    http://www.sciencedirect.com/science/article/pii/S0166223600017148
  - Developmental Remodeling of the Retinogeniculate Synapse
    http://www.sciencedirect.com/science/article/pii/S0896627300001665
- Adam:
  - Electrophysiological Properties of Dorsal Lateral Geniculate Neurons in Brain Slices from ME7 Scrapie-Infected Mice
    http://www.sciencedirect.com/science/article/pii/S0014488697967133?np=y
  - Changes in firing pattern of lateral geniculate neurons caused by membrane potential dependent modulation of retinal input through NMDA receptors
    http://onlinelibrary.wiley.com/doi/10.1113/jphysiol.2007.131540/full

<u>Protocols for LGN slice recordings</u>

- Immunohistochemistry:
  - Excitatory cell marker? CAMKII?

- Biocytin-filled projections:
  - Coronal sections should show axons going rostro-ventro-lateral





- Single cell properties:
  - I-V curve
  - passive properties (input resistance, time constant)
  - resting membrane potential
  - action potential firing threshold
  - action potential shape (spike amplitude, AHP amplitude, spike rise time, spike decay time, spike half width)
  - morphology (biocytin fills)

- Synaptic properties:
  - EPSP shape (amplitude, rise time, decay time)
  - firing patterns evoked by a pulse train of afferent stimuli

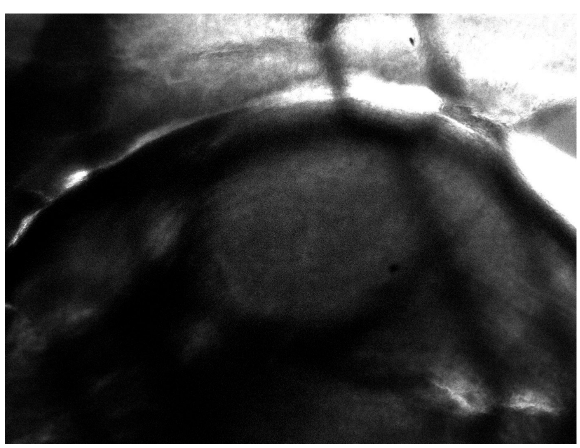
- Protocols:
  - Slicing:
    - **250 um** coronal sections with **caudal down** (cut off cerebellum to form flat end)
  - After pipette is in solution:
    - Amplifier at **V-CLAMP** mode, reading **I**
    - Open **00_VC_gap_free.pro**
    - Reset **Data File Names** to reflect new cell
    - Remove any previous holding voltage on amplifier or Clampex
    - Open default **Membrane Test** (**5 mV** pulse at **10.0 Hz**)
  - Right before breaking in:
    - Reset **pipette offset** so that no current is applied at baseline
    - Keep amplifier at **V-CLAMP** mode, recording **I**
    - Hold voltage at **-70 mV** with **amplifier** (since Clampex can't hold potentials when the default Membrane Test is used)
  - After breaking in:
    - Gap free (**A20170111_0000.abf**):
      - Duration: **60 sec**
    - Switch amplifier to **I = 0**, reading **Vm**
    - **Remove holding voltage** on amplifier
  - Membrane test for passive properties (input resistance, time constant)?
    - Open **01_VC_membrane_test.pro**
    - Make low-pass Bessel filter **100 kHz**
    - Switch amplifier to **V-CLAMP** mode, reading **I**
    - Hold at **-70 mV** with **Clampex**
    - Step (**A20170111_0001.abf**):
      - Amplitudes: **-75 mV**
      - Duration: **20 ms**
      - Frequency: **20 Hz** (every **50 ms**)
      - Repetition: **500** sweeps (**25 sec** total)

- For synaptic events:
  - Keep amplifier at **V-CLAMP** mode, reading **I**
  - Open **02_VC_synaptic_events.pro**
  - Hold at **-70 mV** with Clampex
  - Make low-pass Bessel filter **5 kHz**
  - Step (**A20170111_0002.abf**):
    - Amplitudes: **-70 mV**
    - Duration: **30000 ms**
    - Frequency: **0.033 Hz** (every **30 s**)
    - Repetition: **10** sweeps (**5 min** total)
- For resting membrane potential/spontaneous spiking activity:
  - Switch amplifier to **I = 0**, reading **Vm**
  - Open **03_I0_spontaneous_activity.pro**
  - Step (**A20170111_0003.abf**):
    - Amplitudes: **0**
    - Frequency: **0.1 Hz** (every **10 s**)
    - Repetition: **12** sweeps (**2 min** total)
- For I-V curve/action potential threshold/FI plot:
  - Open **04_CC_IV_curve.pro**
  - Switch amplifier to **I-CLAMP NORMAL**, reading **Vm**
  - Apply holding current with amplifier so that membrane potential is **-55 mV**
  - Step (**A20170111_0004.abf**):
    - Amplitudes: **-200:25:300 pA**
    - Duration: **1000 ms**
    - Frequency: **0.1 Hz** (every **10 s**)
    - Repetition: **21** sweeps (**3.5 min** total)
- For I-V curve:
  - Current clamp
  - Apply holding current so that membrane potential is **-70 mV**
  - Step (**A20170111_0005.abf**):
    - Amplitudes: **-200:25:300 pA**
    - Duration: **1000 ms**
    - Frequency: **0.1 Hz** (every **10 s**)
    - Repetition: **21** sweeps (**3.5 min** total)
- For biocytin fill:
  - 5% biocytin made up in H_2O
  - Retract slowly under membrane test Patch mode to let membrane **reseal** (resistance has to go back to Giga Ohms)
  - Washout excess biocytin with ACSF for **20 min**

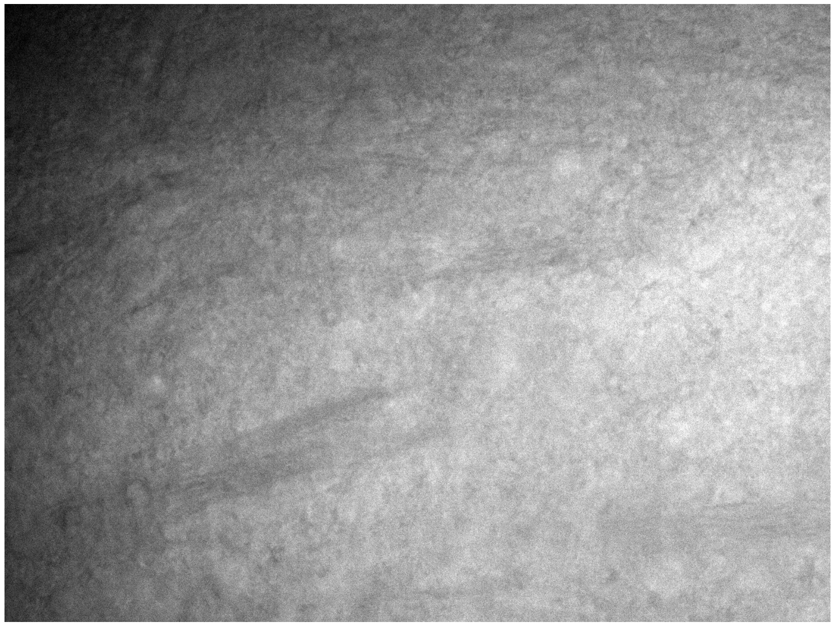
- Backup protocols
  - For EPSP:
    - Current clamp

- Apply holding current so that membrane potential is -60 mV
- Stimulate optic tract with bipolar tungsten electrode:
  - Amplitudes: 1-40 V
  - Duration: 50 ms
  - Frequency: 1 Hz
  - Repetition:
- Biocytin fill for sharp electrode:
  - 2% biocytin made up in 0.05 M Tris/1 M KCl (resistance 70–150 MV)
  - Current clamp
  - Step:
    - Amplitude: 0.6~0.9 nA
    - Duration: 300 ms
    - Frequency: 0.6 Hz (every 1667 ms)
    - Repetition: 540 (a minimum of 15 min)
- Membrane test for sharp electrode:
  - Current clamp
  - Apply holding current so that membrane potential is -60 mV
  - Record holding current value
  - Step:
    - Amplitudes: -50 pA
    - Duration: 100 ms
    - Frequency:
    - Repetition:

- Tested protocols with model cell
- Attempted to record in a 2-month old mouse:
  - ACSF was 298 mmol/kg
  - NMDG was 310 mmol/kg
  - Pipette resistances were 2.4~3.3 MOhm (Thin-wall pipettes with I.D. 1.10 mm and O.D. 1.50 mm were used under previous puller settings)
  - LGN:
    - Under 5X:



- Under 40 x:



- No Gigaohm seal was formed. Possible reasons:
  - The slices were unhealthy (the extracellular matrix is very loose, and the cell boundaries disappear when approached by a pipette). Perfusion might have been imperfect; note color of brain next time.
  - Positive/negative pressure too high (3~5 mL was used for positive pressure; 4~5 mL was used for negative pressure)

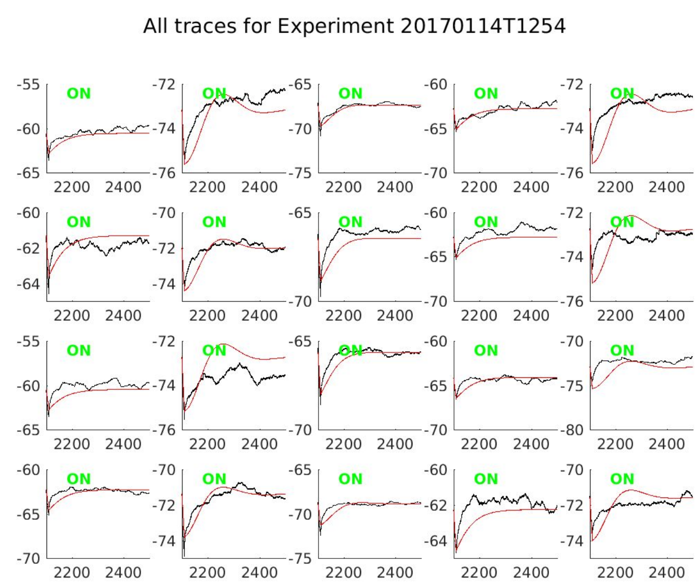
1/4/2017~1/17/2017

Passive Fitting (*cont'd)

- Made geometry (L, diam of soma and dendrite) params:
    - Forced **length of soma** to be equal to the **diameter** to reduce the number of parameters
    - Forced **dend1[1]** and **dend1[2]** (the **middle** and **distal** dendrite, respectively) to have equal diameters **diam_dend2** and equal length ½ * **L_dend2**
    - Initial values and boundaries for each parameter (based on the distribution of the estimated parameters from the curve-fitting method):

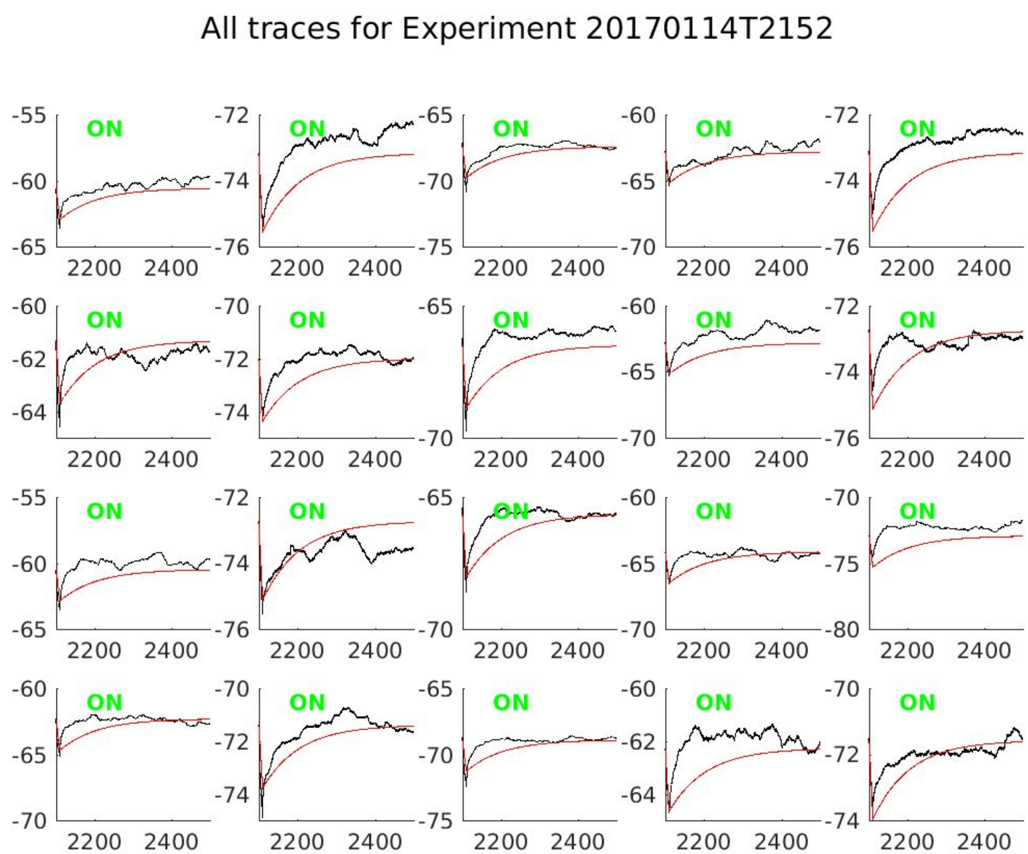
Parameter	Initial value (μm)	Lower bound (μm)	Upper bound (μm)
diam_soma	38.42	30	100
L_dend1	12.49	5	120
diam_dend1	10.28	1	30
L_dend2	84.67	5	120
diam_dend2	8.5	1	30

-
    - Some questions:
        - What bounds would be more physiological?
        - Should we have restrictions on the relative lengths and diameters of each dendritic segment?
    - Made sure fitting still works (the following was for 5 different cells x 4 pharm conditions at 200% g incr):

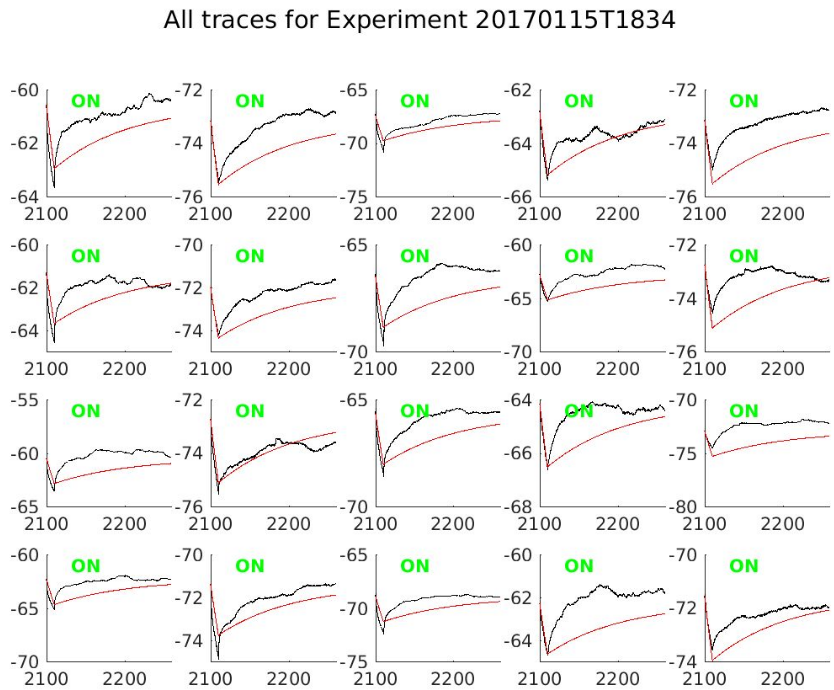


- Difficulty translating the results from the curve-fitting method to the biophysical model:
  - In NEURON, the soma is modeled as a cylinder, not a sphere as in the ball-and-stick model. What is the equivalent length & diameter of the cylinder given the diameter of the sphere?
  - In the biophysical model, there are 2 or 3 dendritic compartments (Destexhe's or Christine's, respectively). However, using only two terms in the curve-fitting method yields estimates for the length and diameter of a single dendritic compartment. How to decide how to convert a single length + diameter pair for the dendrite into two or three pairs?
    - Possible approach #1: Keep equal lengths and diameters for all compartments initially
    - Possible approach #2: Set the lengths and diameters according to original proportions

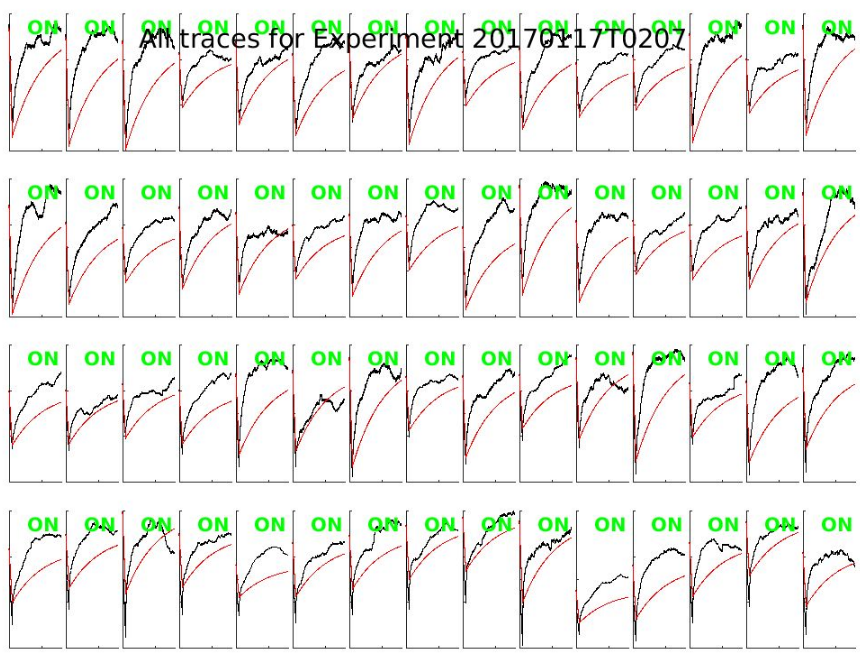
- Removed active channels during passive fitting



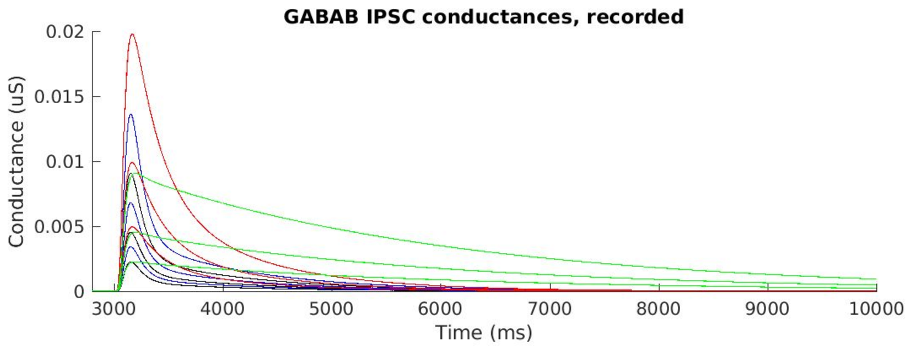
- Change interval of passive fit to just **160 ms** (including the **10 ms** current pulse)

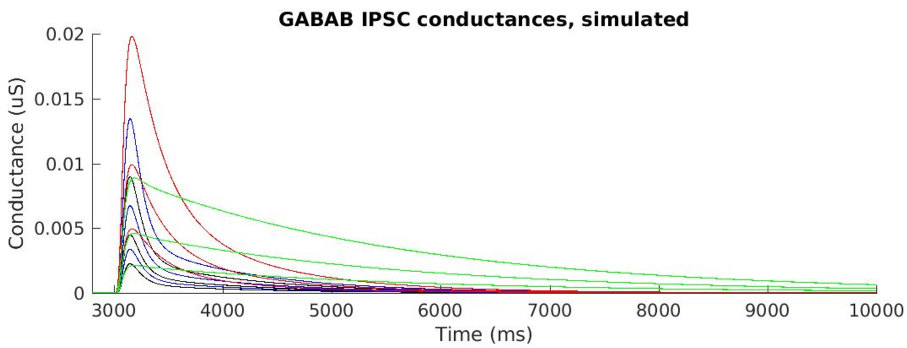


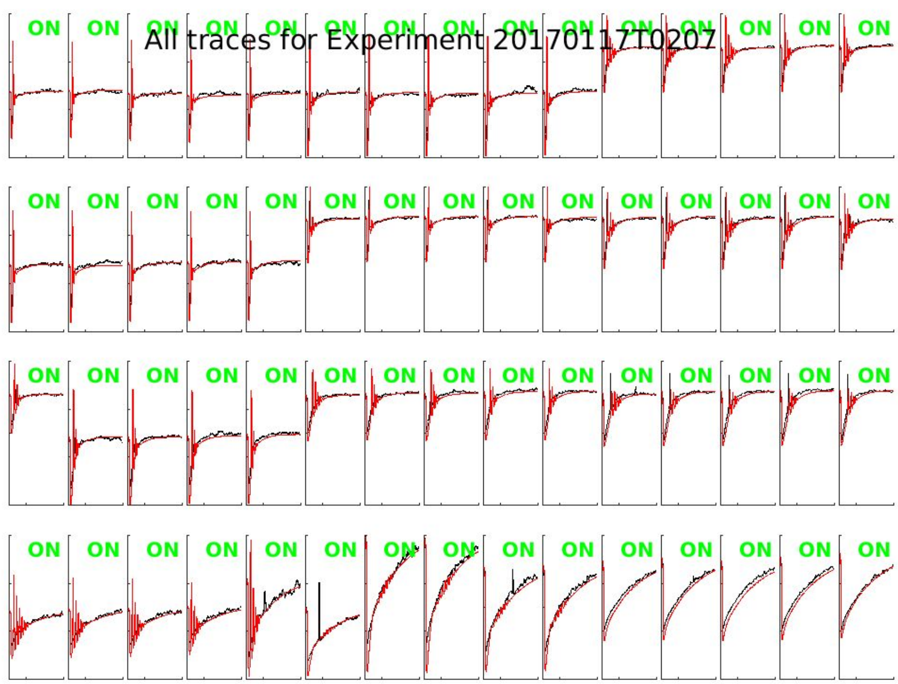
- Fitted all trials from the same cell (**E091710**, which was the cell that the initial parameters were fitted to by Christine)

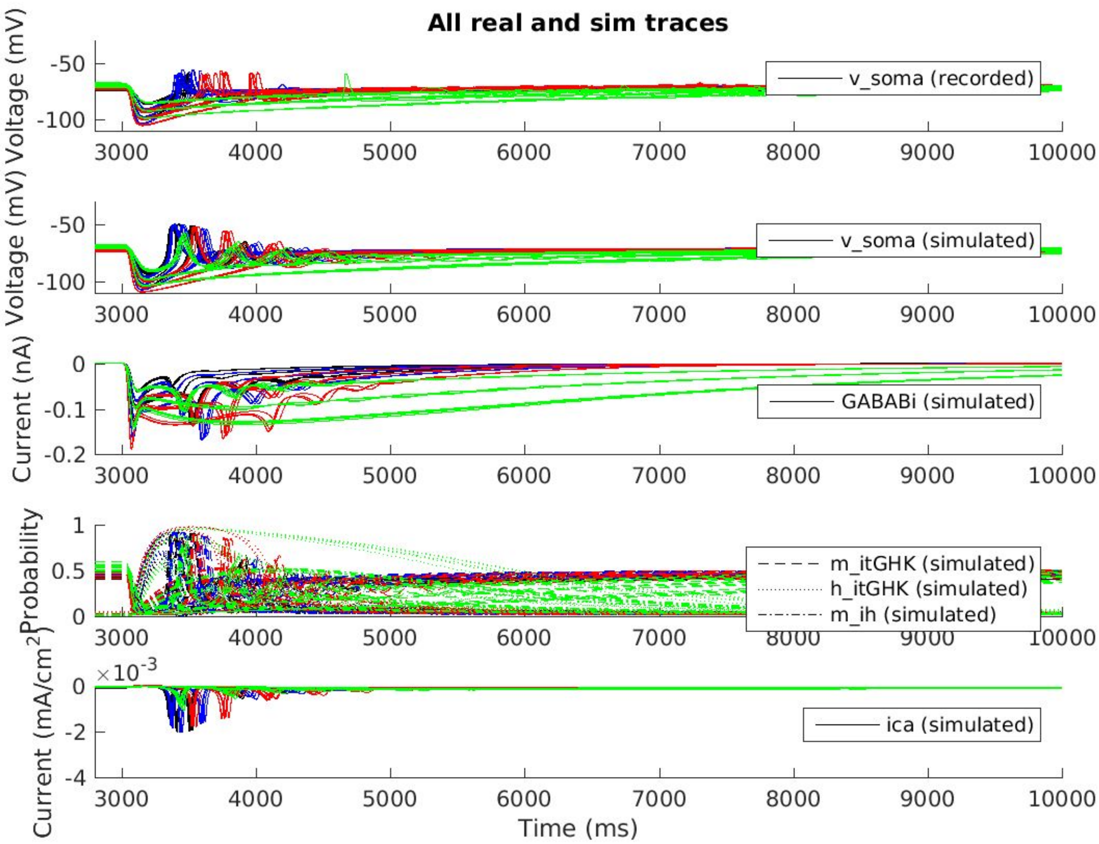


- Just to show that all **12** different GABA IPSC curves (4 pharm x 3 G incr conditions) will be used in the active fit:

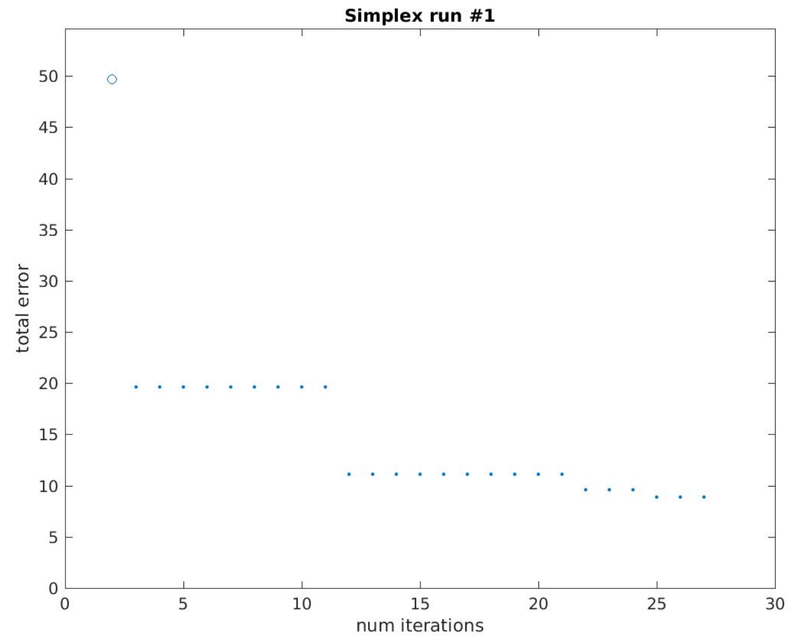


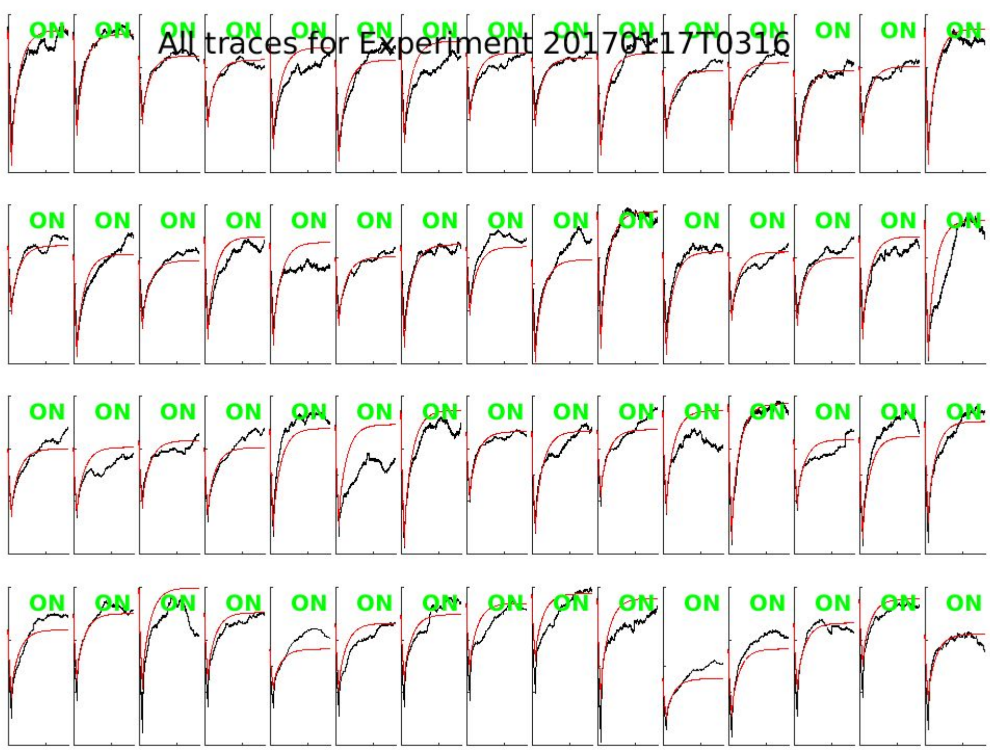




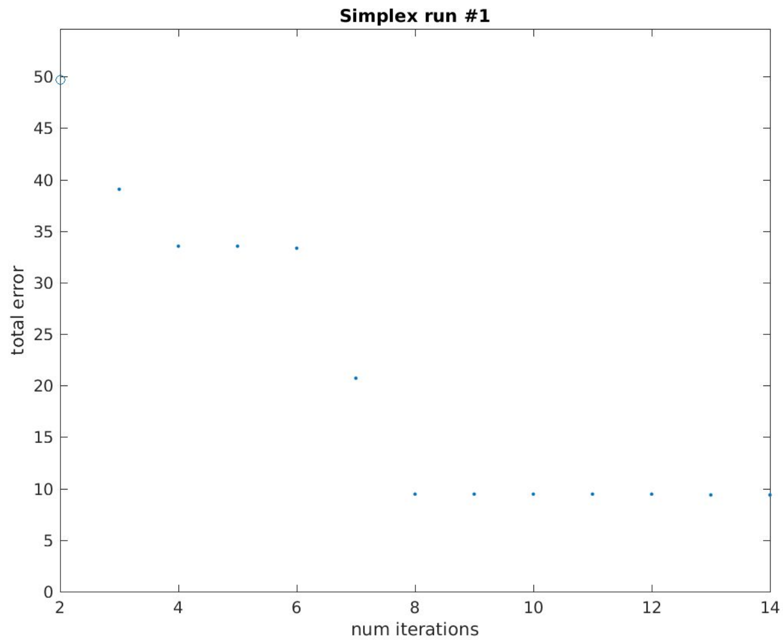

All real and sim traces
Voltage (mV)
v_soma (recorded)
Voltage (mV)
v_soma (simulated)
Current (nA)
GABABi (simulated)
Probability
m_itGHK (simulated)
h_itGHK (simulated)
m_ih (simulated)
Current (mA/cm2)
ica (simulated)
Time (ms)

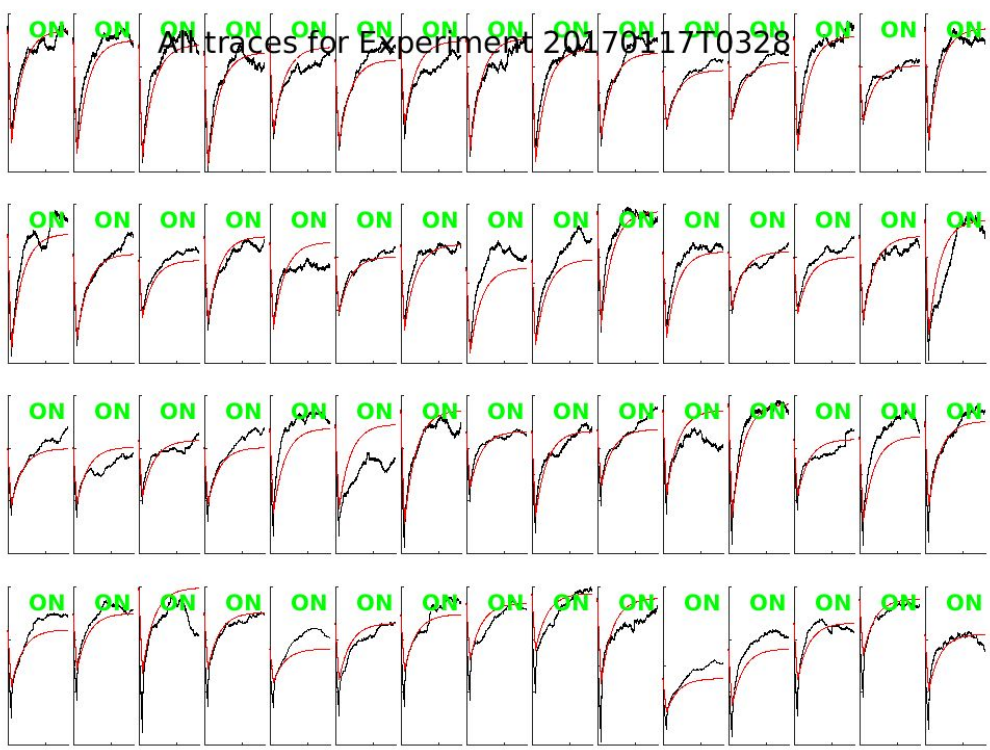
- Fitted E091710's passive traces with all passive params changing



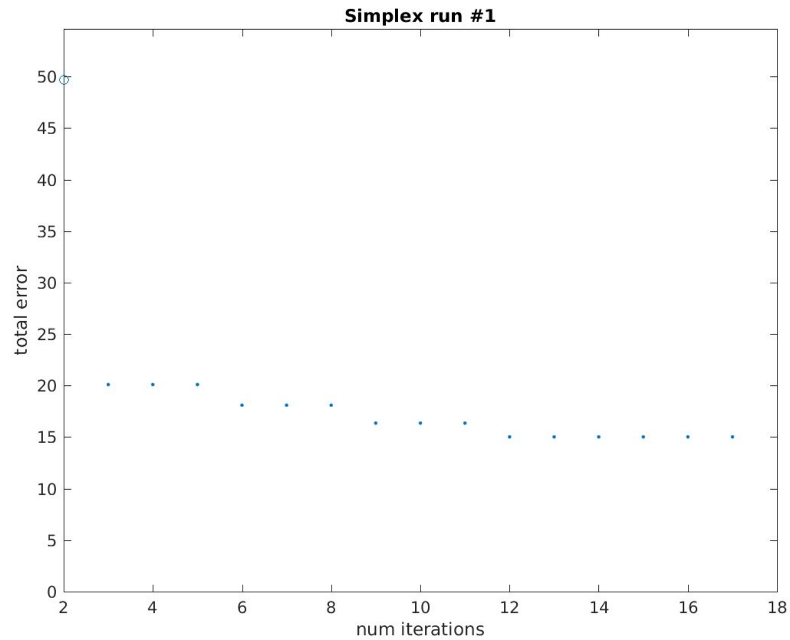


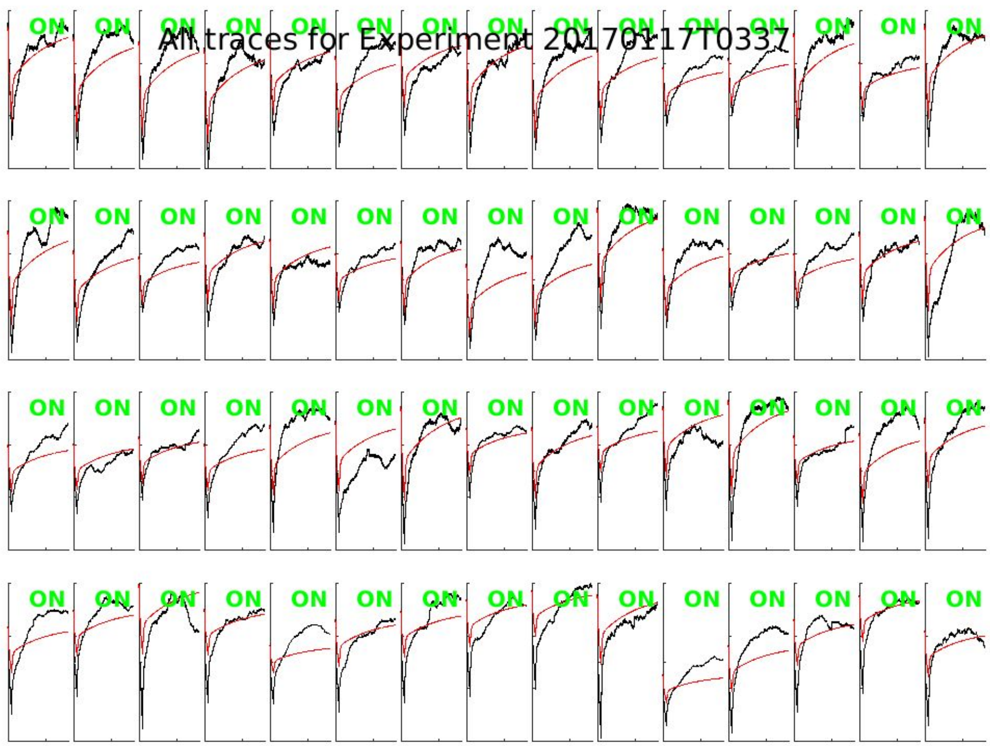
- Fitted E091710's passive traces with only gpas and epas changing



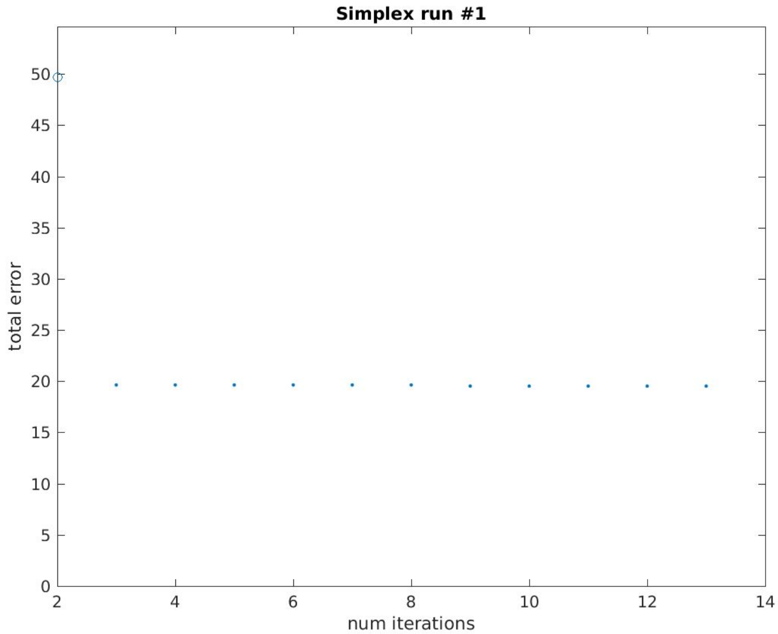


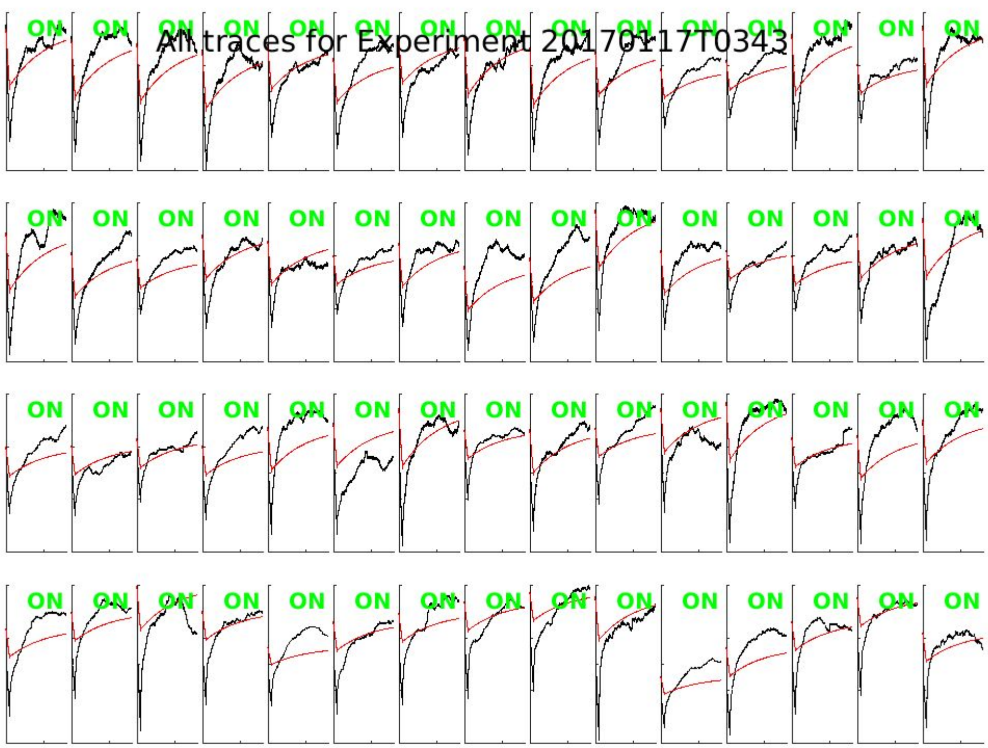
- Fitted E091710's passive traces with only diameters changing



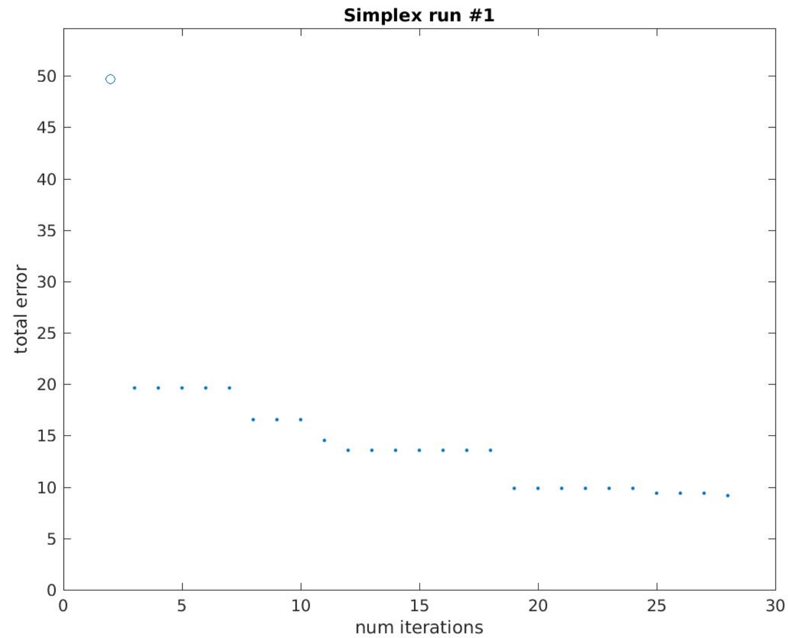


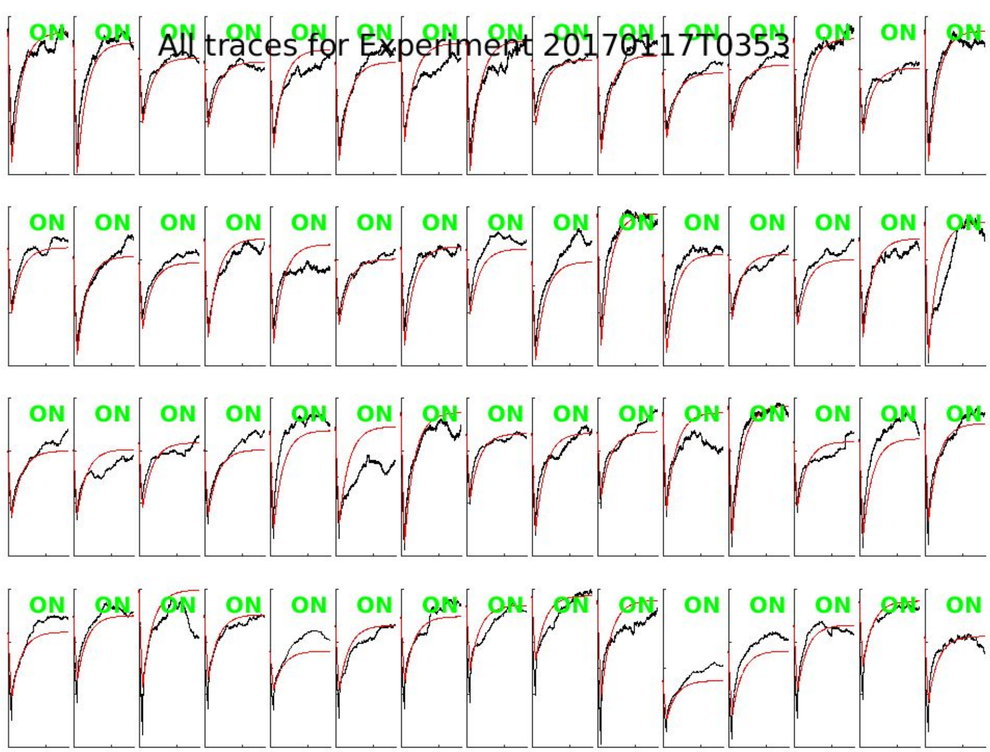
- Fitted E091710’s passive traces with only Lengths of dendrites changing





- Fitted E091710's passive traces with gpas, epas & Lengths of dendrites changing





- Overall comparison:

Condition	Original	All params	gpas epas	All diams	All Ls	gpas epas all Ls
Total error	50	~8	~9	~15	~20	~8
diam_soma	38.4	**50.7**	38.4	**65**	38.4	38.4
L_dend1	12.5	**111**	12.5	12.5	**120**	**57.7**
diam_dend1	10.3	**2.73**	10.3	**1.03**	10.3	10.3
L_dend2	84.7	**17.6**	84.7	84.7	**97.5**	**11.1**
diam_dend2	8.5	**20.1**	8.5	**22.2**	8.5	8.5
gpas	8.21e-6	**3.60e-5**	**2.59e-5**	8.21e-6	8.21e-6	**3.01e-5**
epas	-80.4	**-60**	**-105**	-80.4	-80.4	**-54.9**

- Modified **optimizergui_4compgabab.m**:
    - 2017-01-14 Added **num_buildparams** and added build parameters to paramnames, parammax, parammin, paraminit, dolog
    - 2017-01-15 Shortened **cprwin_orig** from [100, 500] to [100, 260] to be consistent with dclampPassiveFitter.m
    - 2017-01-16 Added **rowmode** so that each pharm, gincr pair is a row for rowmode == 2
    - 2017-01-17 Make **cm** and **Ra** fixed values
    - 2017-01-18 Changed **'MaxIter'** & **'MaxFunEvals'** to **200**
- Modified **run_neuron_once_4compgabab.m**:
    - 2017-01-14 Added **build()** to sim_cmd
    - 2017-01-14 Added **sim_mode** to both build() and sim() of sim_cmd
- Modified **singleneuron4compgabab.hoc**:
    - 2017-01-14 Build the TC neuron with arguments: 'diam_soma', 'L_dend1', 'diam_dend1', 'L_dend2', 'diam_dend2'
    - 2017-01-14 Added **TC4_pas.tem** so that active channels can be turned off when performing passive fitting

- Modified **TC4.tem**:
    - 2017-01-14 Removed tc4.geo and set up geometry in init with arguments
- Created **TC4_pas.tem**:
    - 2017-01-14 Modified from TC4.tem with active mechanisms removed
- Modified **dclampDataExtractor.m**:
    - 2017-01-16 Changed current pulse response to last just 150 ms (cprwin is changed from [95, 500] to [95, 260])

- Modified **FindIndToFit.m**:
  - 2017-01-16 Use all folders of the form **TAKE_OUT_*/*.png**
- Modified **find_LTS.m**:
  - 2017-01-16 Accounted for the condition that **npks == 0** (no local maximums exist)
- Modified **optimizer_4compgabab.m**:
  - 2017-01-17 Modified runauto so that it will fit current pulse response
- Modified **fminsearch3_4compgabab.m**:
  - 2017-01-17 Now saves the error figure and params as .p & .mat files
  - 2017-01-17 Now logs everything using **log_errors_params.m**
  - 2017-01-17 Changed **outparams.runnum_auto** to be current number (removed "+ 1")

1/17/2017~1/21/2017

Optimization algorithm

- Cleaned up code and understood the optimization algorithm implemented in **fminsearch3_4compgabab.m**:
  - Algorithm: "**Nelder-Mead simplex direct search**"
  - Optimization parameters used:

Parameter	Value	Meaning
tolf_rel	0.05	**relative error tolerance** (w.r.t. smallest error)
tolx_rel	0.05	**relative parameter change tolerance** (w.r.t. best set of parameters)
usual_delta	0.5	relevant increment for **non-zero parameters**
zero_term_delta	0.00025	absolute increment for **zero parameters**
rho	1	used in the computation of the **"reflection point"** and others
chi	2	used in the computation of the **"expansion point"**
psi	0.5	used in the computation of the **"contraction points"**
sigma	0.5	used in the performance of **"shrink"**

  - Step 1: Transform parameters to **unconstrained** space
    - For parameters used for fitting, transform initial values into the range $\left[\frac{3\pi}{2}, \frac{5\pi}{2}\right]$nonlinearly using **arcsin:**

      $$p = \arcsin(2\frac{x - LB}{UB - LB} - 1) + 2\pi,$$

      where LB and UB are the lower and upper bounds, respectively.
  - Step 2: Initialize simplex: a convex region in the **n-dimensional space** with **n+1 vertices**:
    - The first vertex is the set of **initial values**
    - Modified each parameter in turn by the following to get the 2nd to n+1th vertices:
      - If the parameter is not zero, increment parameter by:

        usual_delta * parameter value
      - If the parameter is zero, increment parameter by **zero_term_delta**
    - **Sort** vertices in **ascending total error value** so that the first vertex has the lowest total error
  - Step 3: Compute the "reflection point" and determine whether to use it

- Find the worst point (**pworst**) and compute the average of the better n points (**pbar**)
- Compute the "**reflection point**" (**pr**): the point **rho***||pbar - pworst|| away from pbar in the *opposite* direction of pworst
- Compute the error associated with the “reflection point”
- If the error associated with the reflection point is **better** than the **previous best point**, move on to Step 4a
- If the error associated with the reflection point is **not better** than the **previous best point** but **better** than the **second worst point**, **replace the worst point with the “reflection point”**; move on to Step 6
- If the error associated with the reflection point is **not better** than the **second worst point** but **better** than the **worst point**, move on to Step 4b
- If the error associated with the reflection point is **not better** than the **worst point**, move on to Step 4c

- Step 4a: Compute the “expansion point” and determine whether to use it
    - Compute the "**expansion point**" (**pe**): the point **chi*rho***||pbar - pworst|| away from pbar in the *opposite* direction of pworst
    - **Replace the worst point** with the **better of the "expansion point" and the "reflection point"**; move on to Step 6
- Step 4b: Compute the "outside contraction point" and determine whether to use it
    - Compute the "**outside contraction point**" (**pc**): the point **psi*rho***||pbar - pworst|| away from pbar in the *opposite* direction of pworst
    - **Replace the worst point** with the **better of the "outside contraction point" and the "reflection point"**; move on to Step 6
- Step 4c: Compute the "**inside contraction point**" and determine whether to use it
    - Compute the "**inside contraction point**" (**pcc**): the point **psi***||pbar - pworst|| away from pbar in the *SAME* direction as pworst
    - If it's better than the worst point, **replace the worst point** with the **"inside contraction point"**
    - Otherwise, no direction of replacement is better, move on to Step 5
- Step 5: Perform a "**shrink**"
    - Replace all points p other than the best point with the point **sigma***||p - pbest|| away from pbest in the direction of p
- Step 6: Analyze error improvement
    - **Sort** vertices in **ascending total error value** so that the first vertex has the lowest total error
    - Compute **maximum error change**, **maximum parameter change** and respective tolerances
- Step7: Iterate steps 3~6 until **one of** the following occurs:
    - **Both** of these are true:
        - The maximum coordinate difference between the current best point and the next best **ncp** (min(2, n)) other points in the simplex

is less than or equal to **simplexout.tolx**. Specifically, until

$$\max_i\left(\frac{|p_i - p_1|}{|p_1|}\right) \leq \mathrm{TolX}$$

for all parameters p,

where p_1 is the iteration of the parameter corresponding to the best vertex, and p_i is any other iteration of the parameter

- The corresponding maximum improvement in errors is less than or equal to **simplexout.tolf * error of best vertex**

- The **maximum number of iterations** is exceeded
- The **maximum number of function evaluations** is exceeded

- Step 8: Transform back parameters to **original space**

$$x = LB + \frac{\sin(p) + 1}{2}(UB - B)$$

- Logged the **optimization path** in a csv file and tried to improve the algorithm
  - Changed the initial parameter values for **cm** from 0.789 μF/cm^2 (Christine's initial value) to **0.88 μF/cm^2** and refitted E091710's passive traces with **gpas**, **epas** & **Lengths of dendrites** changing

1	itercount	how	func_evals	Error	Maximum error change	Error tolerance	Maximum parameter change	Parameter change tolerance	L_dend1	L_dend2	gpas	epas
2	0	initial	1	45.67	NaN	0.0001	NaN	0.0001	12.49	84.67	8.21E-06	-80.4
3	1	initial simplex	5	20.66	NaN	0.0001	NaN	0.0001	120	84.67	8.21E-06	-80.4
4	2	reflect: < second worst point	6	20.66	20.35	1.033	3.34	0.3921	120	84.67	8.21E-06	-80.4
5	3	reflect: < second worst point	7	20.66	20.35	1.033	3.34	0.3921	120	84.67	8.21E-06	-80.4
6	4	reflect: < second worst point	8	20.66	18.37	1.033	2.752	0.3921	120	84.67	8.21E-06	-80.4
7	5	reflect: < second worst point	9	20.66	15.08	1.033	2.752	0.3921	120	84.67	8.21E-06	-80.4
8	6	contract inside: < worst point	11	20.66	15.08	1.033	2.752	0.3921	120	84.67	8.21E-06	-80.4
9	7	reflect: < best point	13	16.74	18.22	0.837	2.948	0.4754	57.76	30.54	6.49E-05	-120
10	8	reflect: < second worst point	14	16.74	14.89	0.837	2.948	0.4754	57.76	30.54	6.49E-05	-120
11	9	reflect: < second worst point	15	16.74	3.925	0.837	2.948	0.4754	57.76	30.54	6.49E-05	-120
12	10	contract outside: < worst point	17	14.34	5.687	0.7171	1.86	0.4977	33.51	25.78	7.61E-05	-118.6
13	11	reflect: < best point	19	13.34	3.399	0.667	2.581	0.4835	48.53	5.422	7.04E-05	-37.04
14	12	shrink	25	13.34	12.42	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
15	13	reflect: < second worst point	26	13.34	12.42	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
16	14	contract outside: < worst point	28	13.34	12.42	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
17	15	reflect: < second worst point	29	13.34	7.49	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
18	16	contract inside: < worst point	31	13.34	7.438	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
19	17	reflect: < second worst point	32	13.34	5.402	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
20	18	contract inside: < worst point	34	9.785	3.555	0.4893	0.8037	0.4776	55.19	5.437	4.57E-05	-66.05
21	19	reflect: < second worst point	35	9.785	3.555	0.4893	0.8037	0.4776	55.19	5.437	4.57E-05	-66.05
22	20	reflect: < second worst point	36	9.785	3.555	0.4893	0.8037	0.4776	55.19	5.437	4.57E-05	-66.05
23	21	reflect: < second worst point	37	9.785	3.555	0.4893	0.8037	0.4776	55.19	5.437	4.57E-05	-66.05
24	22	contract inside: < worst point	39	9.156	4.181	0.4578	0.5901	0.4755	57.55	13.08	3.33E-05	-56.11
25	23	contract inside: < worst point	41	9.156	2.944	0.4578	0.4134	0.4755	57.55	13.08	3.33E-05	-56.11
26	24	reflect: < second worst point	42	9.156	0.8383	0.4578	0.9844	0.4755	57.55	13.08	3.33E-05	-56.11
27	25	contract inside: < worst point	44	9.156	0.8383	0.4578	0.9844	0.4755	57.55	13.08	3.33E-05	-56.11
28	26	reflect: < second worst point	45	9.156	0.629	0.4578	0.8282	0.4755	57.55	13.08	3.33E-05	-56.11
29	27	contract inside: < worst point	47	9.156	0.629	0.4578	0.8282	0.4755	57.55	13.08	3.33E-05	-56.11
30	28	contract inside: < worst point	49	9.156	0.509	0.4578	0.8282	0.4755	57.55	13.08	3.33E-05	-56.11
31	29	reflect: < second worst point	50	9.156	0.1826	0.4578	0.6848	0.4755	57.55	13.08	3.33E-05	-56.11
32	30	contract inside: < worst point	52	9.134	0.1427	0.4567	0.3548	0.479	53.59	7.175	4.01E-05	-71.48

- Changed the number of points to compare the best point against (**ncp**) from 2 to the **number of parameters** (i.e., all the rest of the points in the simplex)

7	5	reflect: < second worst point	9	20.66	20.35	1.033	3.34	0.3921	120	84.67	8.21E-06	-80.4
8	6	contract inside: < worst point	11	20.66	18.37	1.033	2.752	0.3921	120	84.67	8.21E-06	-80.4
9	7	reflect: < best point	13	16.74	22.05	0.837	2.948	0.4754	57.76	30.54	6.49E-05	-120
10	8	reflect: < second worst point	14	16.74	19.01	0.837	2.948	0.4754	57.76	30.54	6.49E-05	-120
11	9	reflect: < second worst point	15	16.74	18.22	0.837	2.948	0.4754	57.76	30.54	6.49E-05	-120
12	10	contract outside: < worst point	17	14.34	17.28	0.7171	2.11	0.4977	33.51	25.78	7.61E-05	-118.6
13	11	reflect: < best point	19	13.34	7.324	0.667	2.581	0.4835	48.53	5.422	7.04E-05	-37.04
14	12	shrink	25	13.34	731.8	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
15	13	reflect: < second worst point	26	13.34	341.5	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
16	14	contract outside: < worst point	28	13.34	16.47	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
17	15	reflect: < second worst point	29	13.34	16.09	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
18	16	contract inside: < worst point	31	13.34	12.42	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
19	17	reflect: < second worst point	32	13.34	7.49	0.6668	1.161	0.4906	40.8	12.03	7.33E-05	-82.03
20	18	contract inside: < worst point	34	9.785	10.99	0.4893	0.8037	0.4776	55.19	5.437	4.57E-05	-66.05
21	19	reflect: < second worst point	35	9.785	8.954	0.4893	1.014	0.4776	55.19	5.437	4.57E-05	-66.05
22	20	reflect: < second worst point	36	9.785	8.069	0.4893	1.014	0.4776	55.19	5.437	4.57E-05	-66.05
23	21	reflect: < second worst point	37	9.785	6.319	0.4893	0.9307	0.4776	55.19	5.437	4.57E-05	-66.05
24	22	contract inside: < worst point	39	9.156	4.284	0.4578	0.7709	0.4755	57.55	13.08	3.33E-05	-56.11
25	23	contract inside: < worst point	41	9.156	4.184	0.4578	0.5901	0.4755	57.55	13.08	3.33E-05	-56.11
26	24	reflect: < second worst point	42	9.156	4.181	0.4578	0.9844	0.4755	57.55	13.08	3.33E-05	-56.11
27	25	contract inside: < worst point	44	9.156	2.944	0.4578	0.9844	0.4755	57.55	13.08	3.33E-05	-56.11
28	26	reflect: < second worst point	45	9.156	2.183	0.4578	0.9844	0.4755	57.55	13.08	3.33E-05	-56.11
29	27	contract inside: < worst point	47	9.156	0.8383	0.4578	0.9844	0.4755	57.55	13.08	3.33E-05	-56.11
30	28	contract inside: < worst point	49	9.156	0.7013	0.4578	0.8282	0.4755	57.55	13.08	3.33E-05	-56.11
31	29	reflect: < second worst point	50	9.156	0.629	0.4578	0.8282	0.4755	57.55	13.08	3.33E-05	-56.11
32	30	contract inside: < worst point	52	9.134	0.5313	0.4567	0.4734	0.479	53.59	7.175	4.01E-05	-71.48
33	31	contract inside: < worst point	54	9.045	0.2934	0.4523	0.5932	0.4844	47.58	8.736	3.76E-05	-82.17
34	32	contract inside: < worst point	56	9.038	0.2387	0.4519	0.4008	0.4793	53.26	8.805	3.43E-05	-73.54

- Changed the **definition for parameter change** so that the largest parameter doesn't dominate (by normalizing each parameter)

17	15	reflect: < second worst point	29	13.34	16.09	0.6668	0.1895	0.05	40.8	12.03	7.33E-05	-82.03
18	16	contract inside: < worst point	31	13.34	12.42	0.6668	0.1895	0.05	40.8	12.03	7.33E-05	-82.03
19	17	reflect: < second worst point	32	13.34	7.49	0.6668	0.1895	0.05	40.8	12.03	7.33E-05	-82.03
20	18	contract inside: < worst point	34	9.785	10.99	0.4893	0.124	0.05	55.19	5.437	4.57E-05	-66.05
21	19	reflect: < second worst point	35	9.785	8.954	0.4893	0.124	0.05	55.19	5.437	4.57E-05	-66.05
22	20	reflect: < second worst point	36	9.785	8.069	0.4893	0.124	0.05	55.19	5.437	4.57E-05	-66.05
23	21	reflect: < second worst point	37	9.785	6.319	0.4893	0.1925	0.05	55.19	5.437	4.57E-05	-66.05
24	22	contract inside: < worst point	39	9.156	4.284	0.4578	0.09855	0.05	57.55	13.08	3.33E-05	-56.11
25	23	contract inside: < worst point	41	9.156	4.184	0.4578	0.08786	0.05	57.55	13.08	3.33E-05	-56.11
26	24	reflect: < second worst point	42	9.156	4.181	0.4578	0.1466	0.05	57.55	13.08	3.33E-05	-56.11
27	25	contract inside: < worst point	44	9.156	2.944	0.4578	0.1466	0.05	57.55	13.08	3.33E-05	-56.11
28	26	reflect: < second worst point	45	9.156	2.183	0.4578	0.1466	0.05	57.55	13.08	3.33E-05	-56.11
29	27	contract inside: < worst point	47	9.156	0.8383	0.4578	0.1466	0.05	57.55	13.08	3.33E-05	-56.11
30	28	contract inside: < worst point	49	9.156	0.7013	0.4578	0.1233	0.05	57.55	13.08	3.33E-05	-56.11
31	29	reflect: < second worst point	50	9.156	0.629	0.4578	0.1233	0.05	57.55	13.08	3.33E-05	-56.11
32	30	contract inside: < worst point	52	9.134	0.5313	0.4567	0.07441	0.05	53.59	7.175	4.01E-05	-71.48
33	31	contract inside: < worst point	54	9.045	0.2934	0.4523	0.09689	0.05	47.58	8.736	3.76E-05	-82.17
34	32	contract inside: < worst point	56	9.038	0.2387	0.4519	0.06347	0.05	53.26	8.805	3.43E-05	-73.54
35	33	reflect: < second worst point	57	9.038	0.1184	0.4519	0.06511	0.05	53.26	8.805	3.43E-05	-73.54
36	34	contract inside: < worst point	59	9.003	0.131	0.4501	0.06504	0.05	53.97	9.939	3.55E-05	-63.18
37	35	contract inside: < worst point	61	8.992	0.1373	0.4496	0.05186	0.05	52.05	7.65	3.83E-05	-69.97
38	36	contract outside: < worst point	63	8.992	0.05357	0.4496	0.04252	0.05	52.05	7.65	3.83E-05	-69.97

- Lowered **tolx_rel** & **tolf_rel** from 0.05 to **0.01**

31	29	reflect: < second worst point	50	9.156	0.629	0.09156	0.1233	0.01	57.55	13.08	3.33E-05	-56.11
32	30	contract inside: < worst point	52	9.134	0.5313	0.09134	0.07441	0.01	53.59	7.175	4.01E-05	-71.48
33	31	contract inside: < worst point	54	9.045	0.2934	0.09045	0.09689	0.01	47.58	8.736	3.76E-05	-82.17
34	32	contract inside: < worst point	56	9.038	0.2387	0.09038	0.06347	0.01	53.26	8.805	3.43E-05	-73.54
35	33	reflect: < second worst point	57	9.038	0.1184	0.09038	0.06511	0.01	53.26	8.805	3.43E-05	-73.54
36	34	contract inside: < worst point	59	9.003	0.131	0.09003	0.06504	0.01	53.97	9.939	3.55E-05	-63.18
37	35	contract inside: < worst point	61	8.992	0.1373	0.08992	0.05186	0.01	52.05	7.65	3.83E-05	-69.97
38	36	contract outside: < worst point	63	8.992	0.05357	0.08992	0.04252	0.01	52.05	7.65	3.83E-05	-69.97
39	37	contract inside: < worst point	65	8.985	0.05324	0.08985	0.04979	0.01	50.43	8.963	3.67E-05	-77.01
40	38	contract inside: < worst point	67	8.985	0.02712	0.08985	0.04979	0.01	50.43	8.963	3.67E-05	-77.01
41	39	reflect: < second worst point	68	8.985	0.01832	0.08985	0.05773	0.01	50.43	8.963	3.67E-05	-77.01
42	40	contract inside: < worst point	70	8.985	0.01179	0.08985	0.05773	0.01	50.43	8.963	3.67E-05	-77.01
43	41	contract inside: < worst point	72	8.98	0.01612	0.0898	0.03505	0.01	52.21	8.598	3.63E-05	-70.87
44	42	contract outside: < worst point	74	8.98	0.01213	0.0898	0.02145	0.01	52.21	8.598	3.63E-05	-70.87
45	43	contract inside: < worst point	76	8.974	0.01439	0.08974	0.01985	0.01	52	8.268	3.74E-05	-71.33
46	44	reflect: < second worst point	77	8.974	0.01157	0.08974	0.01985	0.01	52	8.268	3.74E-05	-71.33
47	45	contract inside: < worst point	79	8.974	0.01067	0.08974	0.01985	0.01	52	8.268	3.74E-05	-71.33
48	46	reflect: < second worst point	80	8.974	0.01035	0.08974	0.03283	0.01	52	8.268	3.74E-05	-71.33
49	47	reflect: < second worst point	81	8.974	0.006988	0.08974	0.03283	0.01	52	8.268	3.74E-05	-71.33
50	48	contract inside: < worst point	83	8.974	0.006914	0.08974	0.03283	0.01	52	8.268	3.74E-05	-71.33
51	49	contract inside: < worst point	85	8.974	0.005825	0.08974	0.02063	0.01	52	8.268	3.74E-05	-71.33
52	50	shrink	91	8.971	0.01415	0.08971	0.00949	0.01	52.1	8.431	3.68E-05	-71.1

Condition	Previous	Changed **cm**	Changed **ncp**	Modified **parameter change**	Lowered **tolx** & **tolf** to **0.01**
Total error	~8	**9.134**	**9.038**	**8.992**	**8.971**
L_dend1	**57.7**	**53.59**	**53.26**	**52.05**	**52.1**
L_dend2	**11.1**	**7.715**	**8.805**	**7.65**	**8.431**
gpas	**3.01e-5**	**4.01e-5**	**3.43e-5**	**3.83e-5**	**3.68e-5**
epas	**-54.9**	**-71.48**	**-73.54**	**-69.97**	**-71.1**

- Modified **fminsearch3_4compgabab.m**:
    - 2017-01-21 Cleaned up code
    - 2017-01-21 Changed the **number of parameters to compare** against to n (from min(2, n))
    - 2017-01-21 Changed definition of **maxparamchange** & **tolx** so that the largest parameter doesn't dominate
    - 2017-01-21 Replace by the **"reflection point"** as long as it is better than the worst point
    - 2017-01-21 Decrease **tolf_rel** && **tolx_rel** from 0.05 to 0.01
- Created **log_errors_params.m**
    - 2017-01-17 Created

Plan for next week

- Patching:
  - Add a **positive/negative pressure system**. Use the manometer to check performance
  - Add an **audio monitor**
  - Prepare a **battery charger** for the 12-volt Pb battery
  - Ascertain whether the center is also off using the **image under AxoCam**
  - Find an **excitatory cell marker** for LGN recordings
  - (Wed or the following week) Practice patching LGN neurons from **2-month old mice** provided by Geoff

- Passive fitting with simulations:
  - Create a concise log file; add timestamp to log file name
  - Figure out what **bounds** would be physiological and impose any necessary restrictions on the relative lengths and diameters of each segment
  - Use results from the curve-fitting method as the starting points for the biophysical model. What is the equivalent length & diameter of the cylinder given the diameter of the sphere? How to decide how to convert a single length + diameter pair for the dendrite into two or three pairs?
  - **Bootstrap** the optimization procedure for the current pulse response fit by varying the **initial values** for the parameters
  - Further improve the optimization algorithm
    1. Apply stochasticity in each step? (Perhaps not a good idea for reproducibility)
    2. Systematically sample across entire space initially? (to avoid converging on local minimums)
    3. **Cross-entropy optimization** algorithm
    4. Implement the **control variable u(t)** in the error function
  - **Compare** the fitted passive parameters across cells
  - Await response from John on questions about the **passive fitting**

- Data analysis:
  - Decide what to do with CONTESTED_TAKE_OUT_More_than_one_LTS_no_spont
  - Ask everyone to score Word files
  - Fix **find_LTS.m** to enforce overrules.
  - Rerun dclampDataExtractor.m with all the **overrules enforced** (**dclampDataExtractor14.slurm**, giving the version **old15**)

- Brian's tasks:
  - Write **Microsoft Visual Basic code** for analyzing scored Word files (already done)

- Analyze scoring results (after everyone finishes scoring)
- **Fit Gaussians** to find a threshold in the RMSE histograms from the curve fitting method
- Figure out whether the traces with **high RMSE** in the rising phase are the same traces with high RMSE in the falling phase
- Devise a good threshold for **"noisy recordings"**
- Take out any trace with error greater than the threshold from the trace averaging. Compute the **mean recorded voltage change** ($\Delta \bar{V}_{rec}$), the **mean current pulse amplitude** (**cpa_mean**), the **mean pulse width** (**pw_mean**) by averaging over all traces remaining.
- Fix **plot_traces_abf.m**:
  i. Suppress aberrant output
  ii. Automatically detect whether a voltage or current is recorded (based on the maximum absolute values and label the axes appropriately (esp. Voltage clamp recordings, see '**A20161216_0008.abf**' for example)

- SWD detection w/ Vignesh & Mark:
  - Figure out how to **screen** through detection results

- Computational Neuroscience:
  - Computational Neuroscience (University of Washington Coursera): Week 6 Quiz
  - Computational Neuroscience (University of Washington Coursera): Week 7

- Patch Clamp Electrophysiology:
  - 6.002.1x Circuits and Electronics (MITx): Week 2

- Neuroscience in General:
  - NESC 7030 Molecular, Cellular, and Developmental Neuroscience: Week 3

- Research in General:
  - Molecular Foundations of Medicine (Stanford EdX): Molecular Techniques
  - Mathematical Biostatistics Bootcamp 1 (Johns Hopkins Coursera): Week 3