

Supporting information for: *Cyclodextrin Ion Channels*

Jonathan K.W. Chui and Thomas M. Fyles*

Voltage Clamp Data Acquisition

A model BC-525A bilayer clamp (Warner Instrument Corp.) was used for planar bilayer experiments. The analogue output was filtered with an 8-pole Bessel filter (Frequency Devices, model 902) and digitized with a 330 kHz digitizer (Axon Instruments, Digidata 1200A). Data acquisition was controlled by the pClamp8 software package (Axon Instruments). Data were collected at 10 Hz, analogue filtered at 1 Hz, and digitally filtered at 50 Hz. The headstage and the bilayer chamber (3 mL polystyrene cuvette with 250 μm diameter aperture held in a 5 mL PVC holder) were placed on a floating table and electrically shielded by a grounded aluminum Faraday cage. Agar salt bridges (2 M KNO_3 in 1% Agar) were used to stabilize junction potentials and were employed between the electrolyte in each well of the cell and Ag/AgCl electrodes. Electrolyte solutions were prepared from high purity salts and nanopure water.

A stock solution of diphytanoyl phosphatidylcholine (diPhyPC) in chloroform (Avanti Polar Lipids; shipped on dry ice) was divided into sealed glass vials under an argon atmosphere and stored at $-12\text{ }^\circ\text{C}$. For use in an experiment, a stream of dry nitrogen was passed through the vial for 1 hour. The dried lipid was diluted with decane to give a solution concentration of 25 mg/mL in lipid.

Bilayers were formed by either brushing or dipping: after lipid in decane had been introduced by brushing, a lipid/decane film formed on the surface of the electrolyte, and bilayers could then be formed by withdrawal of 2-3 mL of electrolyte from the cell holder by syringe to expose one face of the aperture to the air-water interface held in the cell holder, followed by reintroduction of the electrolyte to oppose monolayers across the aperture in the cuvette. Bilayer quality was monitored via the capacitance and stability under applied potential, using the criteria previously described¹. The measured voltage was applied with respect to the *trans* (cuvette) side of the bilayer, making the *trans* side the relative ground. Digitized data files were analyzed using the pClamp10 suite of programs.

The compounds are introduced to the membrane in two ways, depending on the solvent in which the compound can be dissolved:

Direct injection - all injection experiments utilized bilayers that were apparently stable at 100 mV for periods of 20 minutes or more. Aliquots (1-5 μL of transporter solutions in MeOH) were injected with a microliter syringe as close as possible to the bilayer in the free well of the cuvette holder (*cis* side), and gently stirred with a stream of nitrogen for 5 minutes.

Pre-mixed into lipid - in this method, 1mol% of compound (in CDCl_3 or MeOH-d_4) was added to the diPhyPC/ CHCl_3 solution, and solvent removed with a stream of N_2 , and bilayer membrane prepared by brushing/dipping as described above. Most of the bilayers formed with this method gave bilayers with good quality.

Of the two methods, direct injection is preferable, as it allows monitoring of pristine bilayer prior to compound introduction. Following direct injection, channel behaviour typically appears within 20

minutes of compound introduction, and persists over period of hours. Once stabilized, continuous data acquisition of at least 30-60 minutes is required to provide sufficient statistical power for the power-law analysis; shorter acquisition periods (10 minutes) are sufficient to characterize other types of behaviors.

Power Law Fitting Procedure

Fitting experimental data to a power law requires two distinct steps. The first step transforms the irregular current trace into a list of opening times; this list is then fitted to a power law distribution.

Event List Generation Manipulation of the digitally filtered traces was carried out using Clampfit 10 of the pClamp suite. A customized threshold search was used to generate the list of events. The threshold was set across the fluctuating section of the trace to maximize the number of events. Within that segment, α is insensitive to the choice of threshold. A minimum duration was fixed at 50ms. The threshold search automatically logs *event start* and *event end* from which the duration can be calculated. The resultant values were exported to the fitting program.

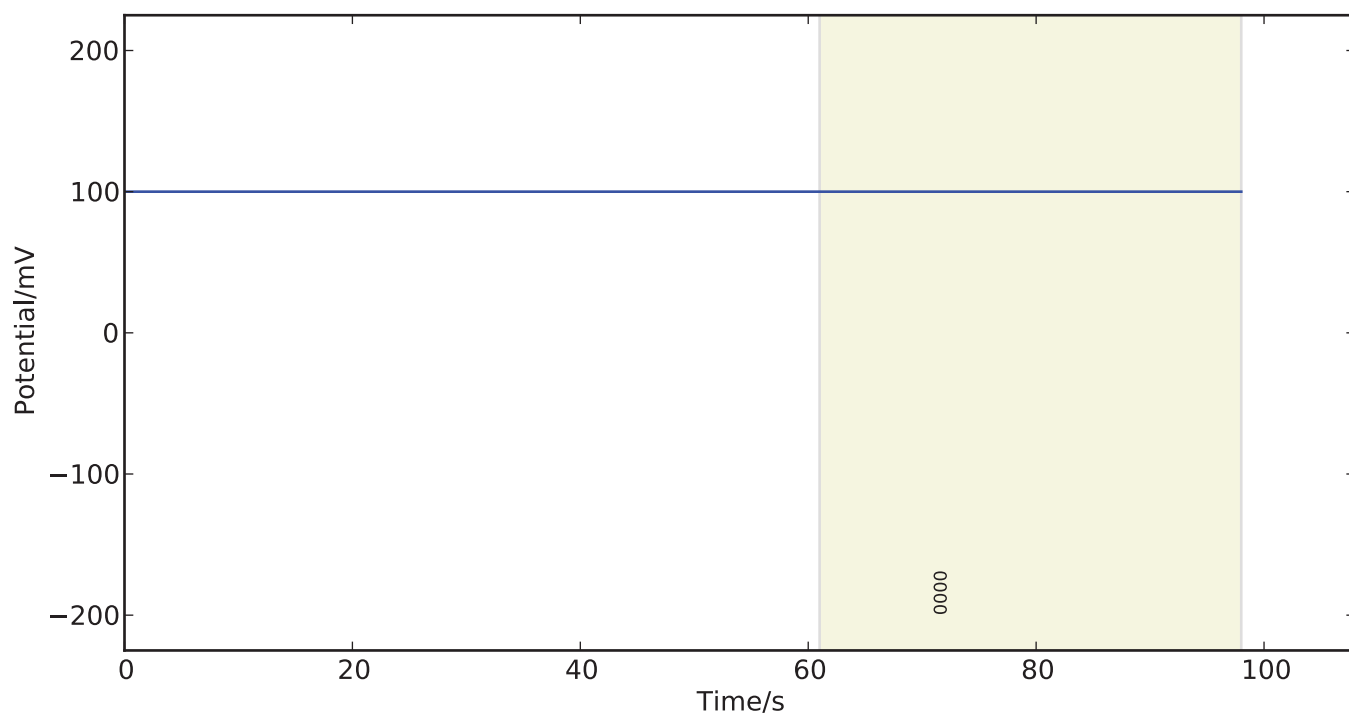
Power Law Fitting The list of opening durations, obtained above as a plain-text file, can then be fitted using the method of Clauset *et al*², implemented in python³. The code performs the Maximum Likelihood Estimate fit, and provides α , x_{\min} , n , and p-value as outputs.

Summary of bilayer activity

Annotated activity grids, as well as full conductance records (and expansions where appropriate), are provided below for every compound studied. The activity grids were prepared as previously described⁴. The summaries are arranged first by compound, then individual experiments. Within each experiment, the first page(s) summarizes the experimental conditions as well as activity grids charted; subsequent pages shows the full conductance record as the top panel, with expansions indicated by corresponding letters.

1. Fyles, T. M.; Knoy, R.; Müllen, K.; Sieffert, M., Membrane activity of isophthalic acid derivatives: ion channel formation by a low molecular weight compound. *Langmuir* **2001**, *17*, 6669-6674.
2. Clauset, A.; Shalizi, C. R.; Newman, M. E. J., Power-law distributions in empirical data. *SIAM Rev.* **2009**, *51*, 661-703.
3. Ginsberg, A. <<http://code.google.com/p/aqpy/wiki/PowerLaw>> (accessed November 7).
4. (a) Chui, J. K. W. A New Paradigm for Voltage-Clamp Studies of Synthetic Ion Channels. University of Victoria, Victoria, 2011; (b) Chui, J. K. W.; Fyles, T. M.; Luong, H., Planar bilayer activities of linear oligoester bolaamphiphiles. *Beilstein J. Org. Chem.* **2011**, *7*, 1562-1569.

JC-130 JC-W-2 bCD-6AmF5 1M CsCl pH 7



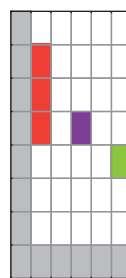
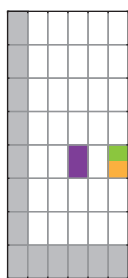
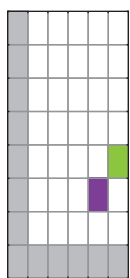
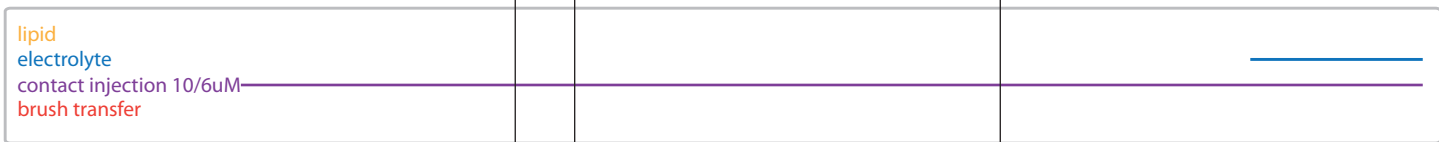
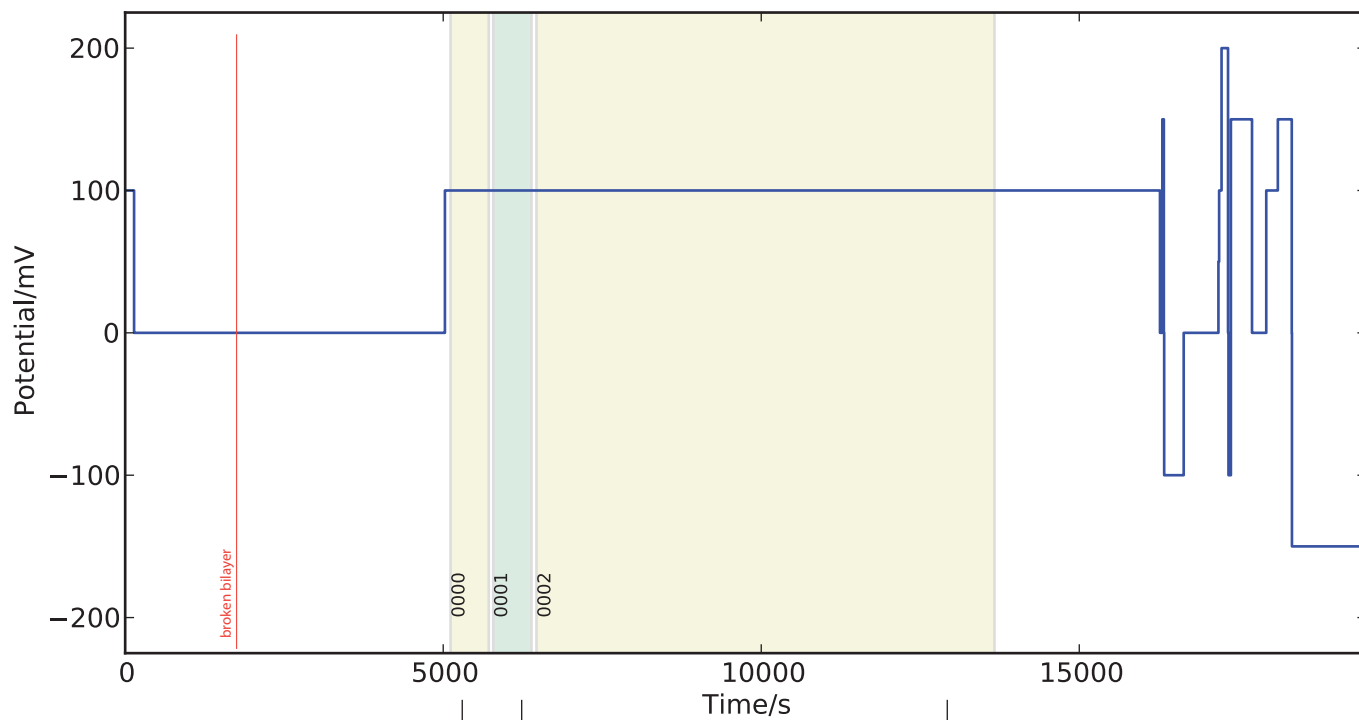
lipid
electrolyte
contact injection
brush transfer

Adamantyl guest

lipid
electrolyte

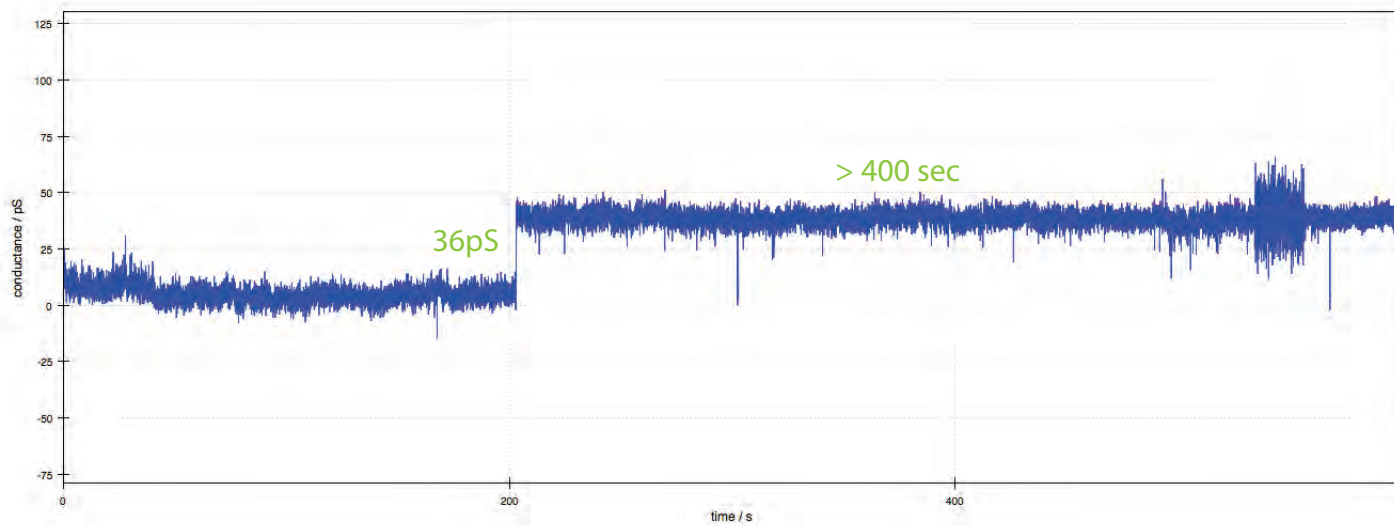
bad bilayer - no compound added

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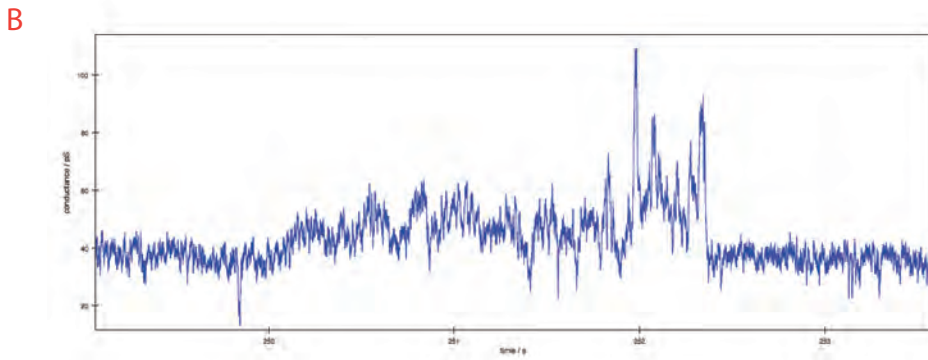
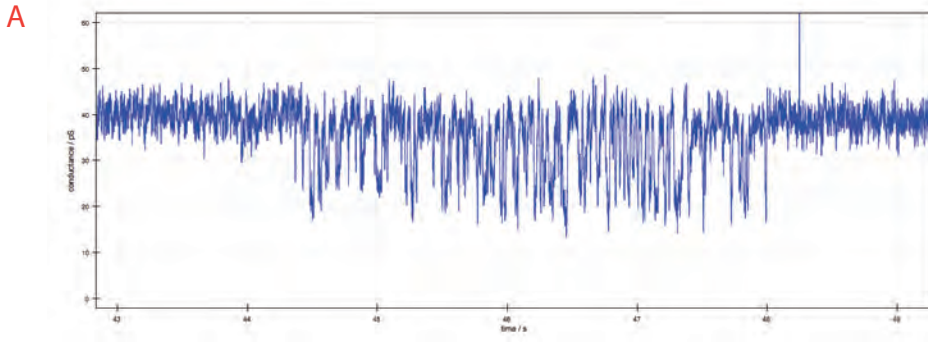
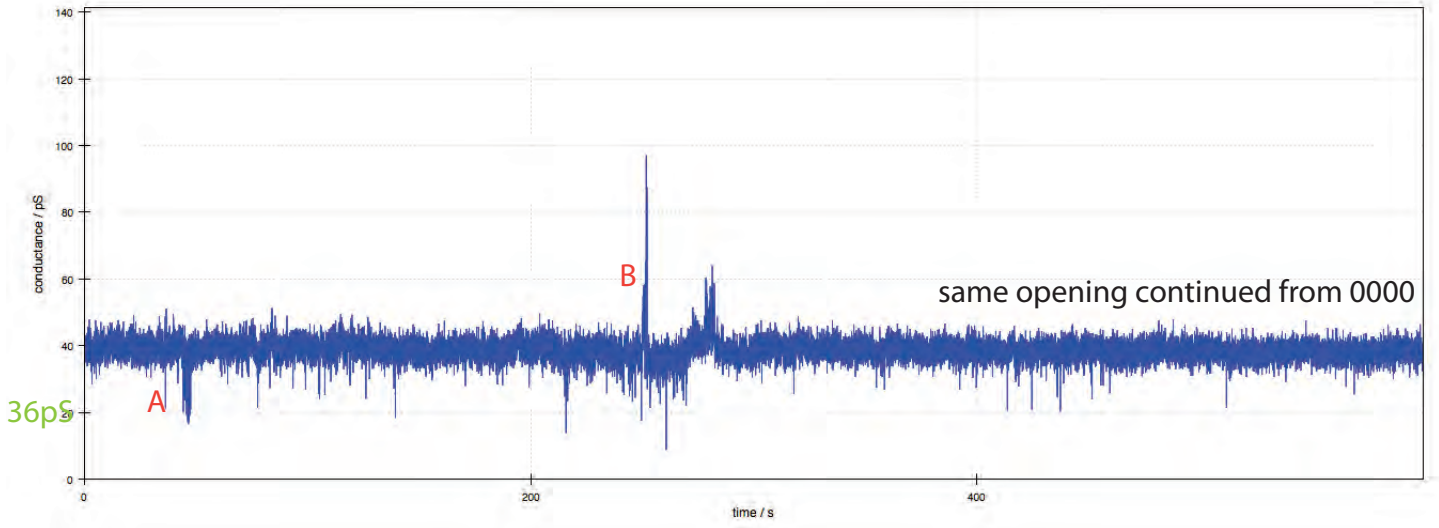


opening continued in 0001

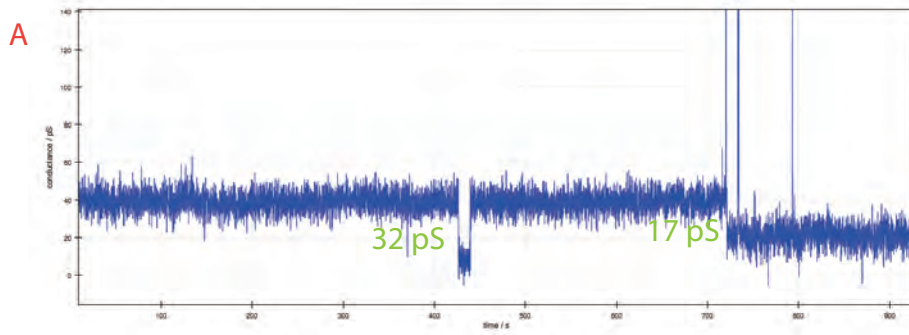
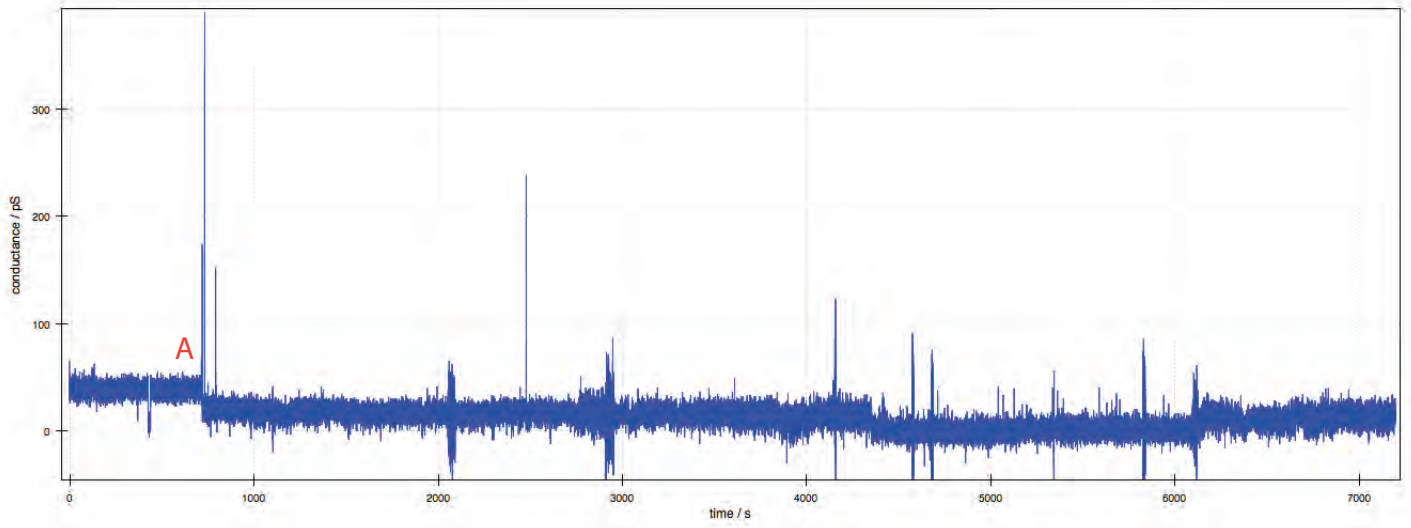
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131-0001

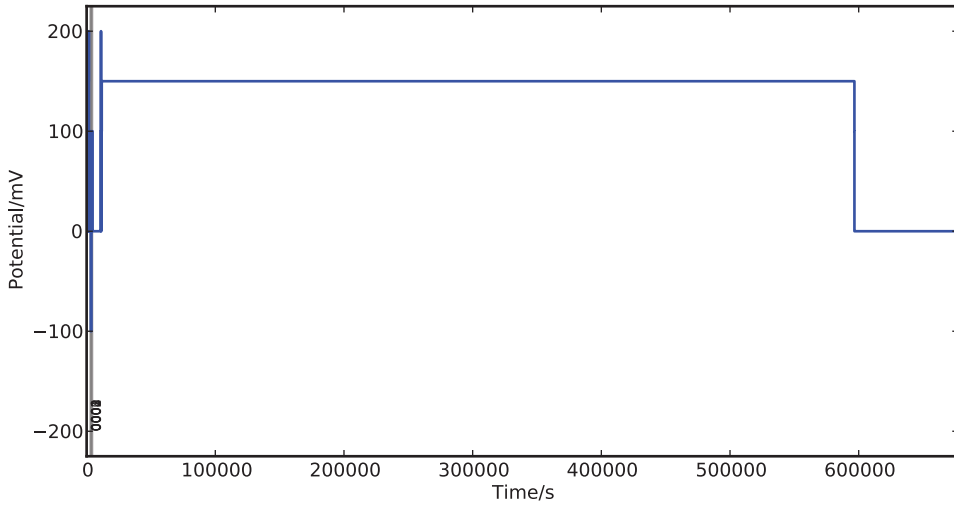


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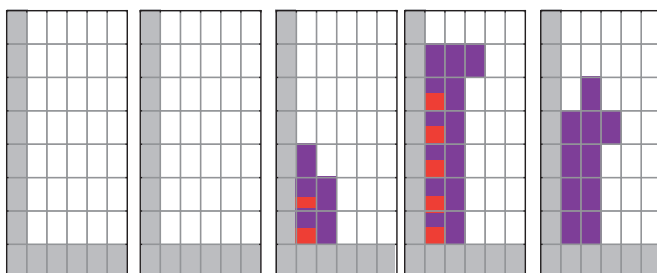
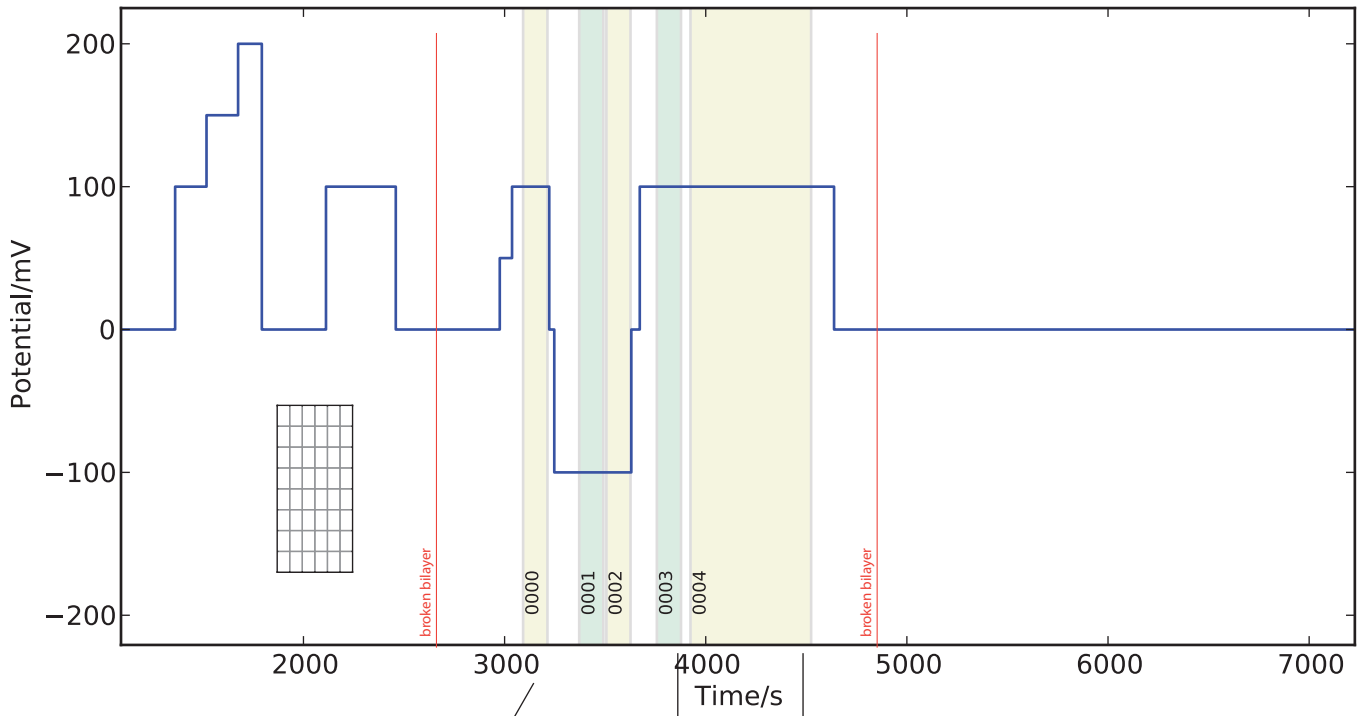


very large noise

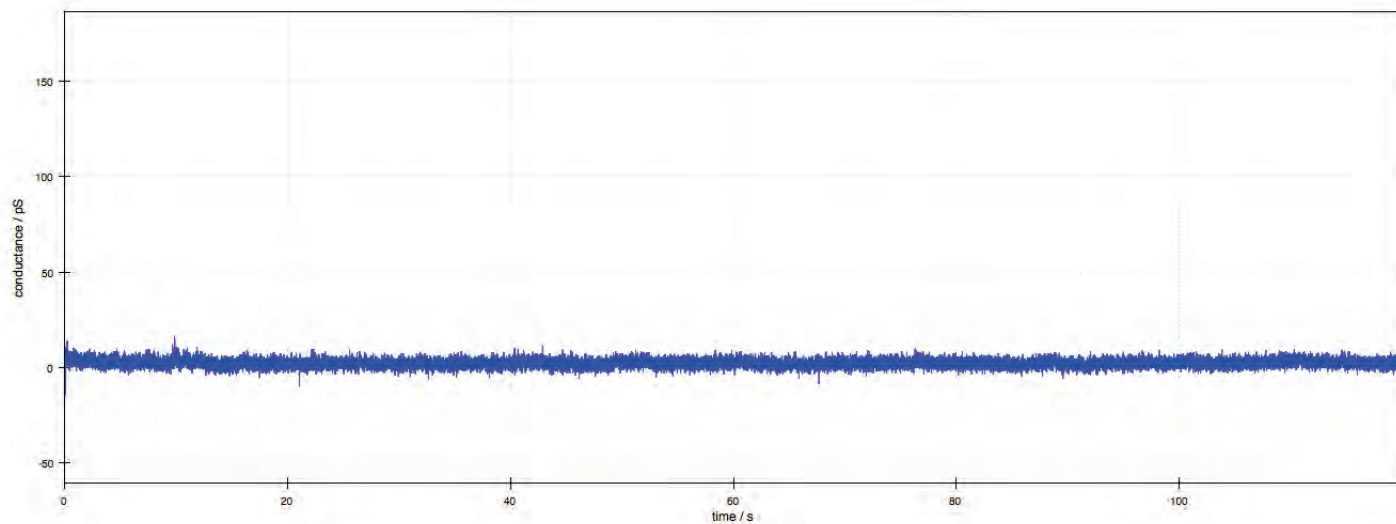
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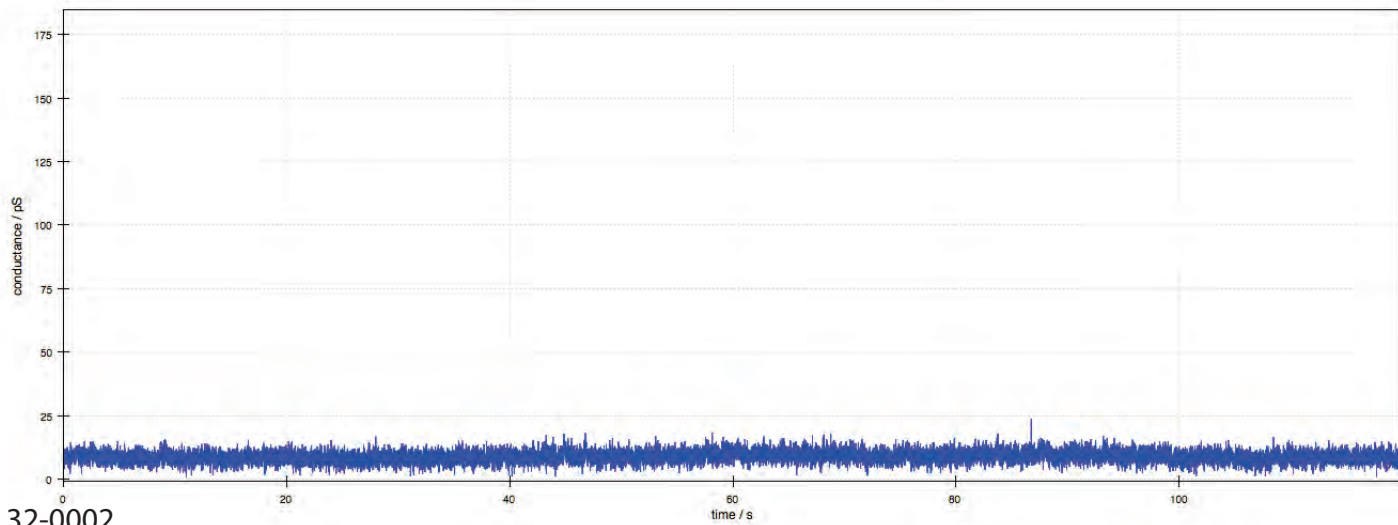
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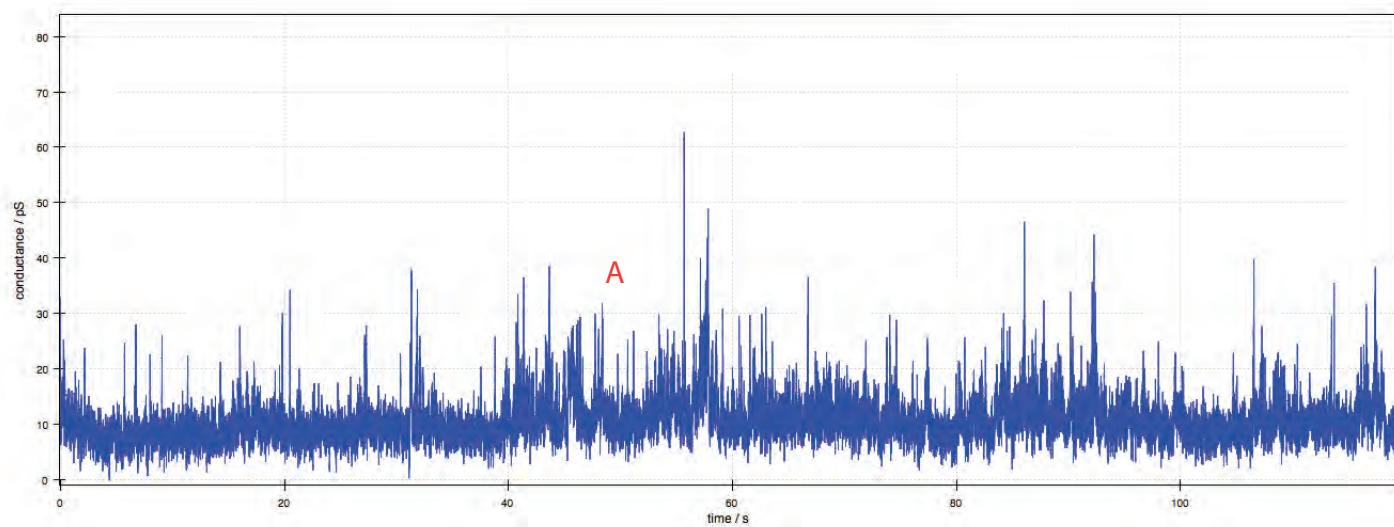
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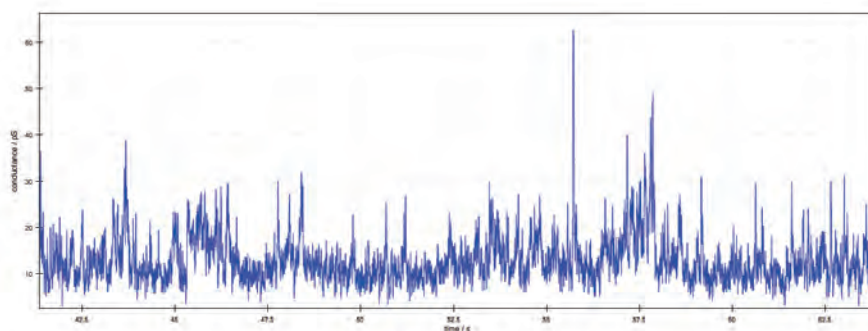
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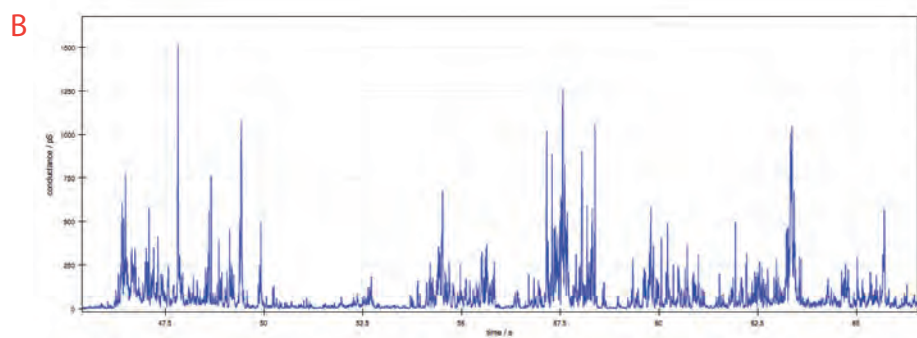
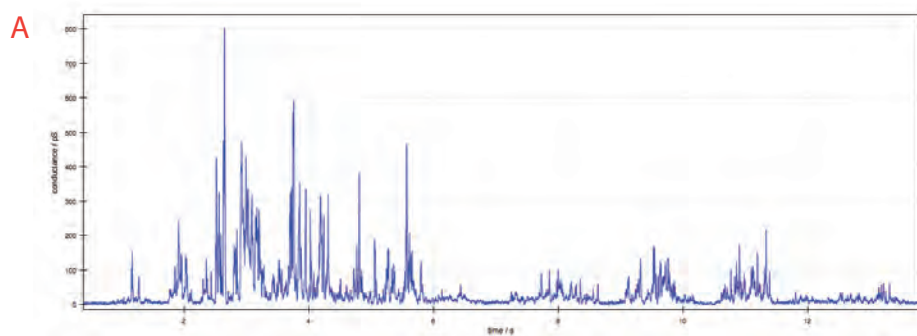
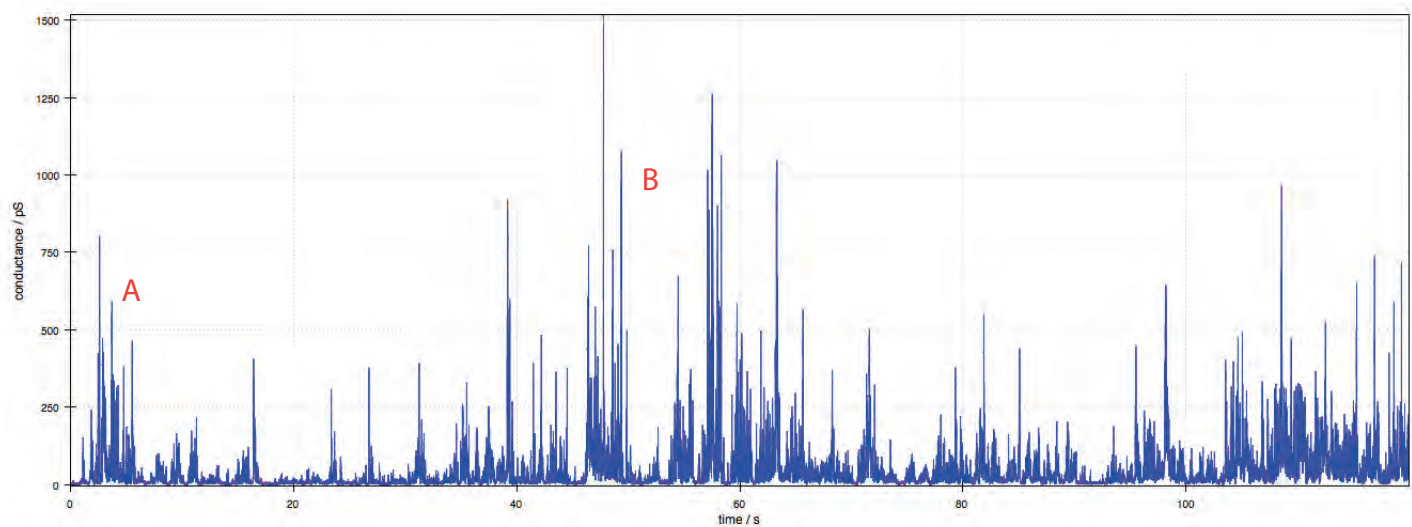


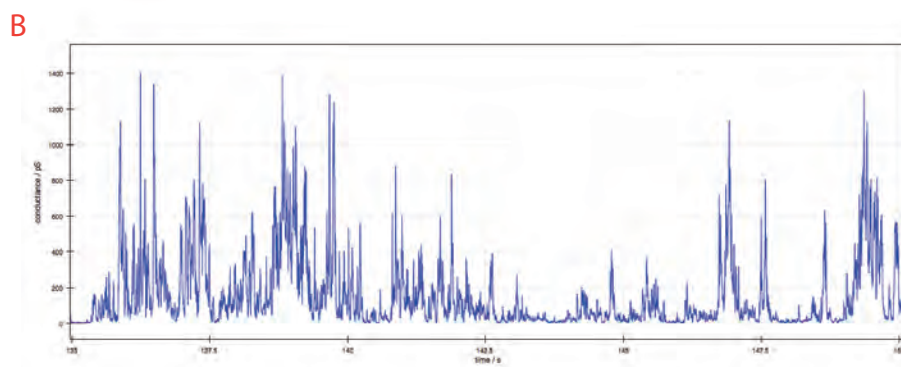
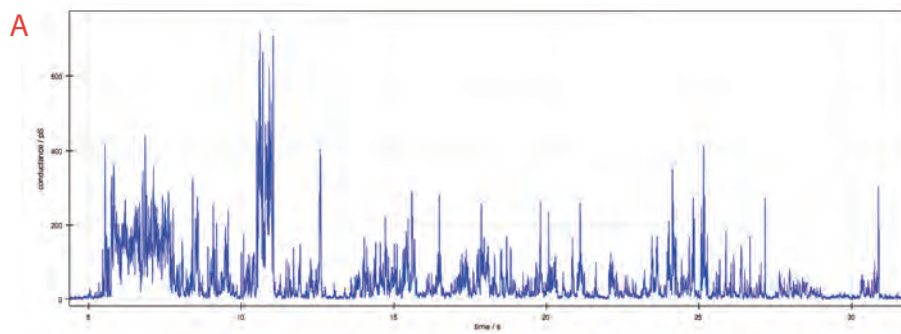
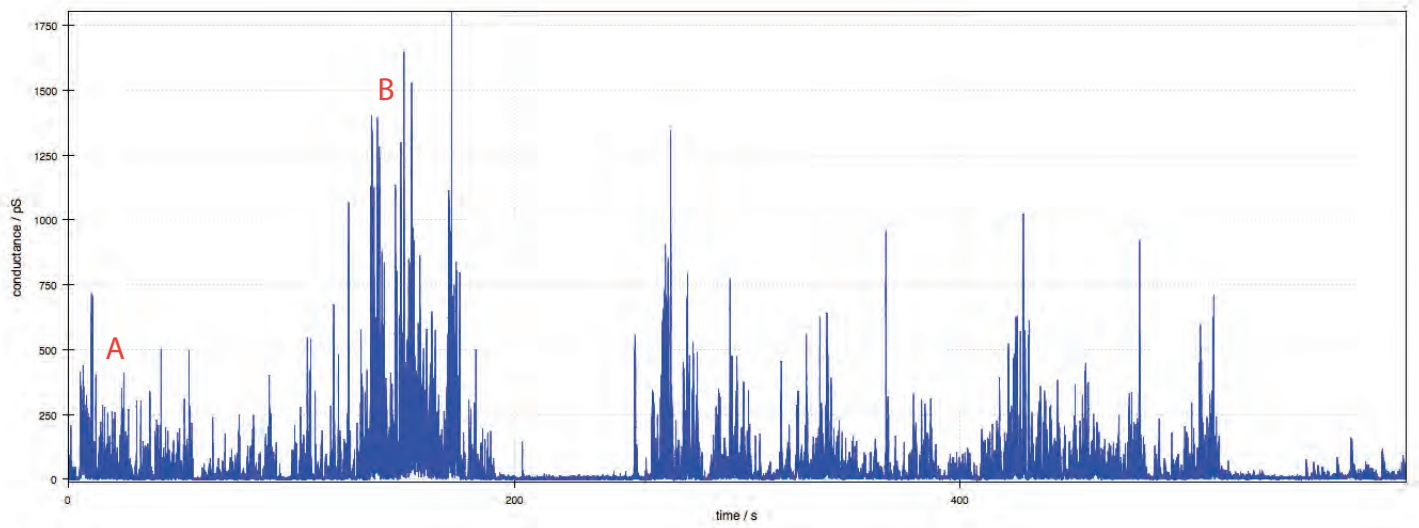
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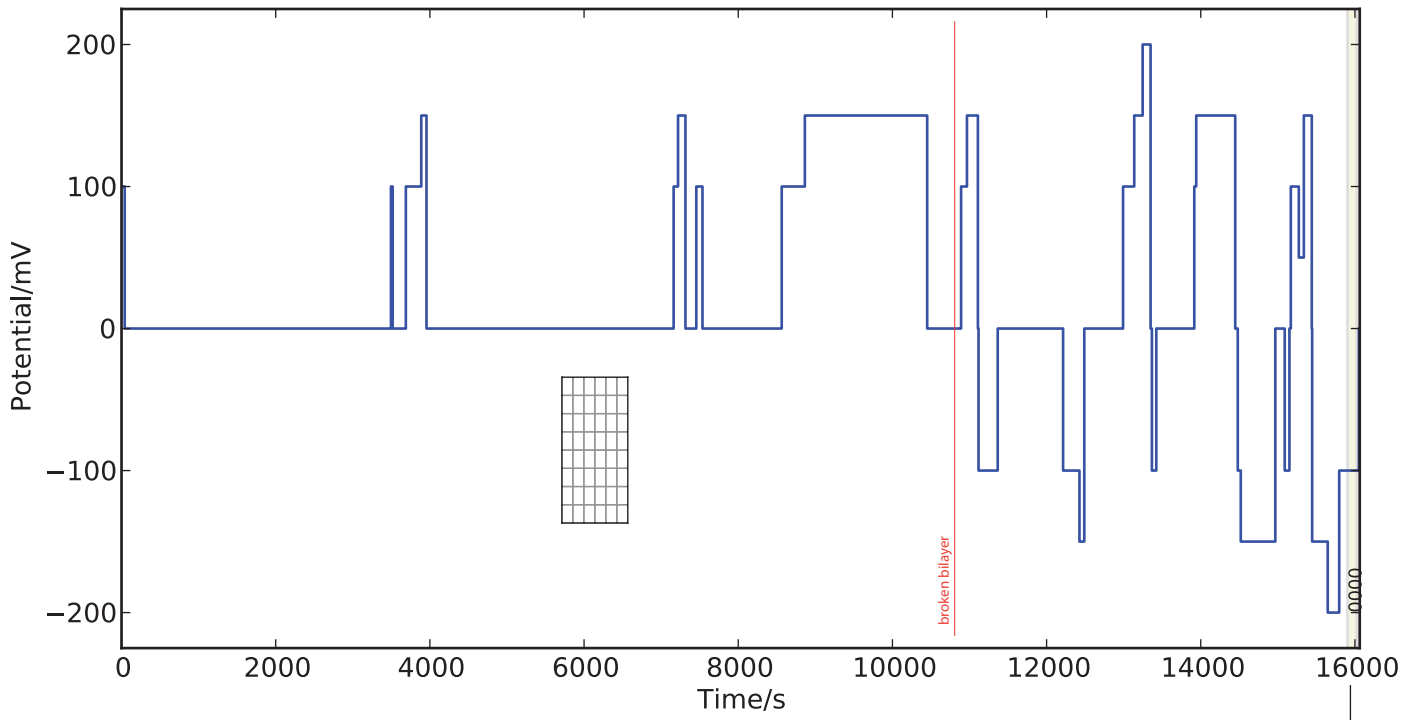
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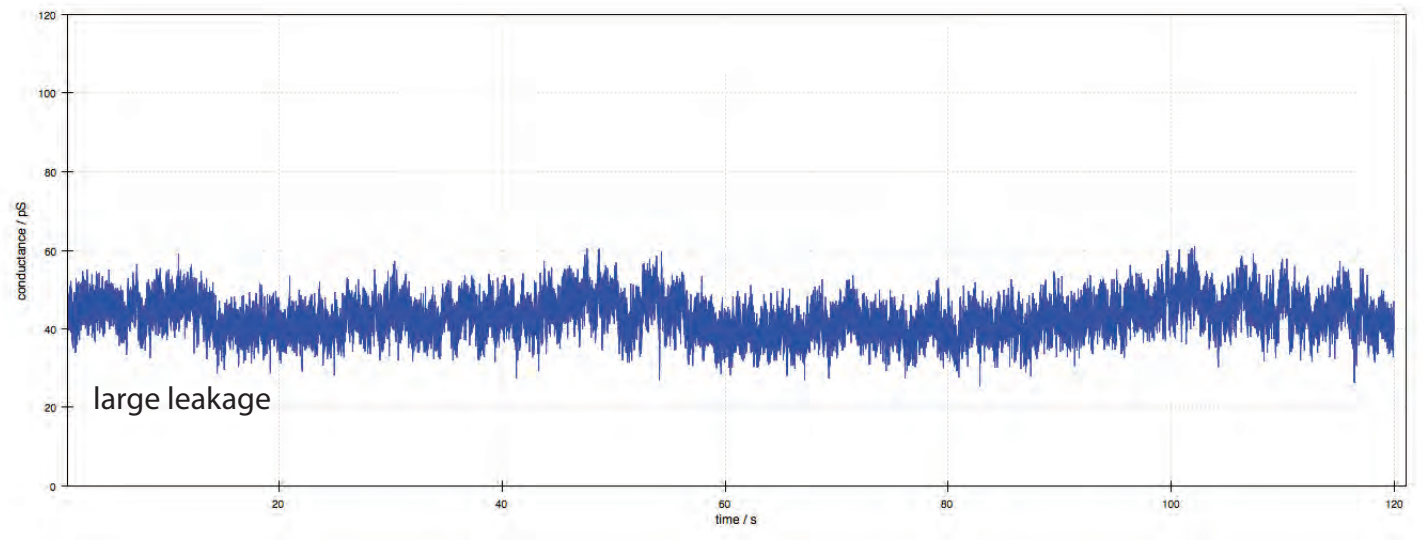


JC-133 JC-W-2 bCD-6AmF5 1M CsCl pH 7

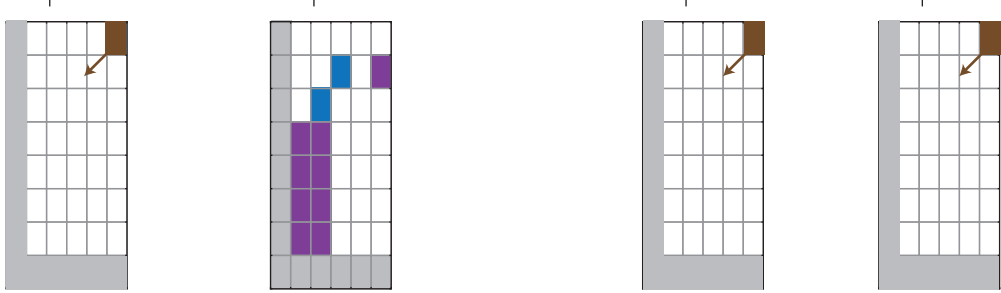
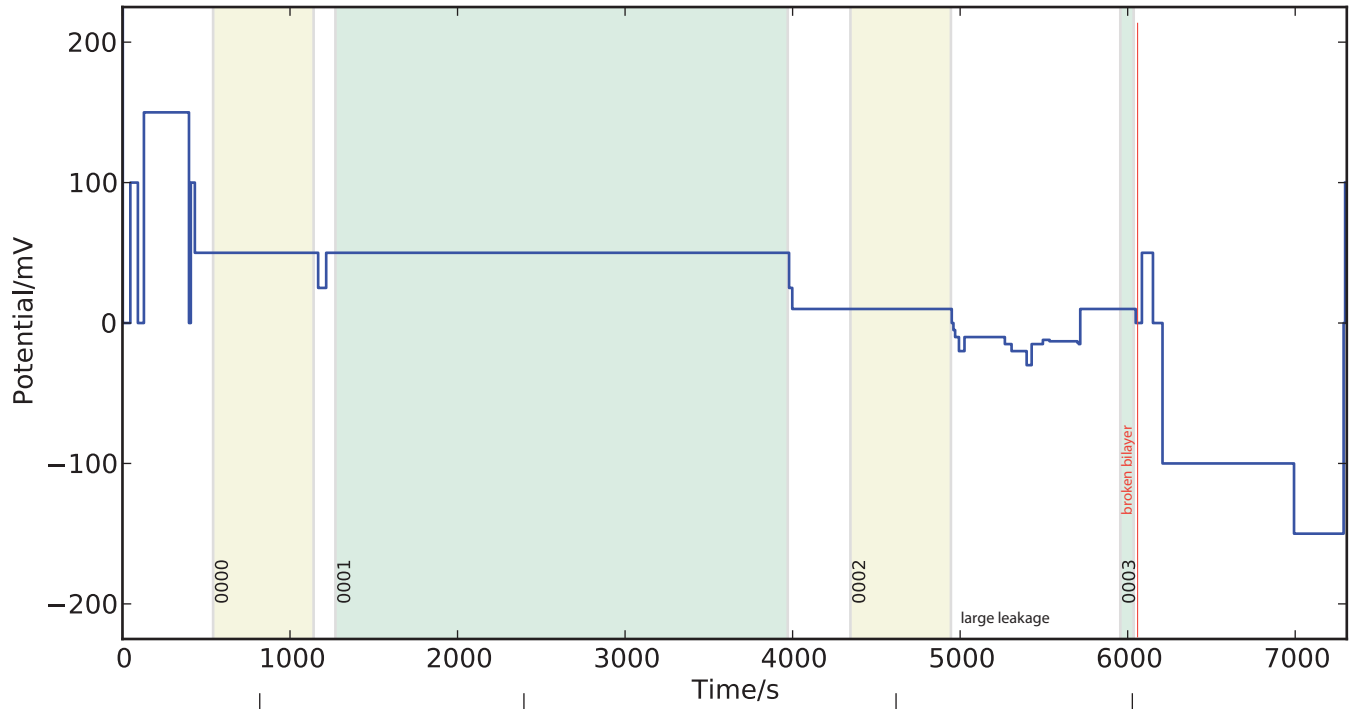


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electrolyte 2.7/4.2uM
contact injection
brush transfer
Adamantyl guest
lipid
electrolyte 0.88/1.35mM

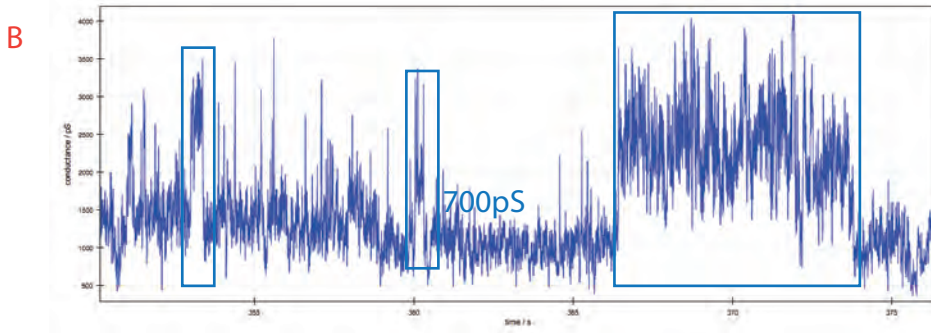
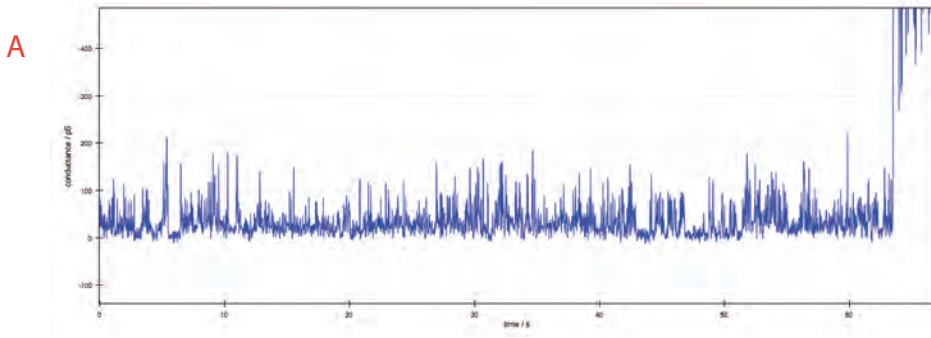
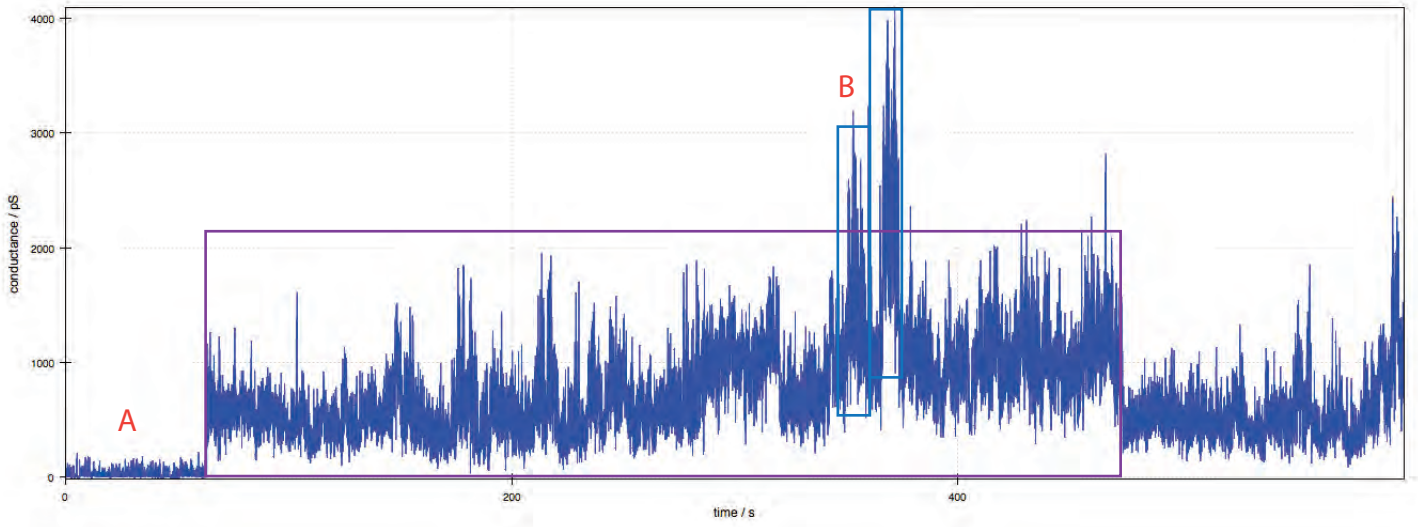
baseline drift,
large leakage

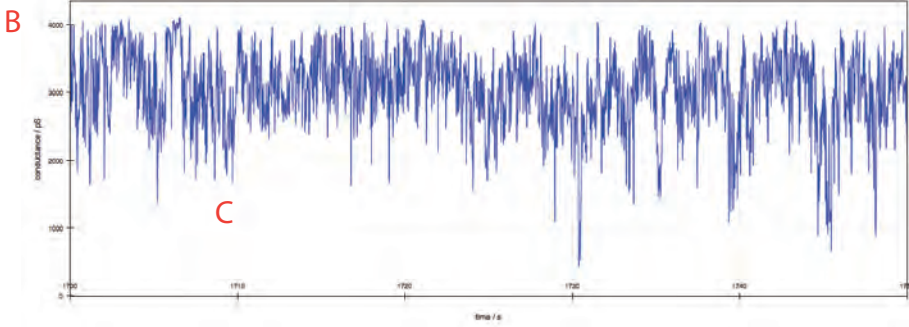
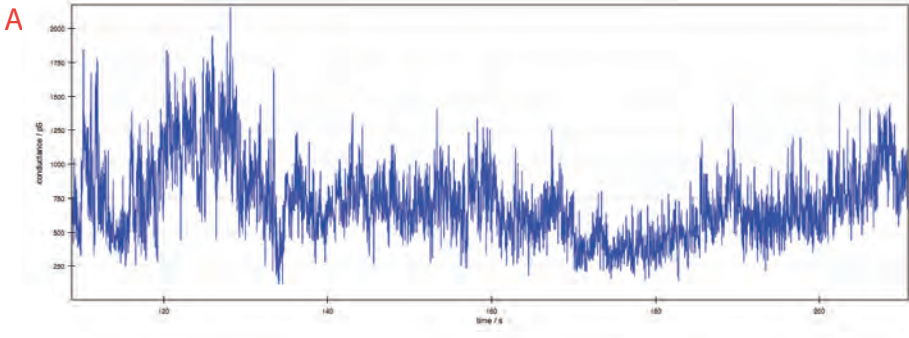
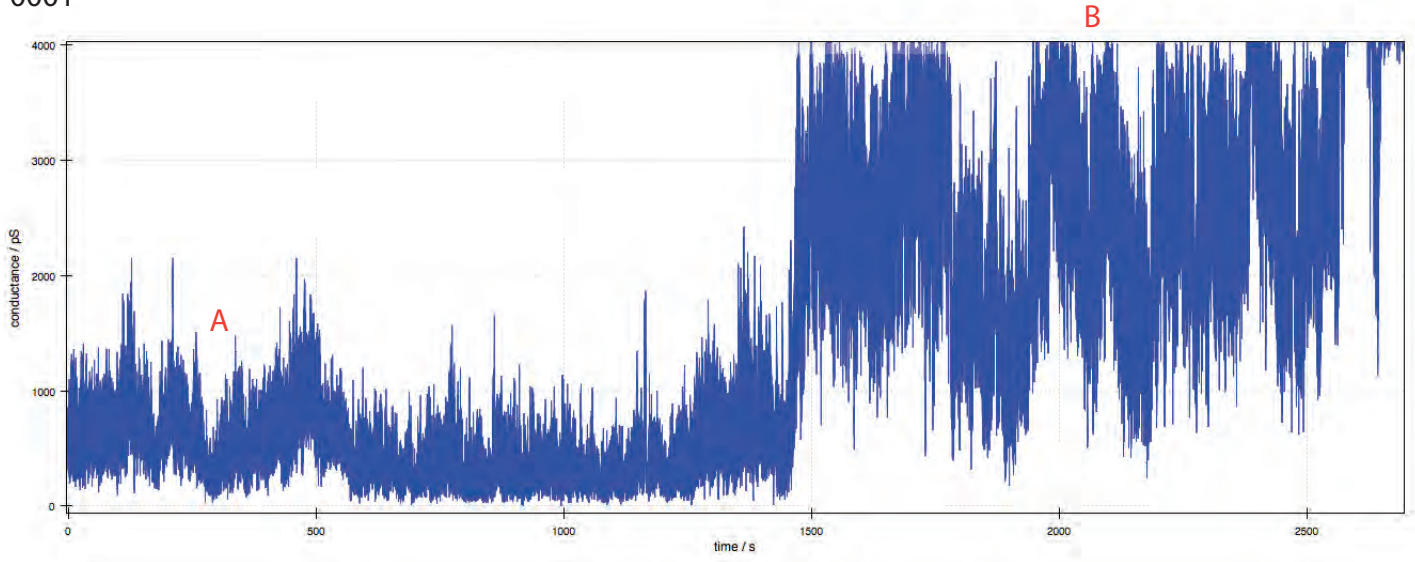


JC-135 JC-W-2 bCD-6AmF5 1percent 1M CsCl pH 7

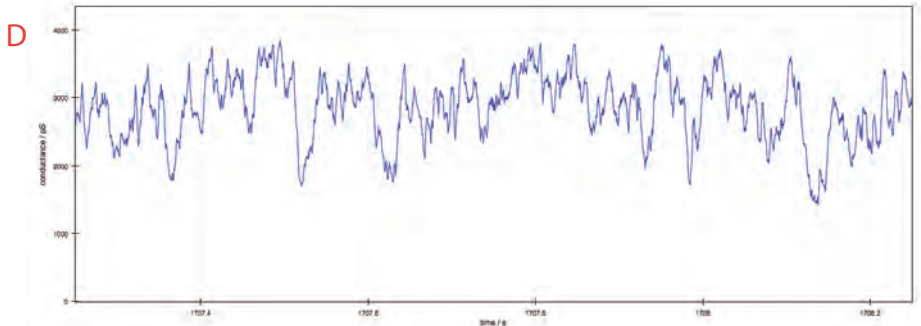
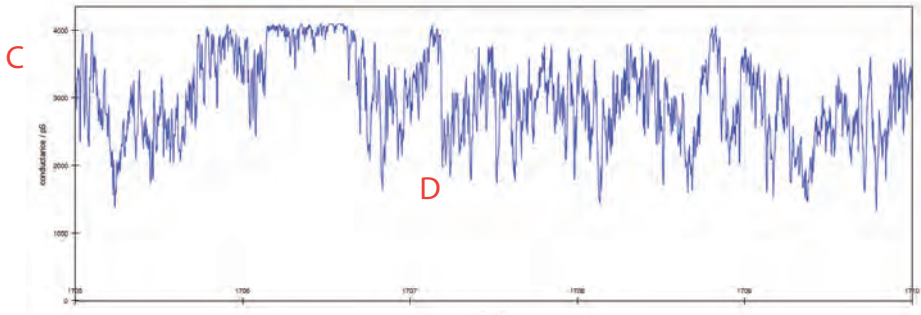


AdNH2 addition made halfway through expt.

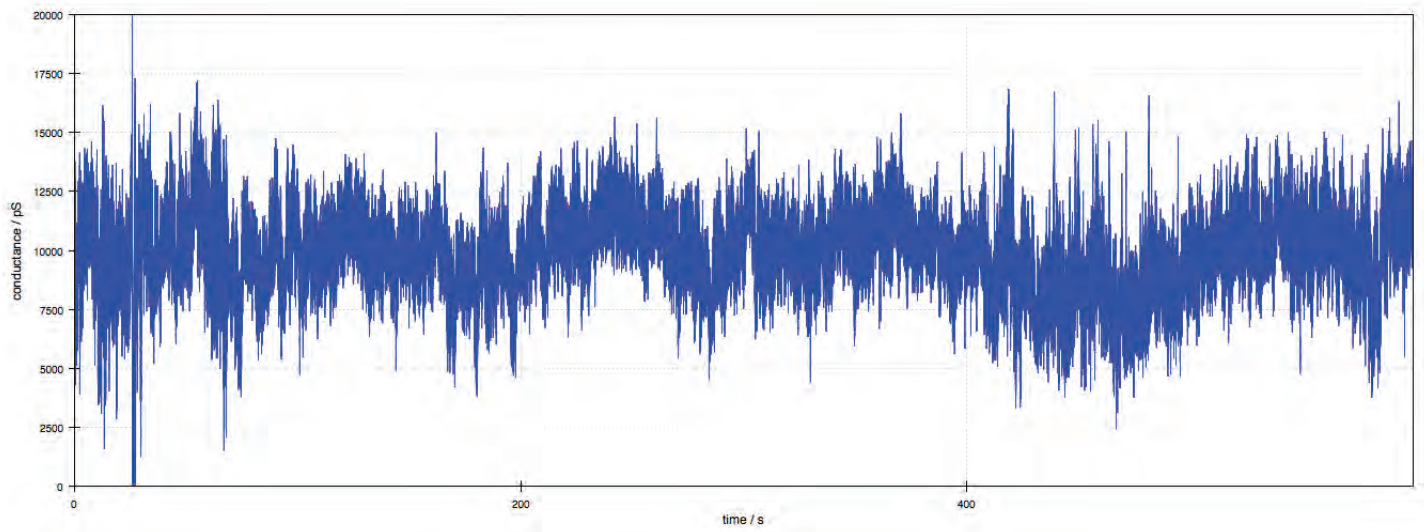




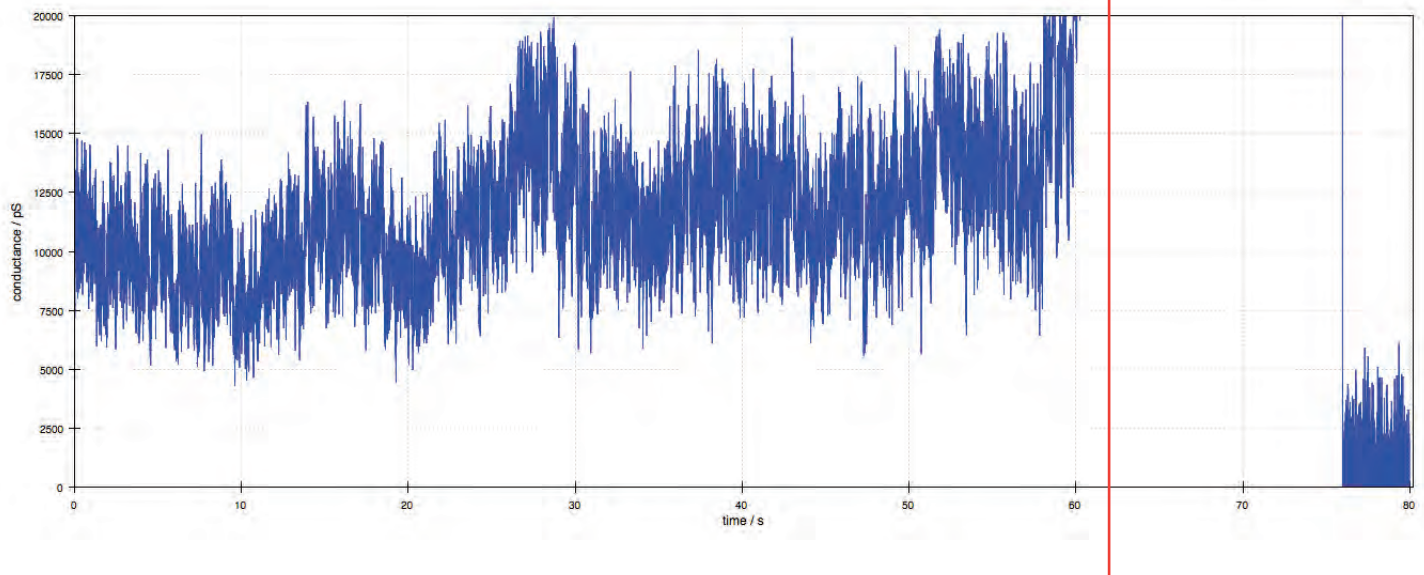
fractal?



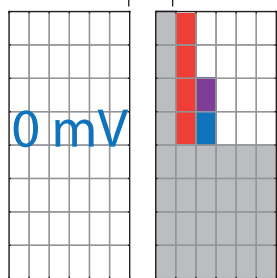
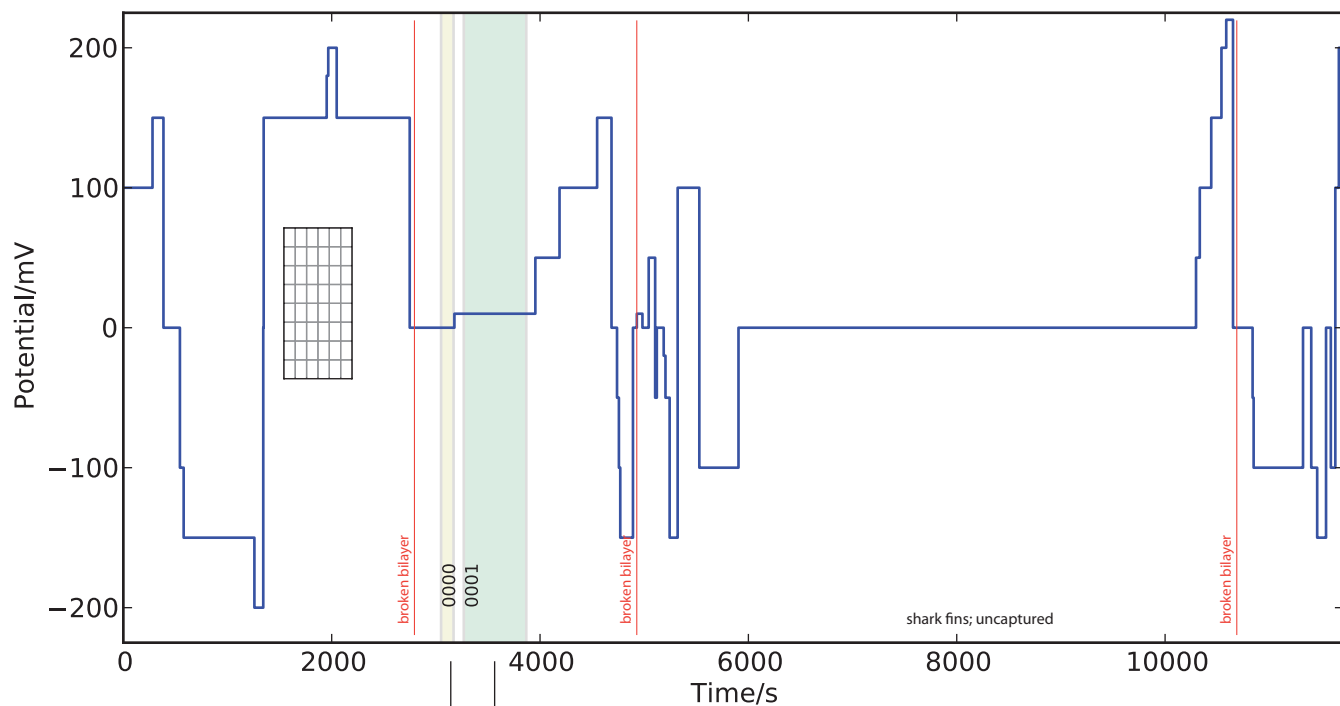
135-0002



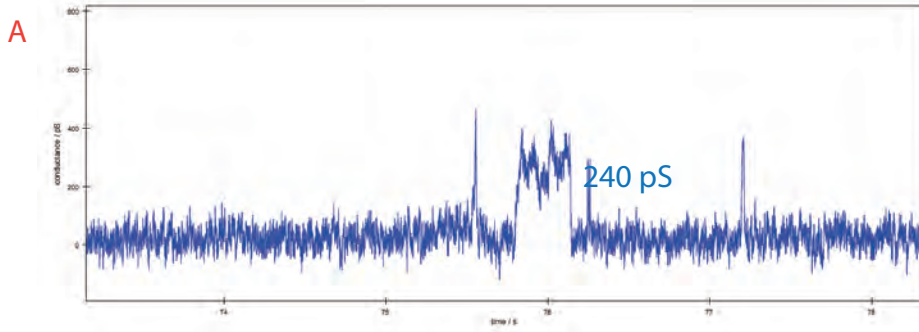
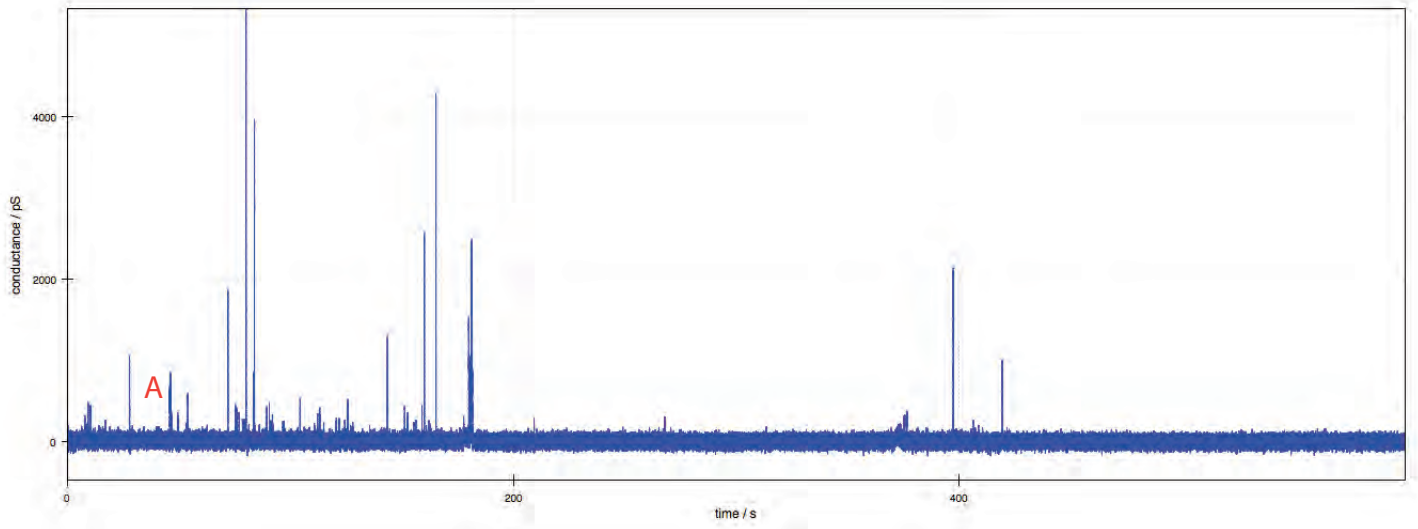
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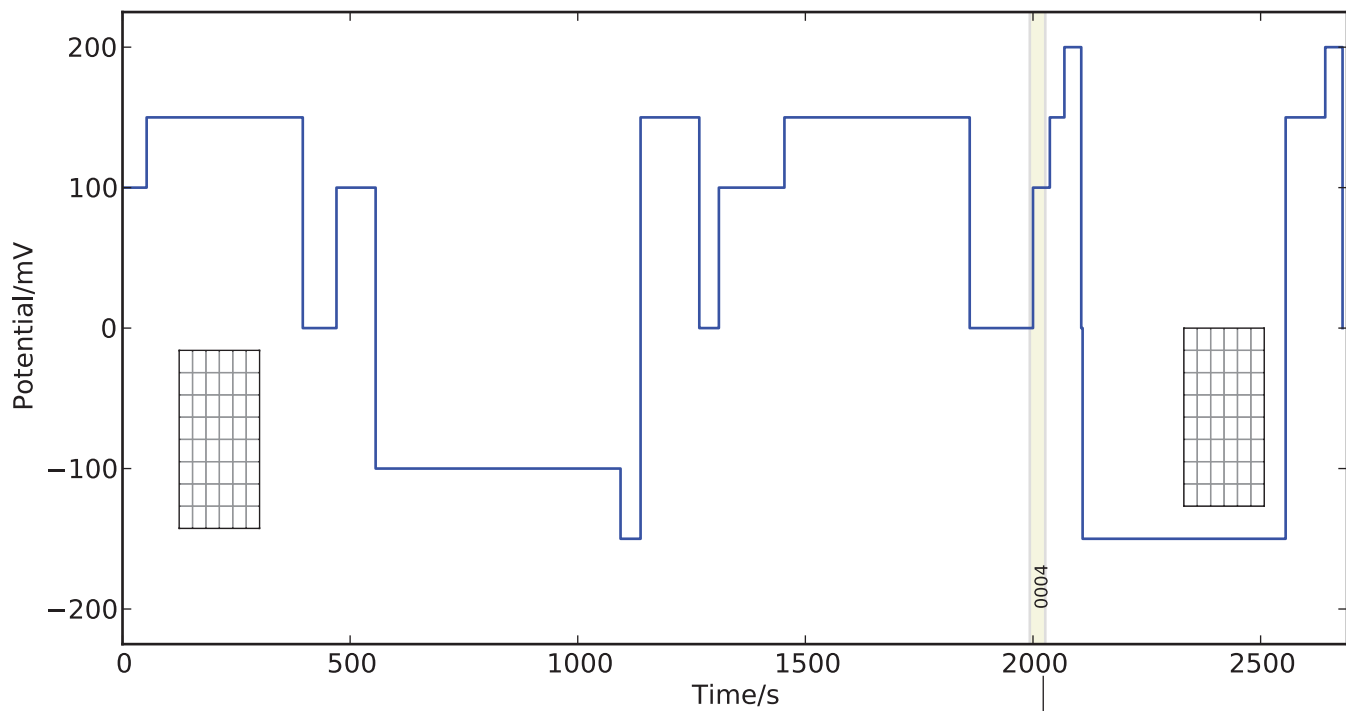
JC-136 JC-W-2 bCD-6AmF5 0-5percent premix AdNH2 1M CsCl pH7



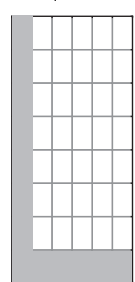
136-0001



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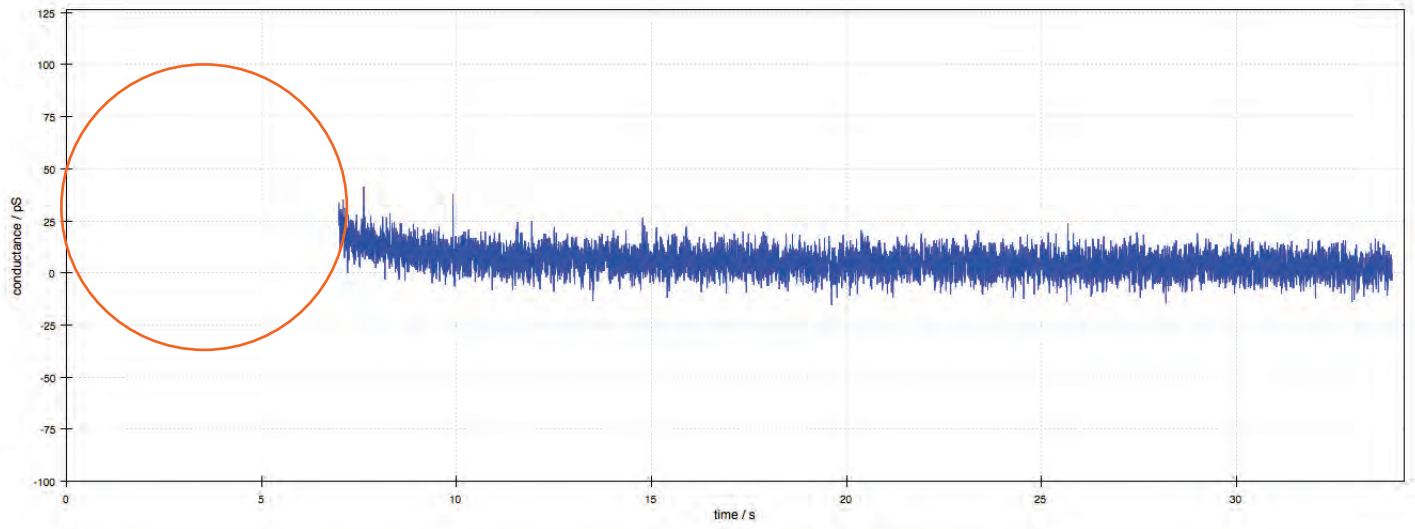


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electrolyte	—
contact injection 17/10.6uM	—
brush transfer	—
Adamantyl guest	—
lipid	—
electrolyte 1.4/0.9mM	—

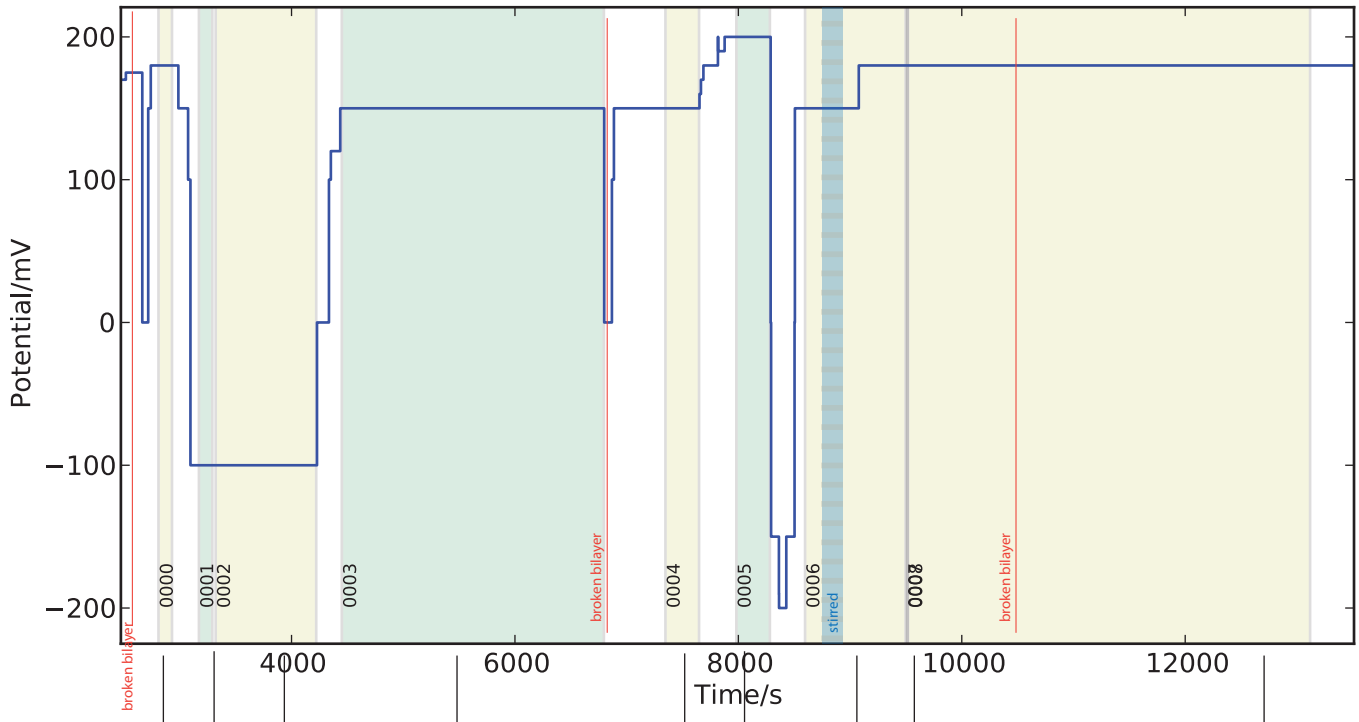


no activity

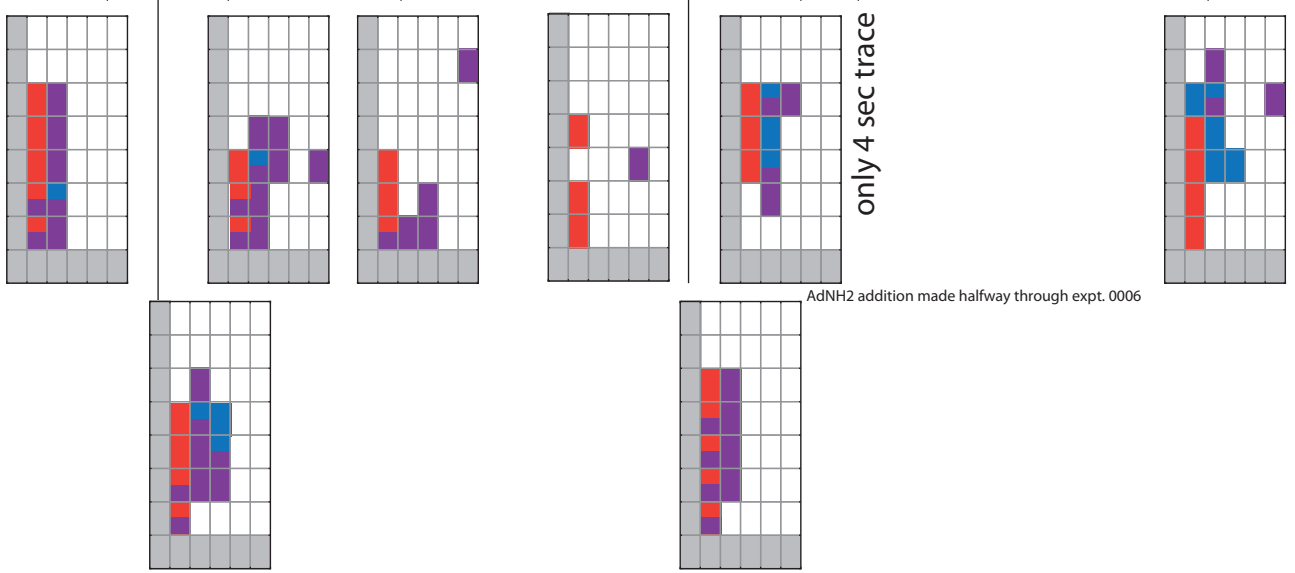
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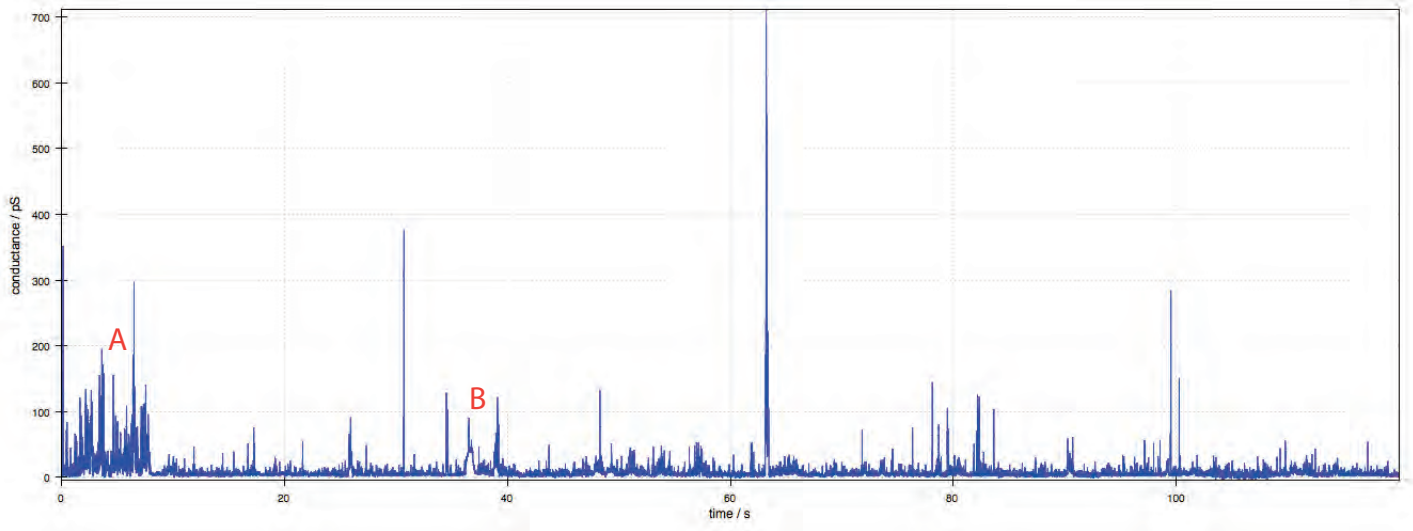
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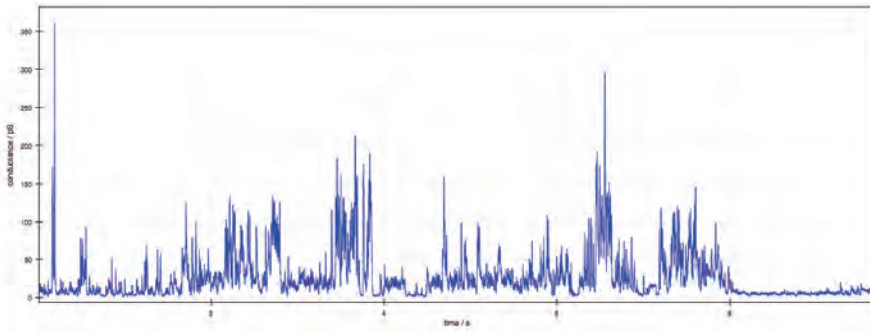
lipid 1%	lipid
electrolyte	electrolyte 1.4/0.9uM
contact injection	
brush transfer	
Adamantyl guest	



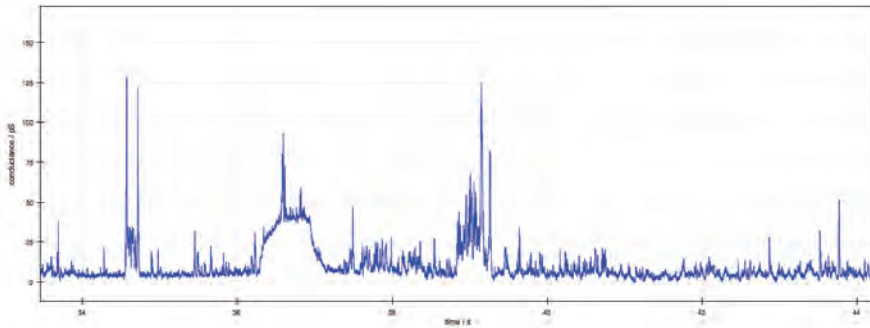
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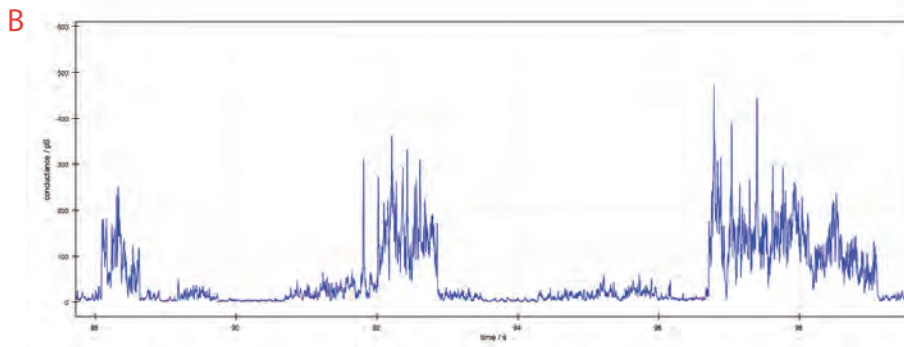
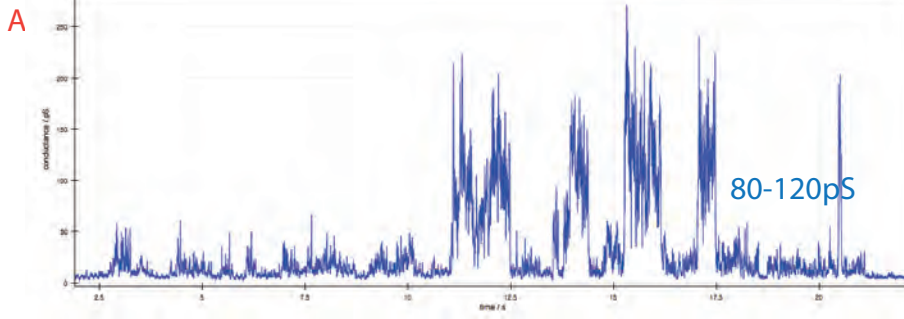
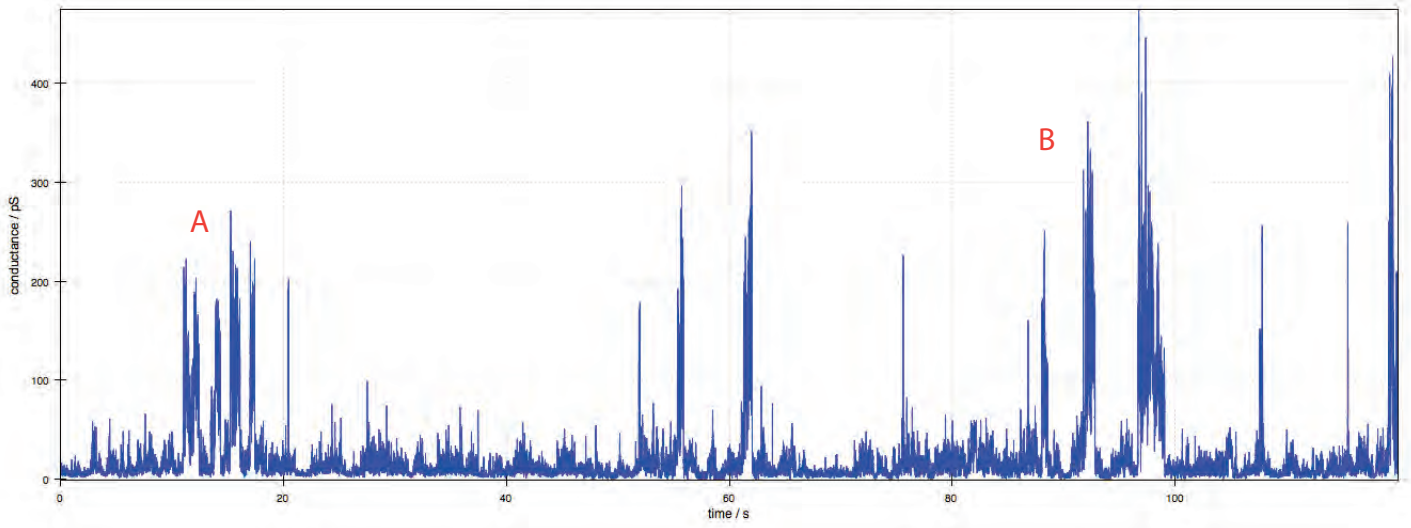
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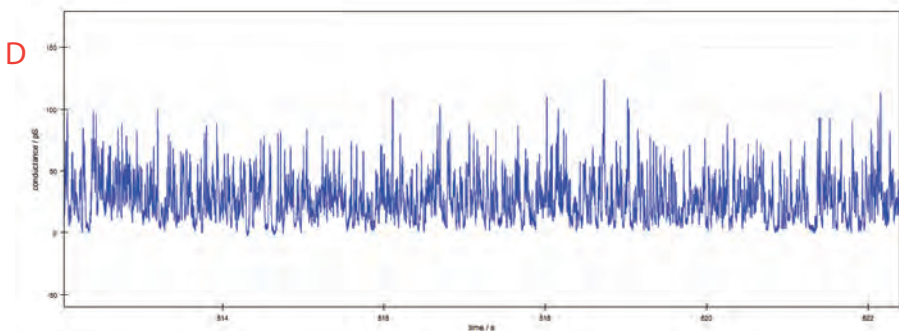
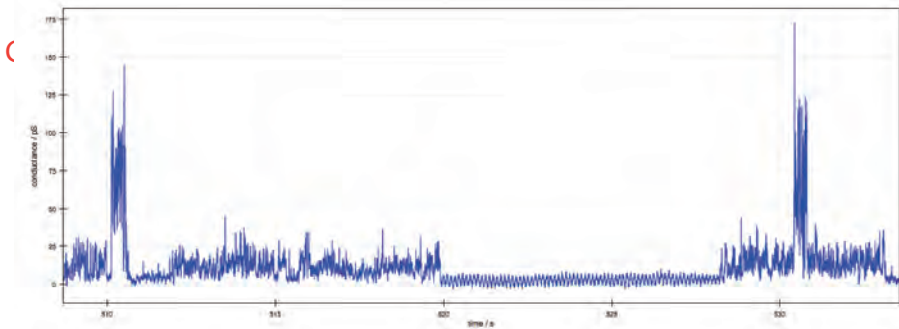
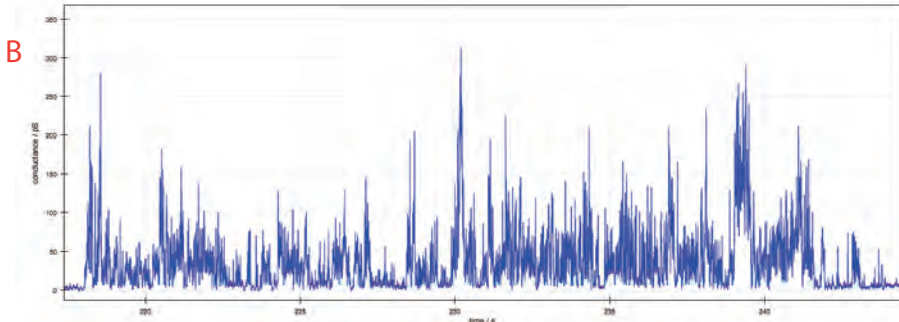
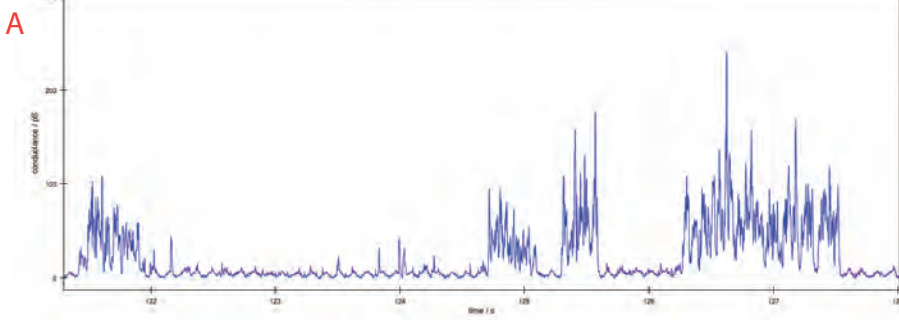
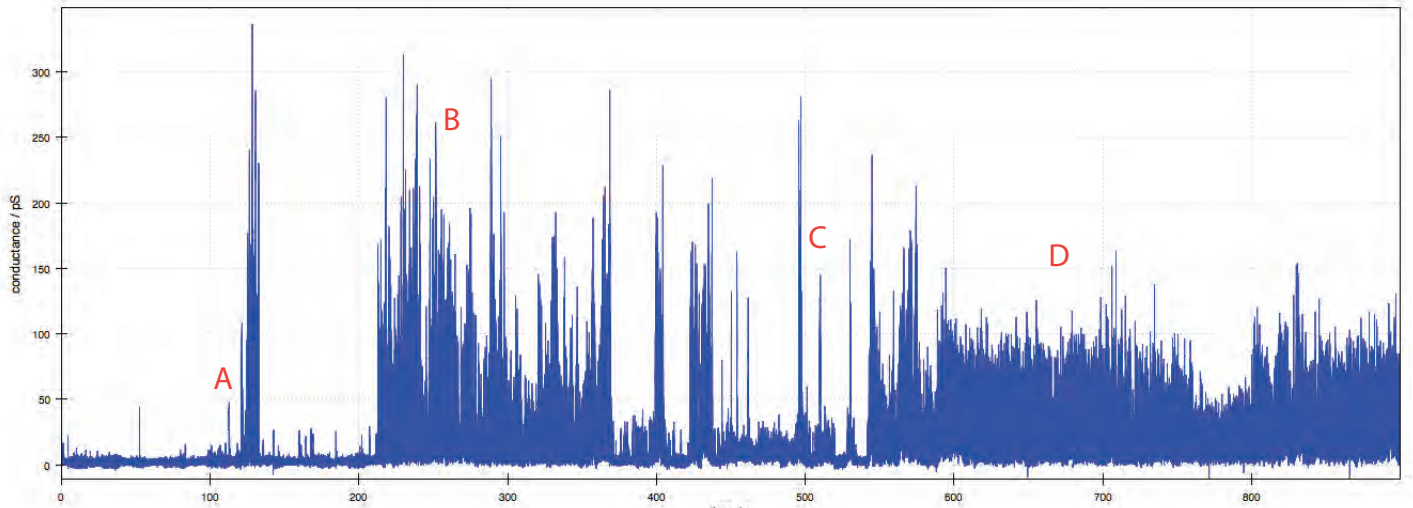


B

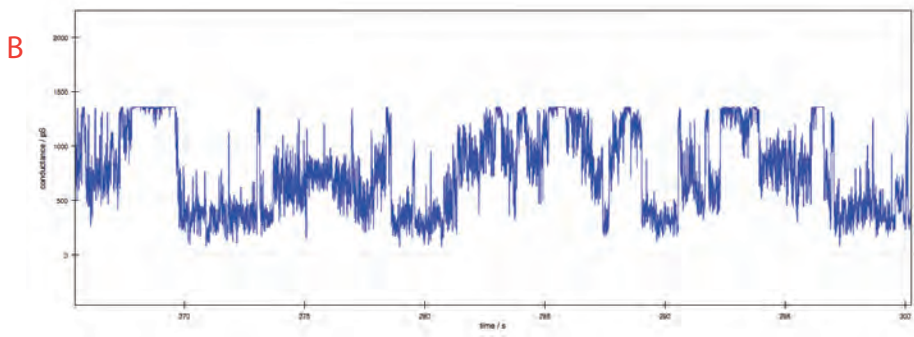
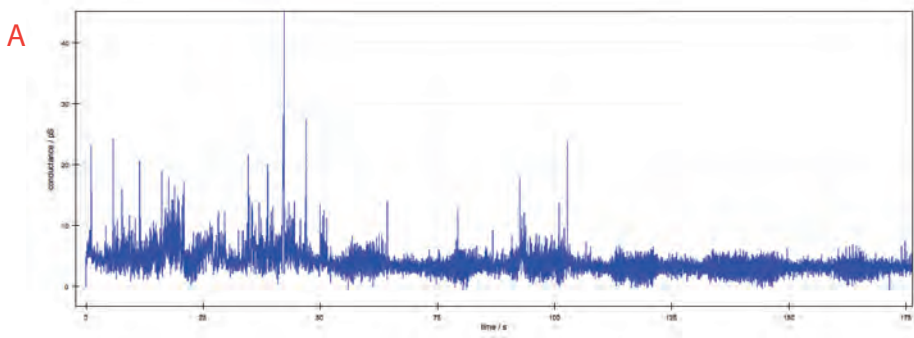
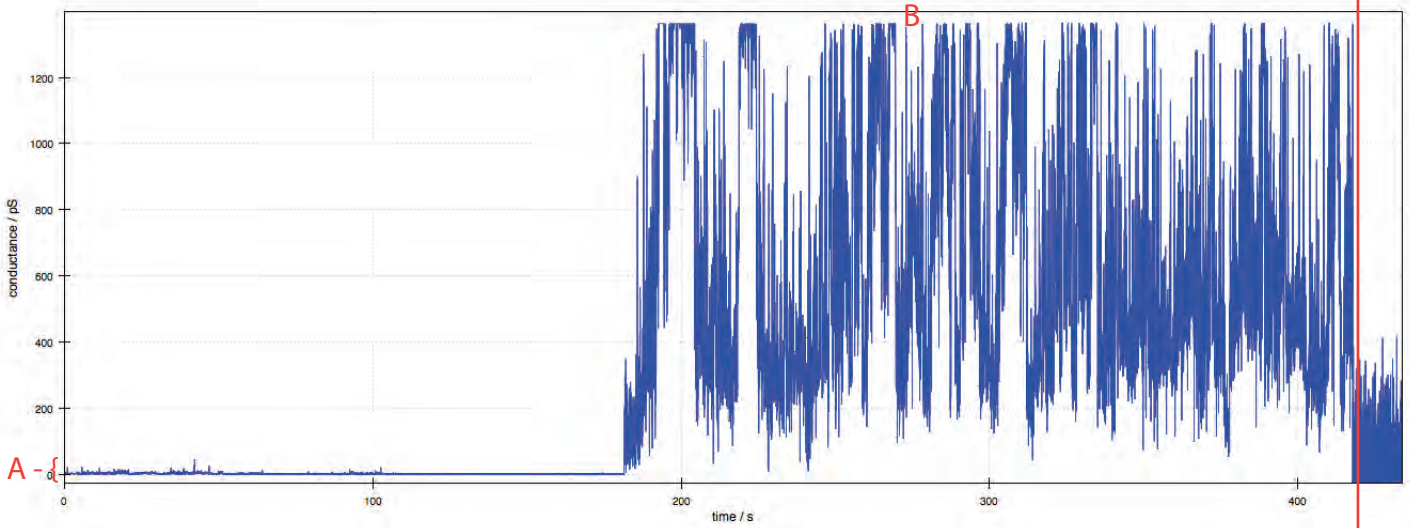


150-0001



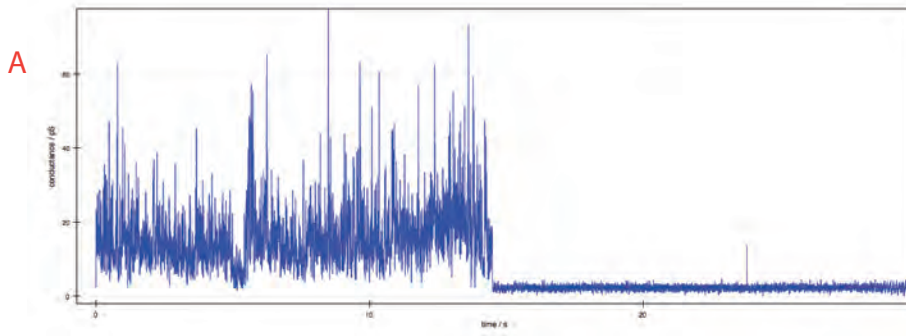
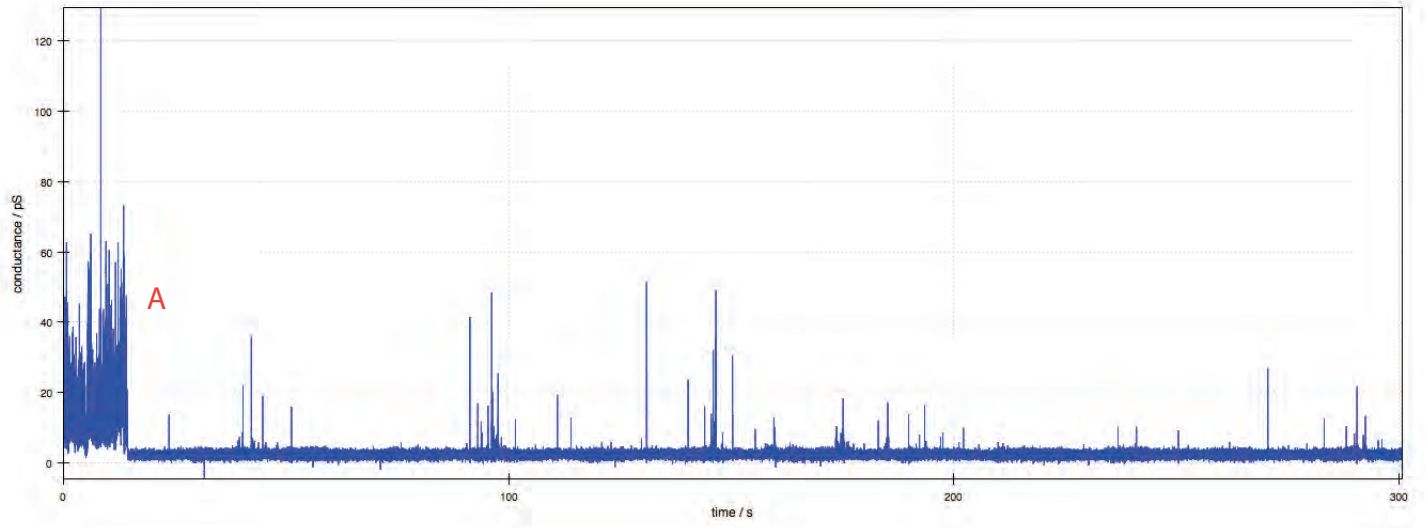


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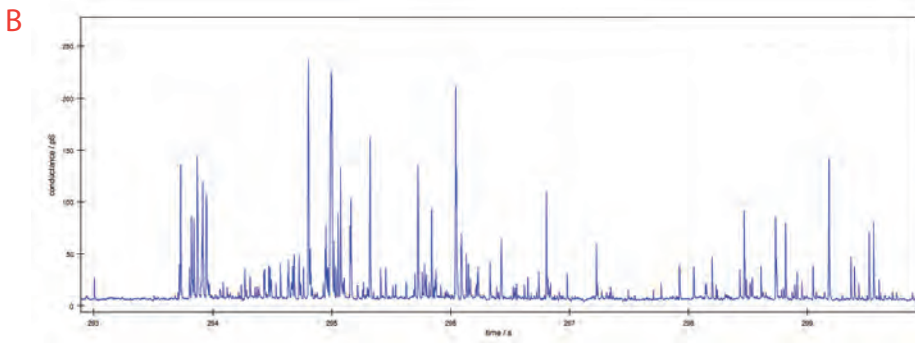
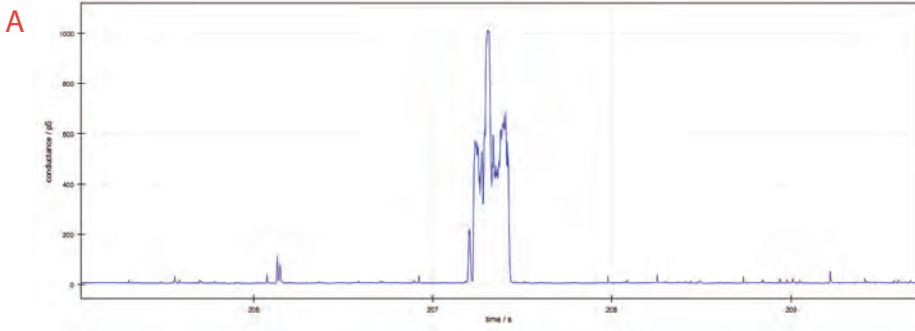
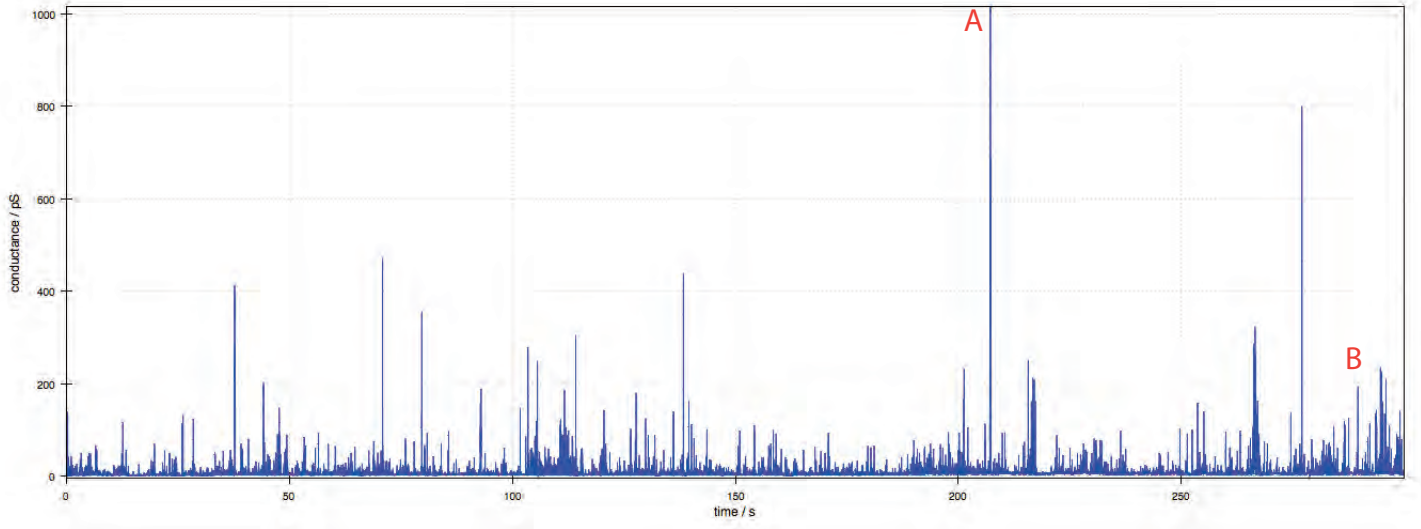


There may be structure under there, but it's not obvious where to start/end.

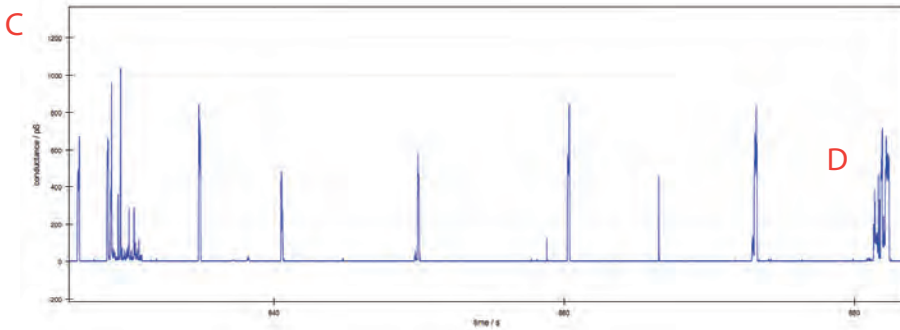
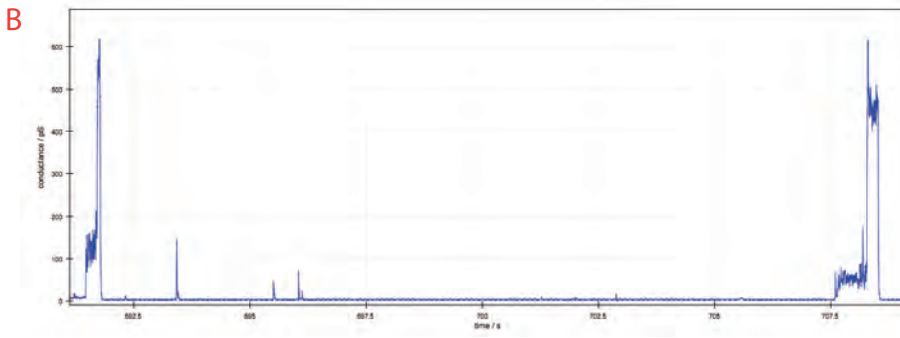
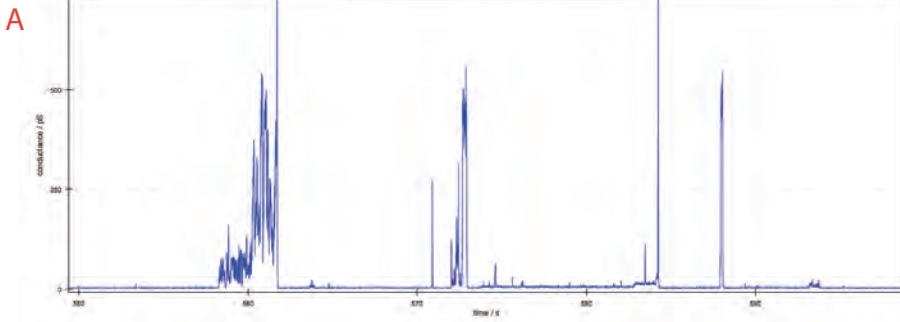
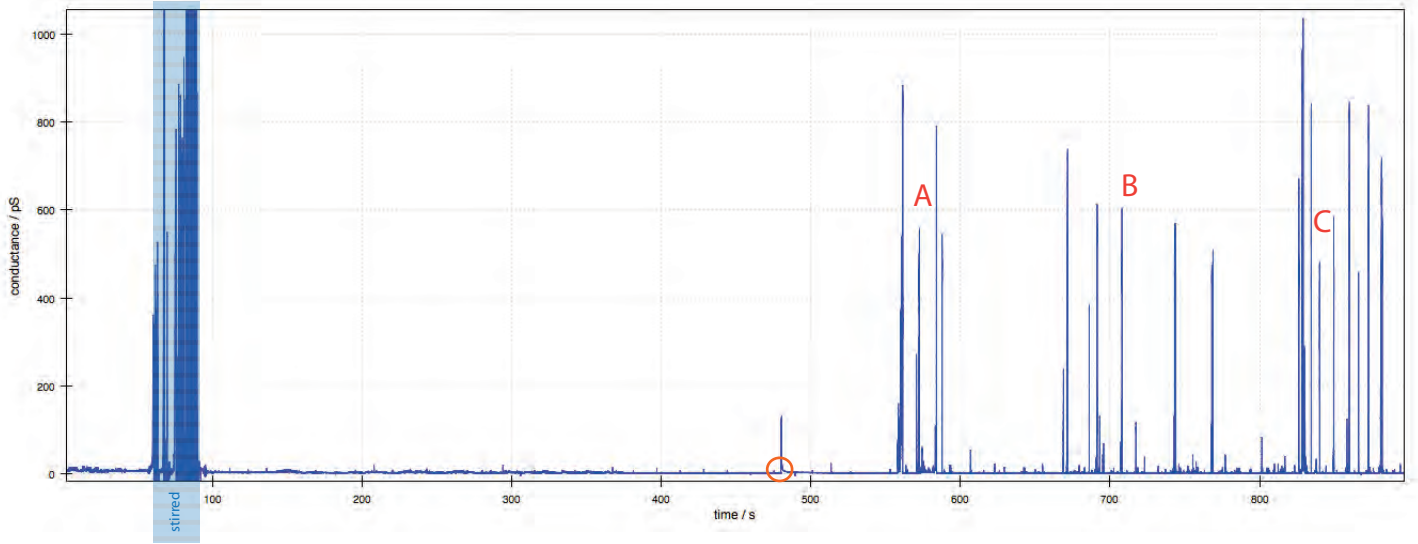
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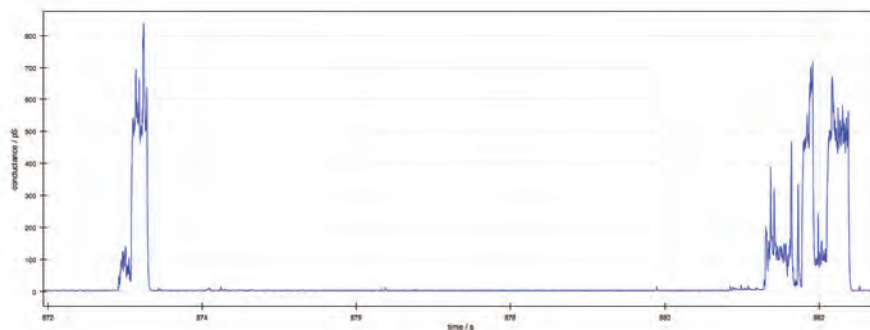
150-0005

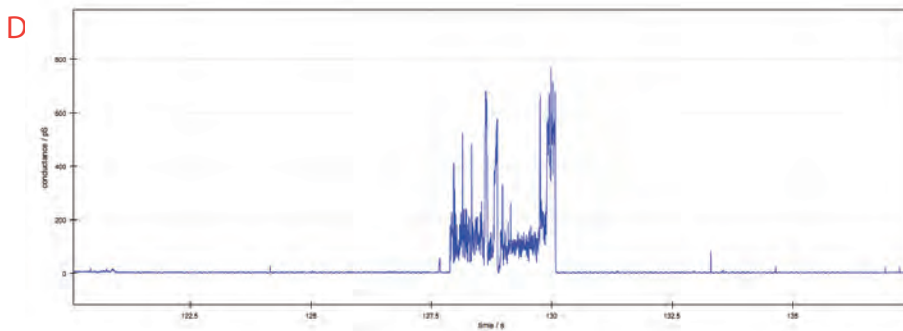
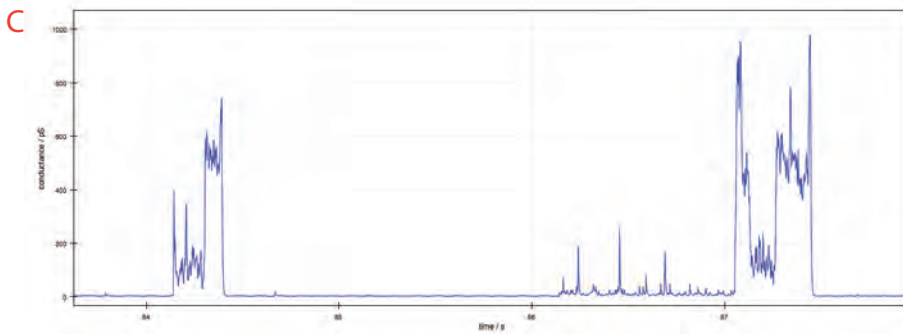
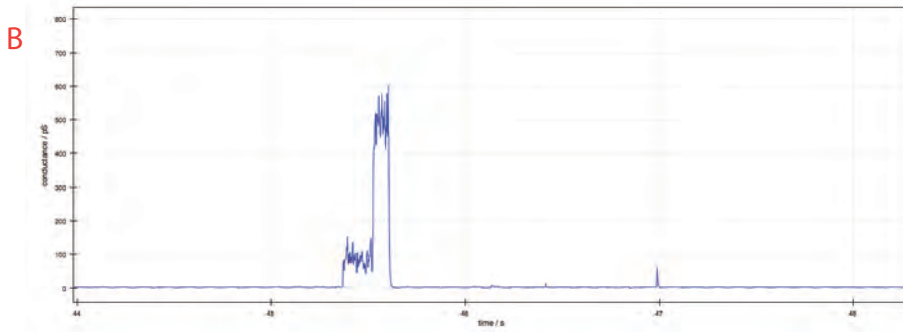
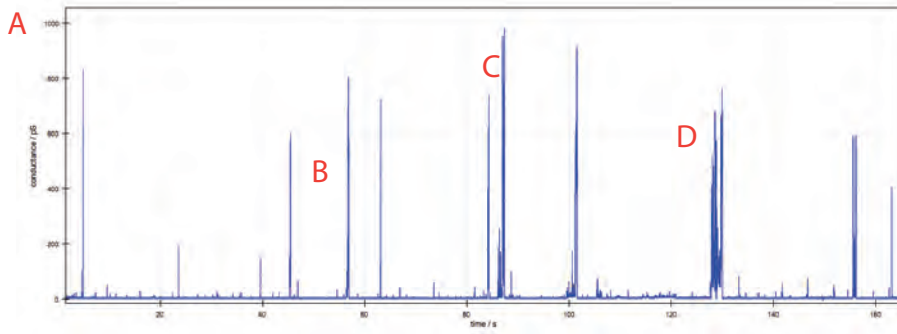
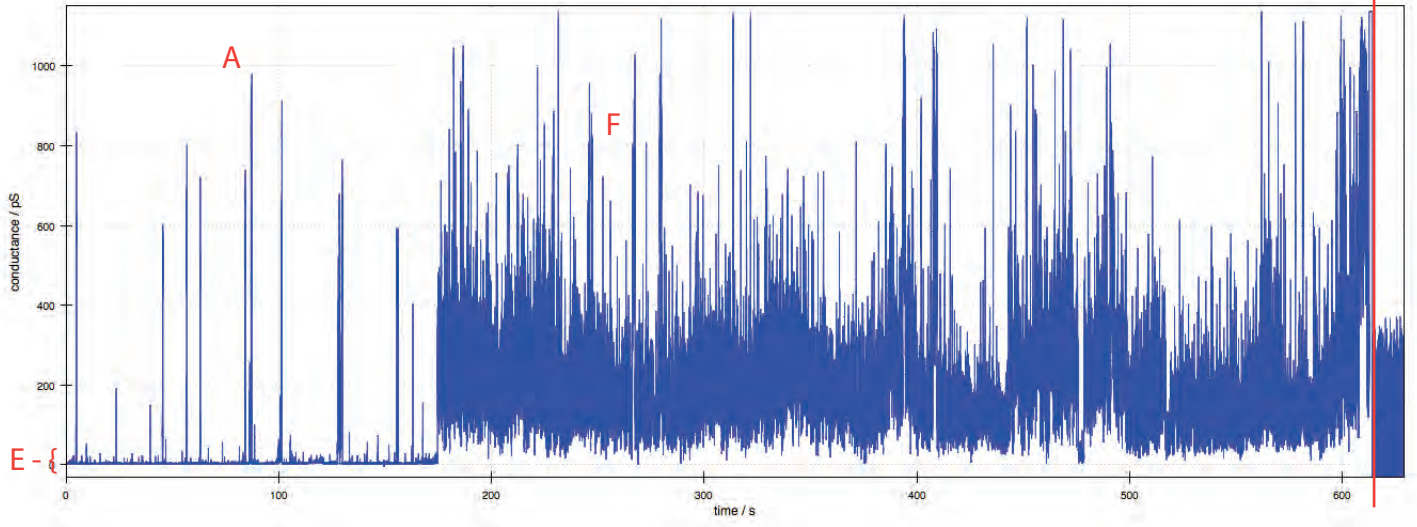


105-0006

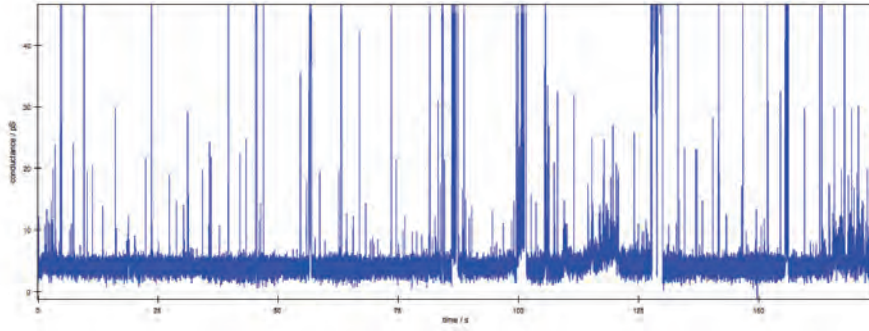


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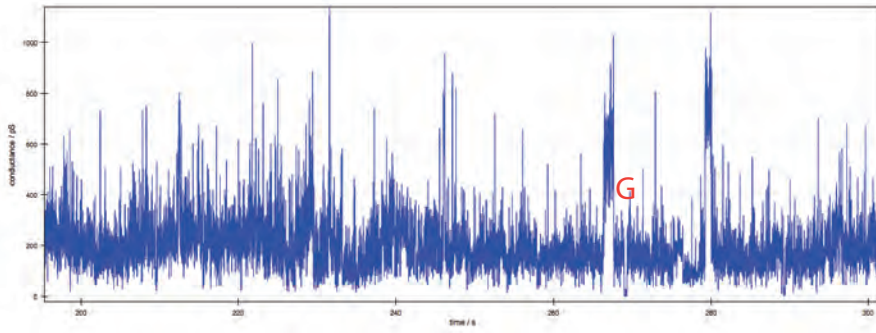




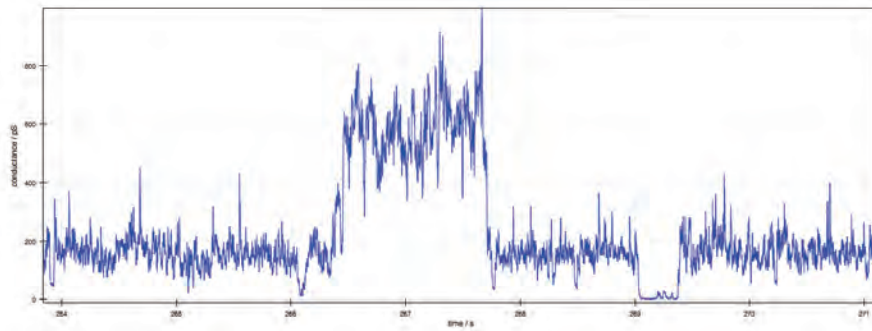
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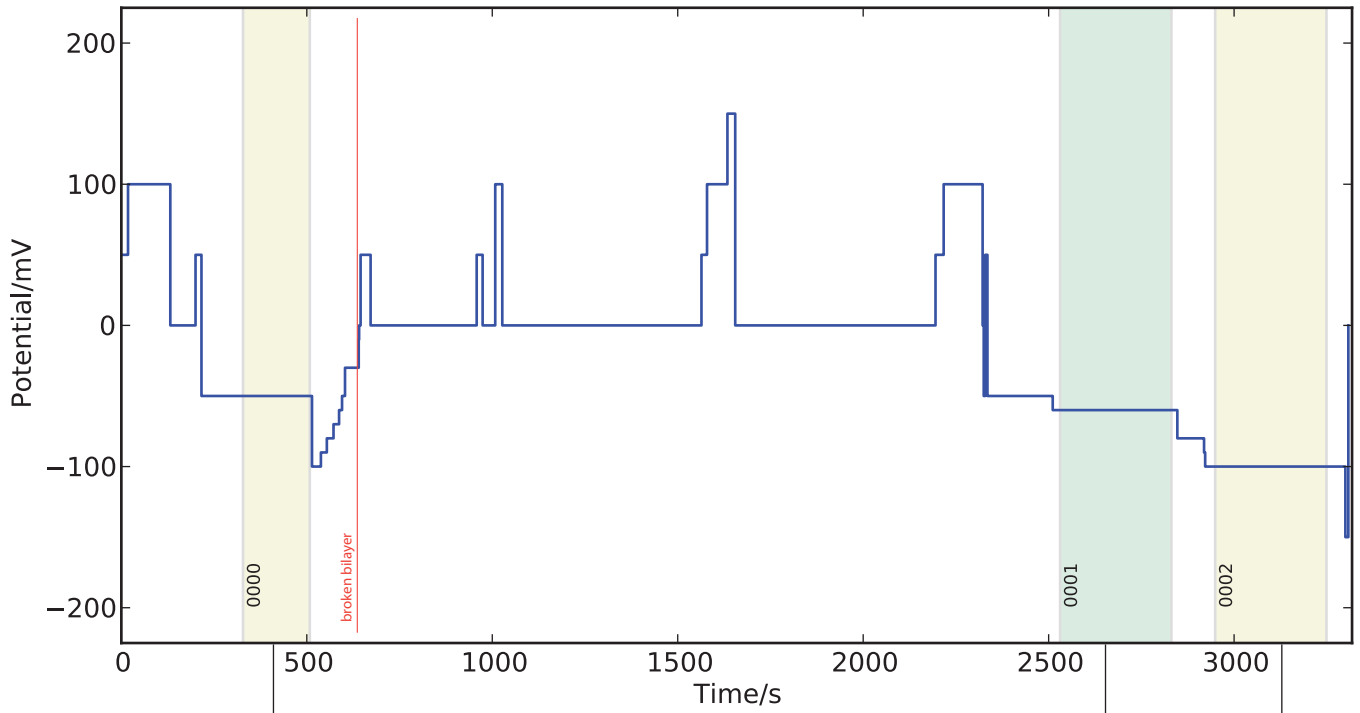
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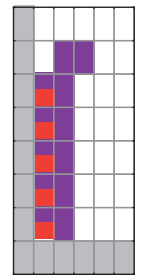
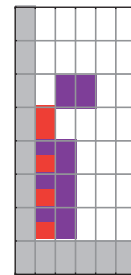
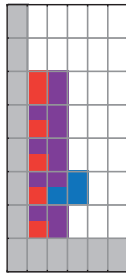
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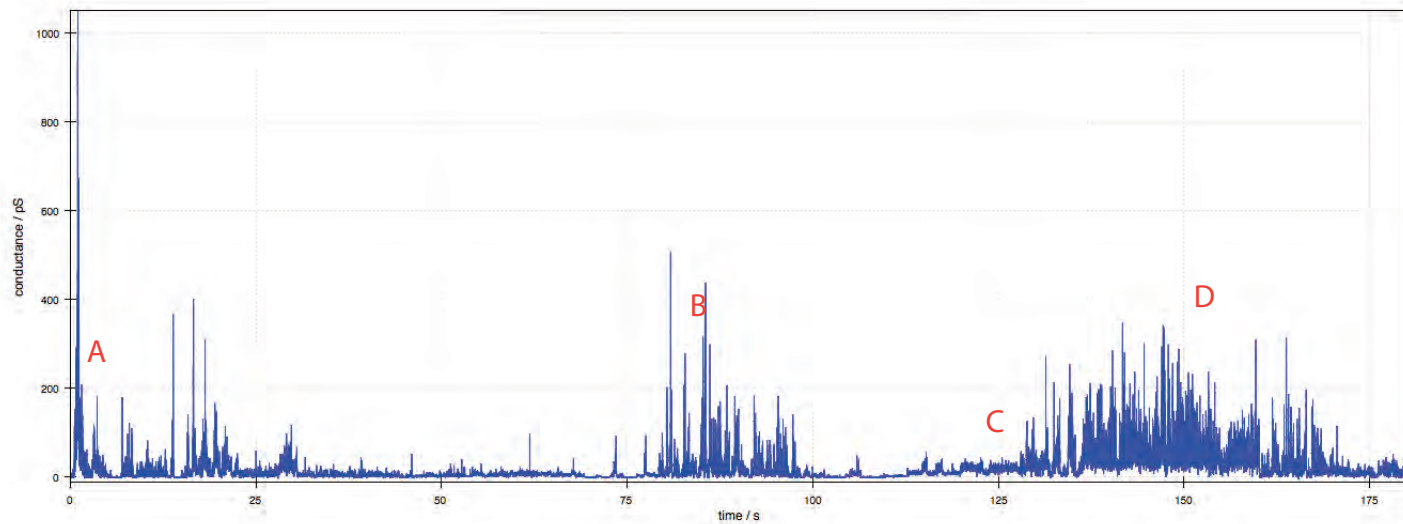
[JC-108] bCD6Es6Es2 1M CsCl pH 7 homoAdd



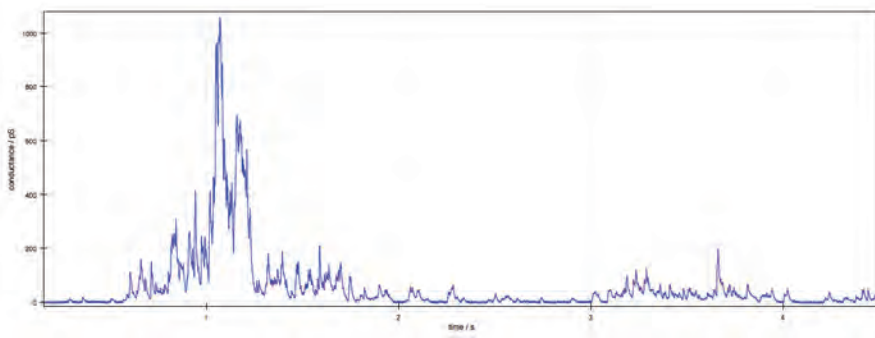
lipid
electrolyte 27/18uM
contact injection
brush transfer
Adamantyl guest
lipid
electrolyte



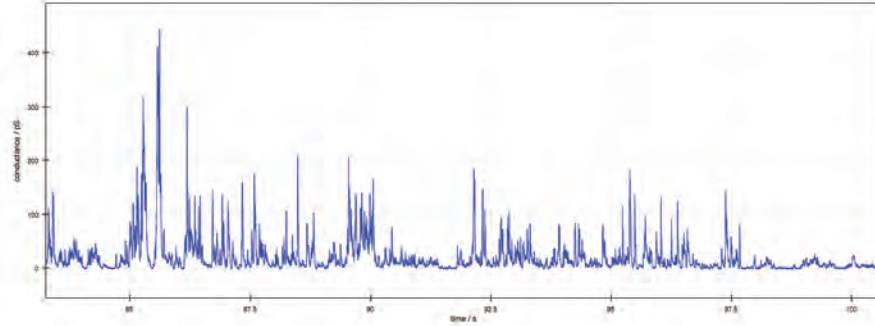
spikes potential dependent



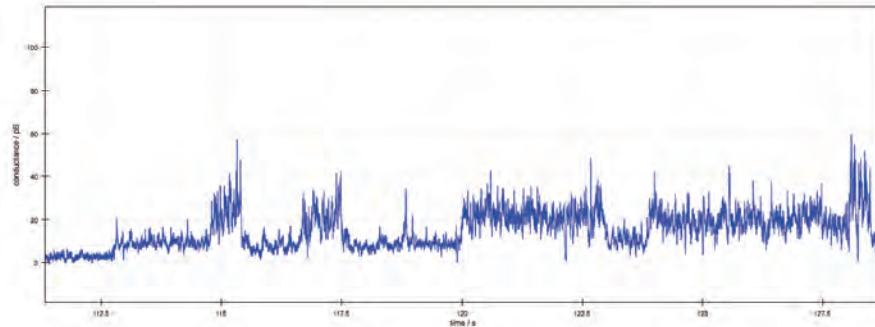
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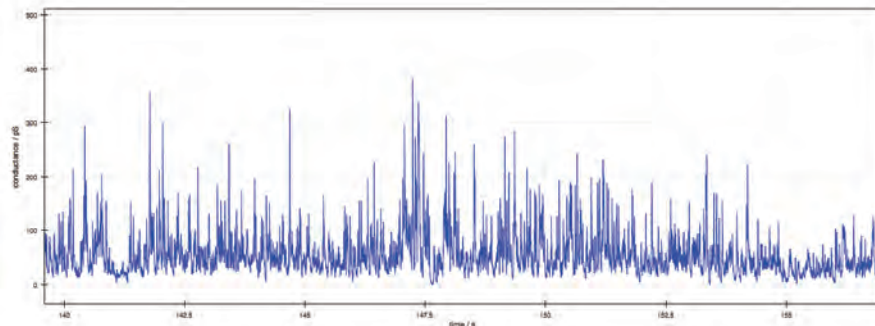
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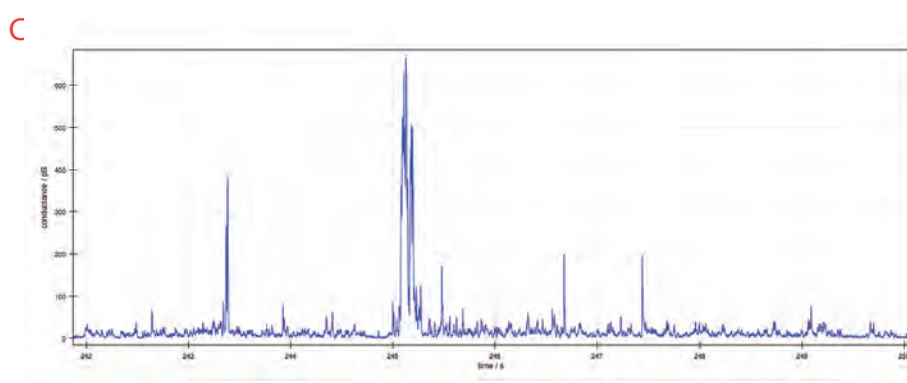
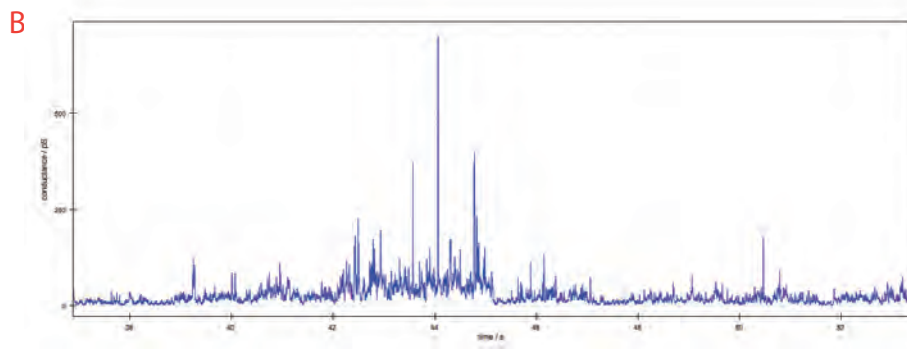
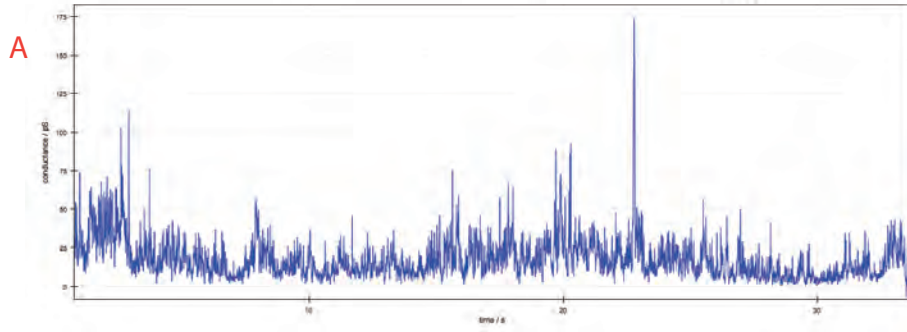
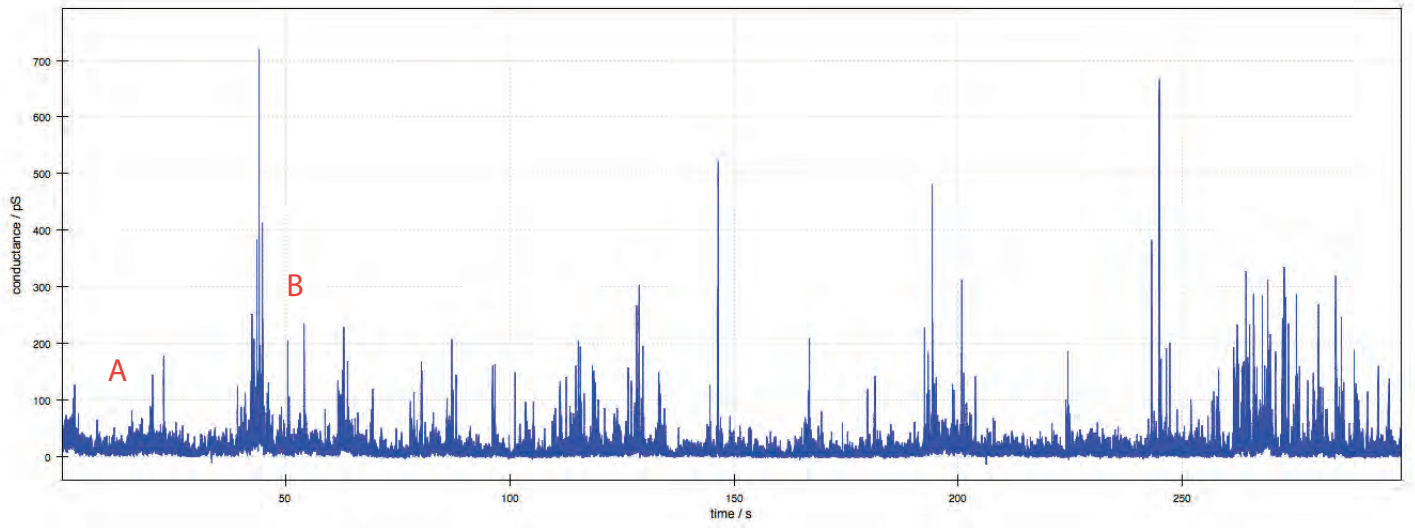


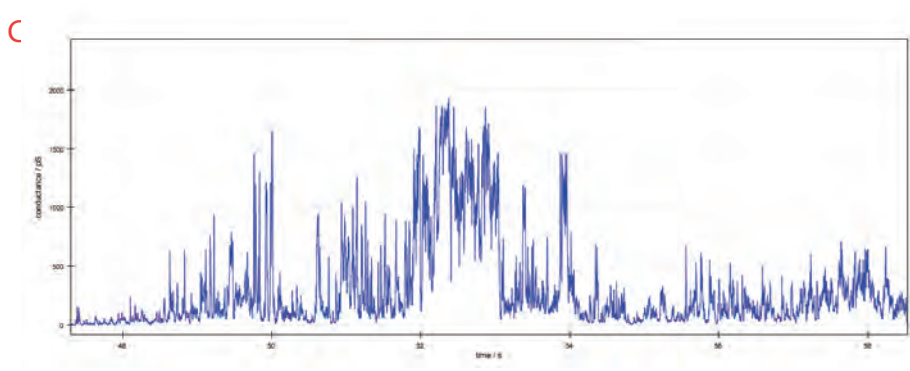
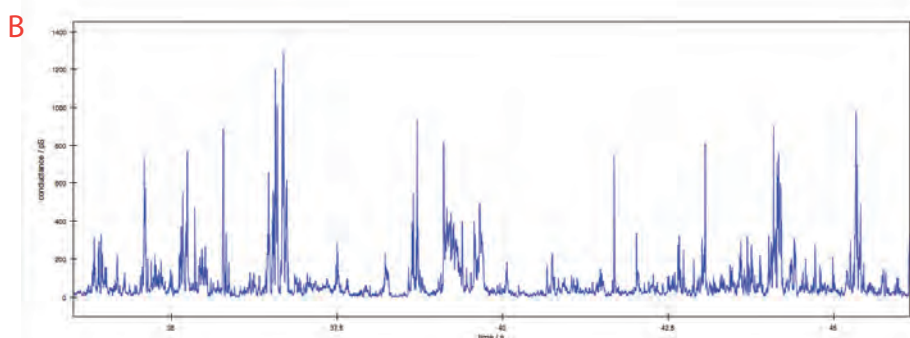
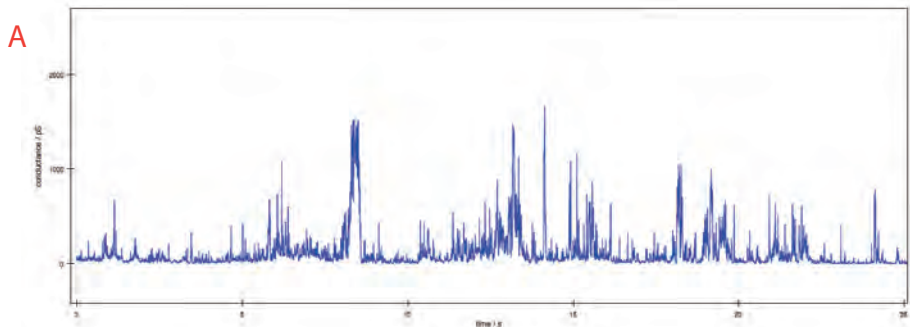
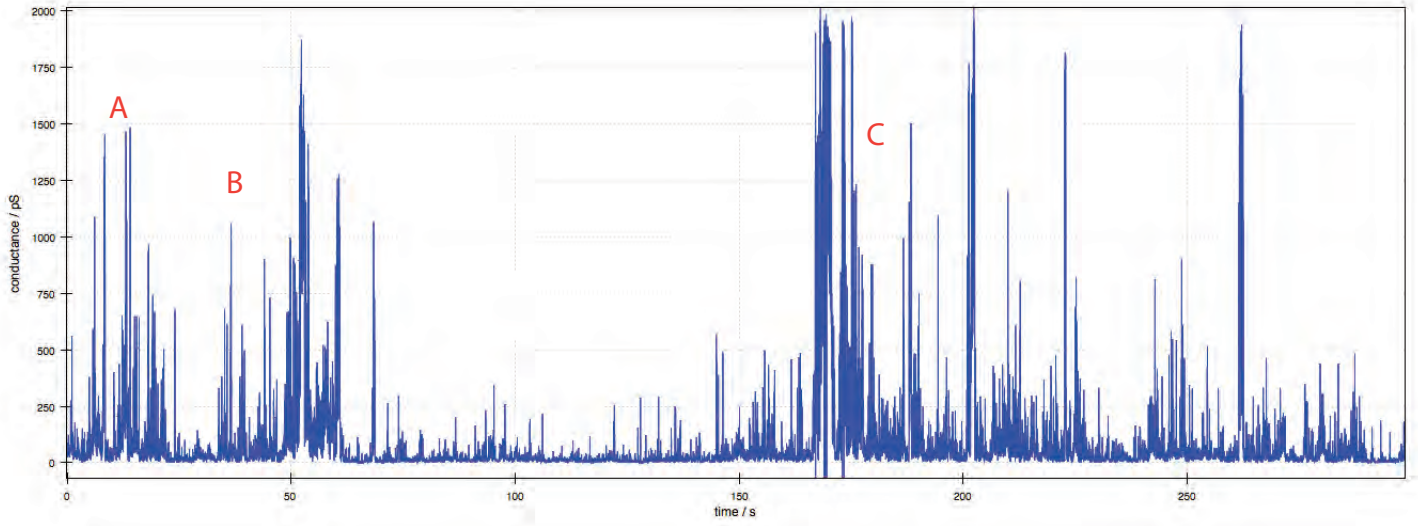
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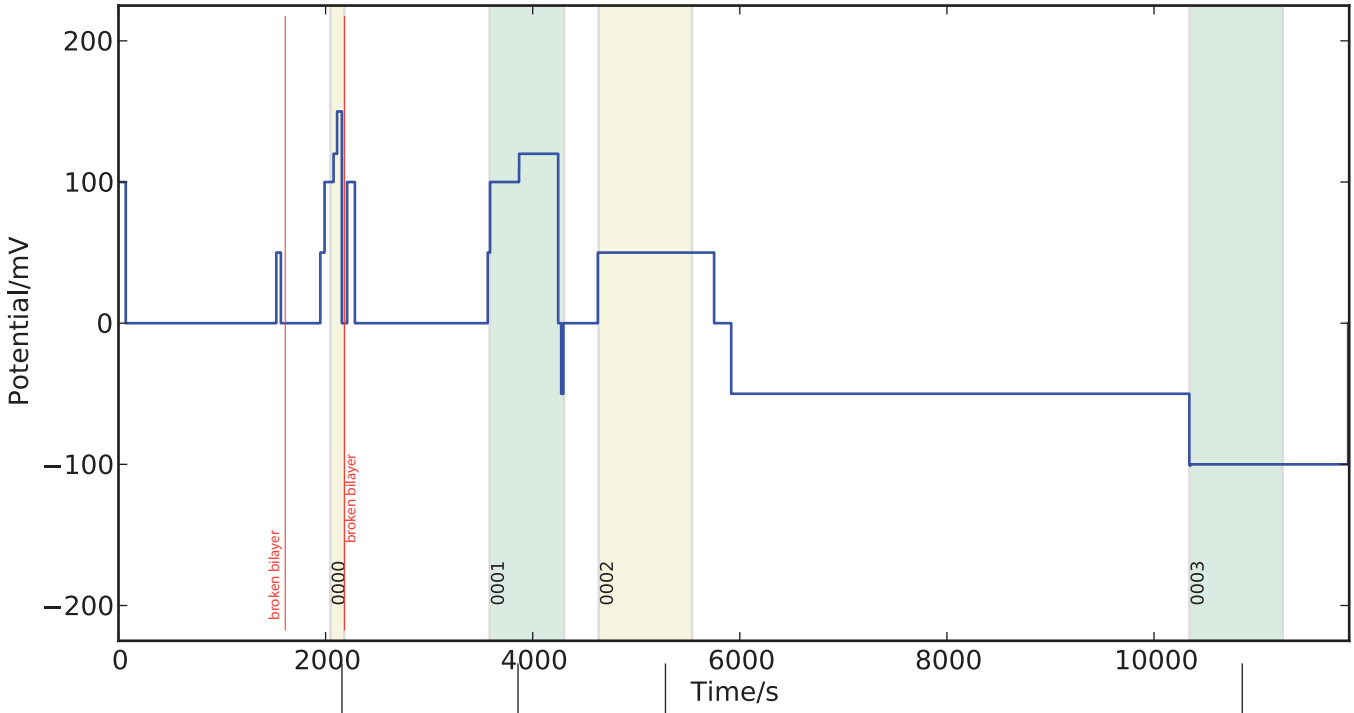
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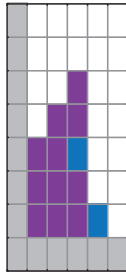
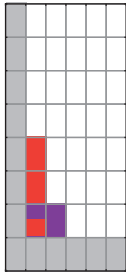




[JC-72] bCD-6-Es-8 1M CsCl pH 7 survey

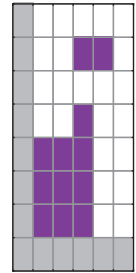


lipid
electrolyte
contact injection 14.6uM (insol)
brush transfer



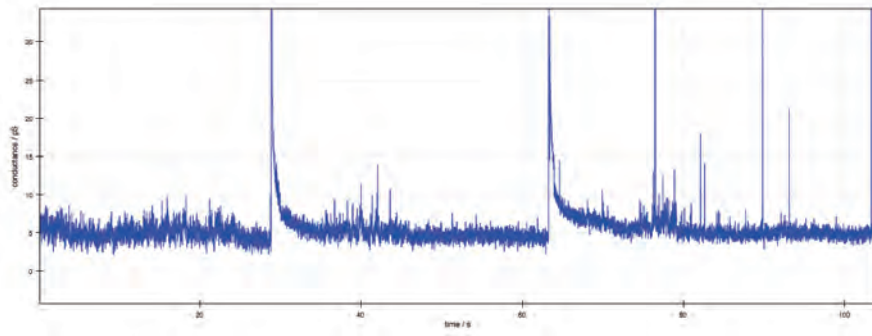
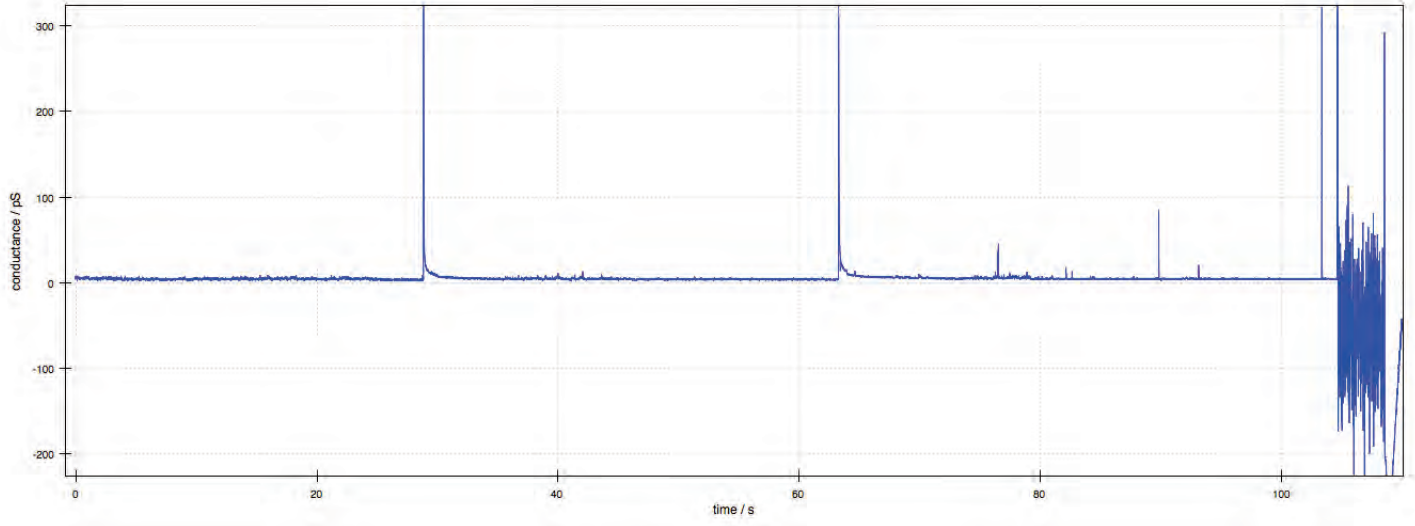
structure instable to potential changes

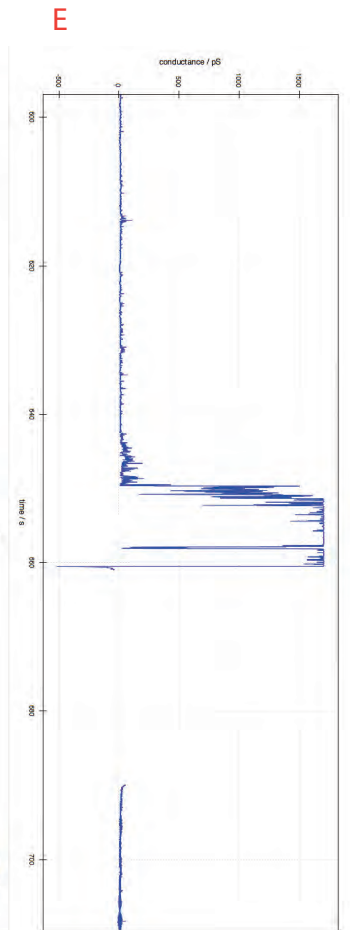
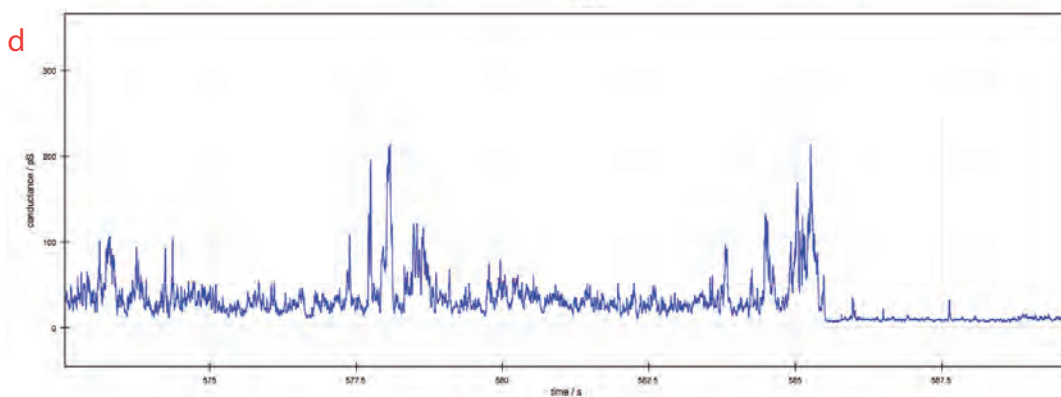
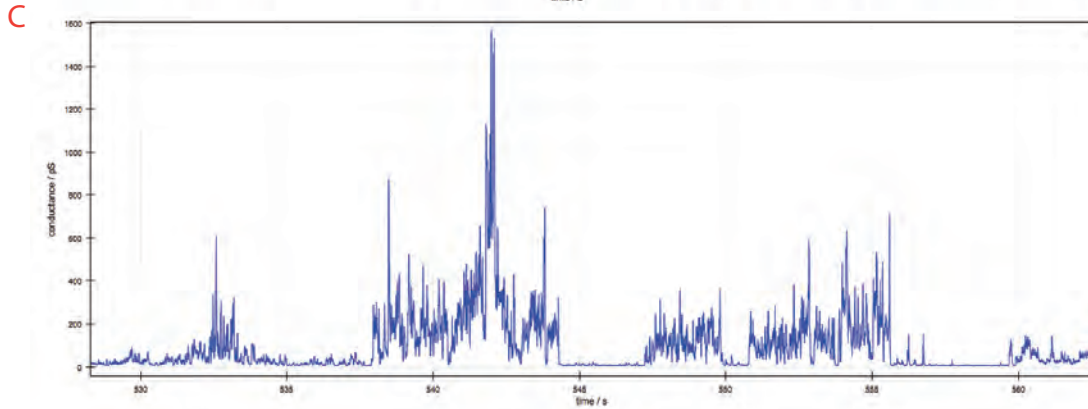
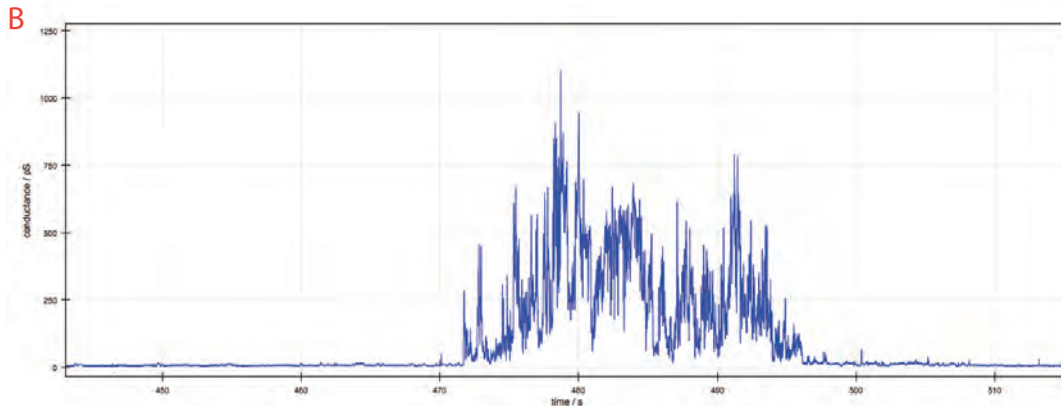
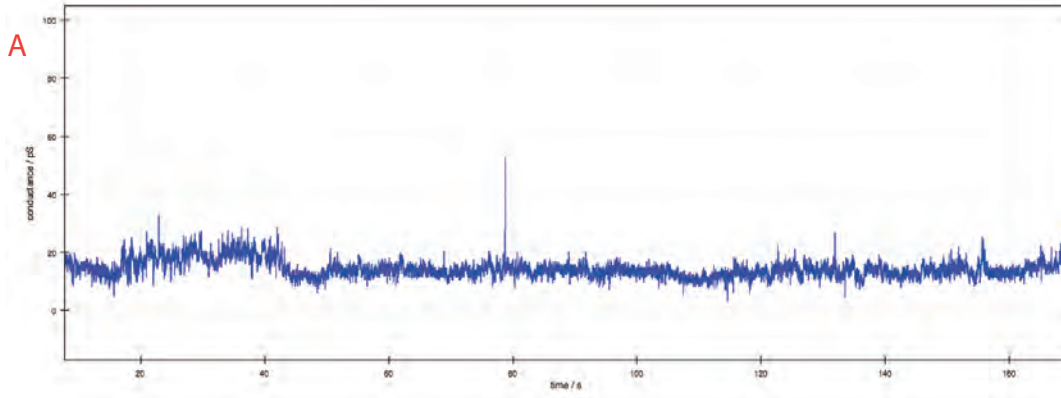
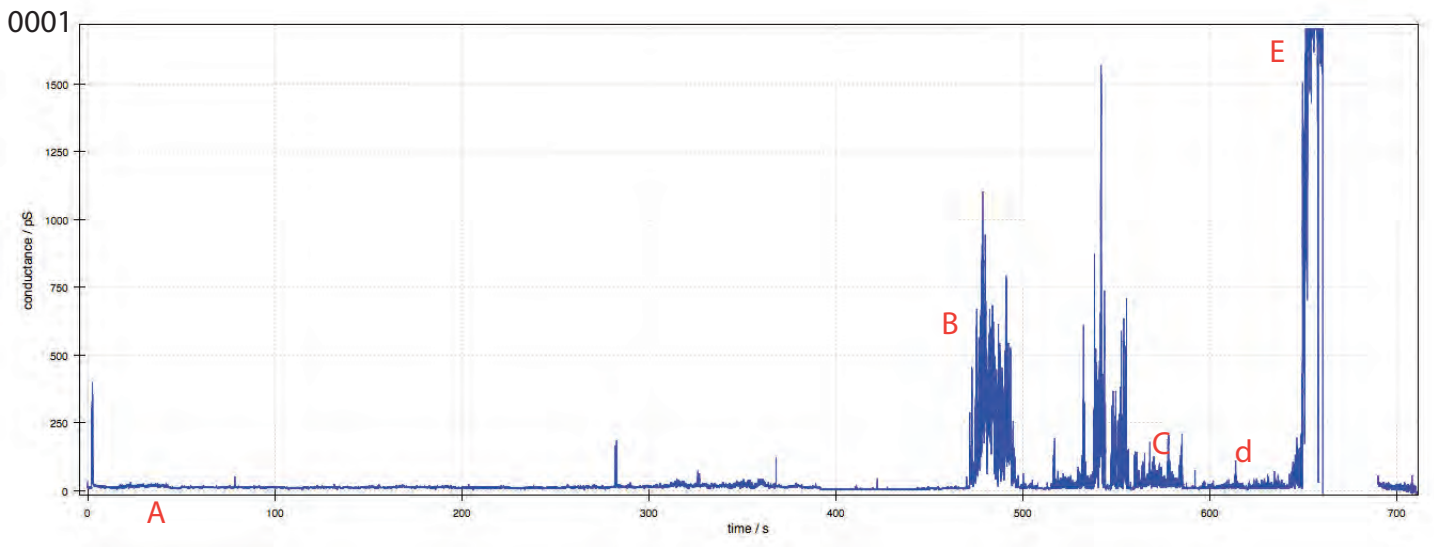
inexplicable noise
or genuine small, frequent activity?



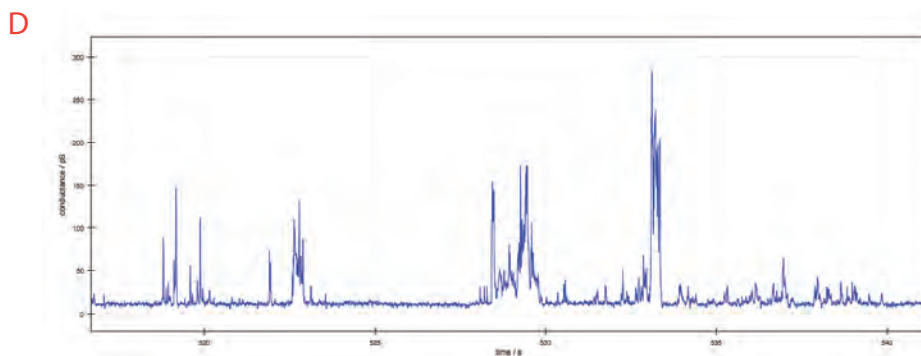
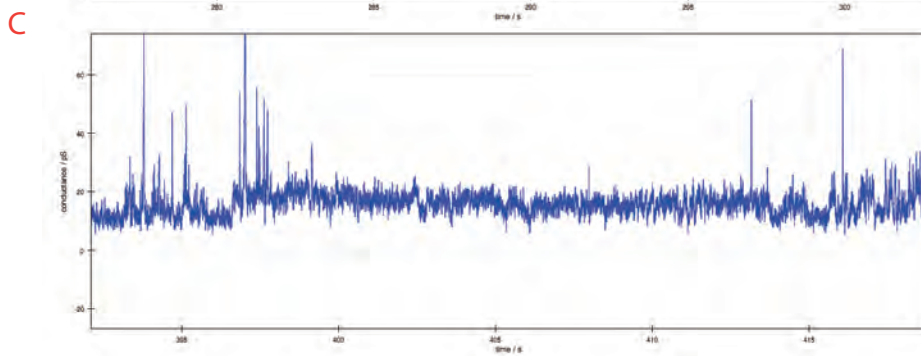
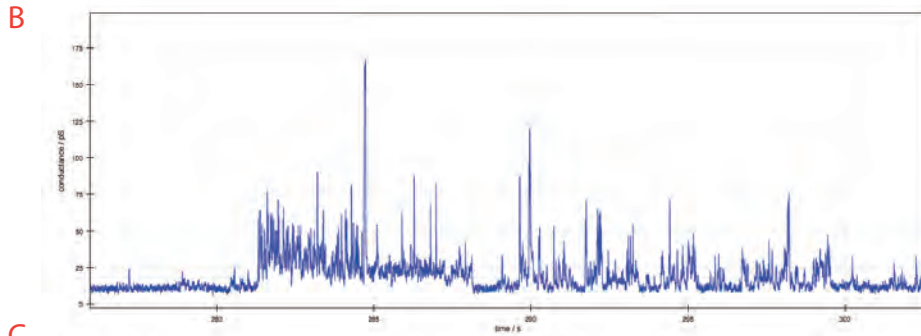
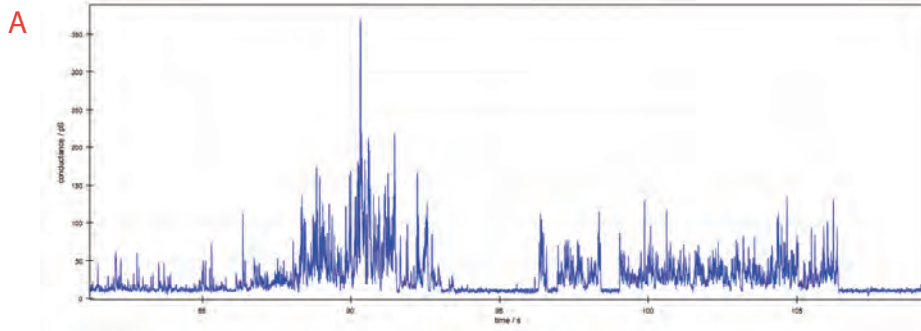
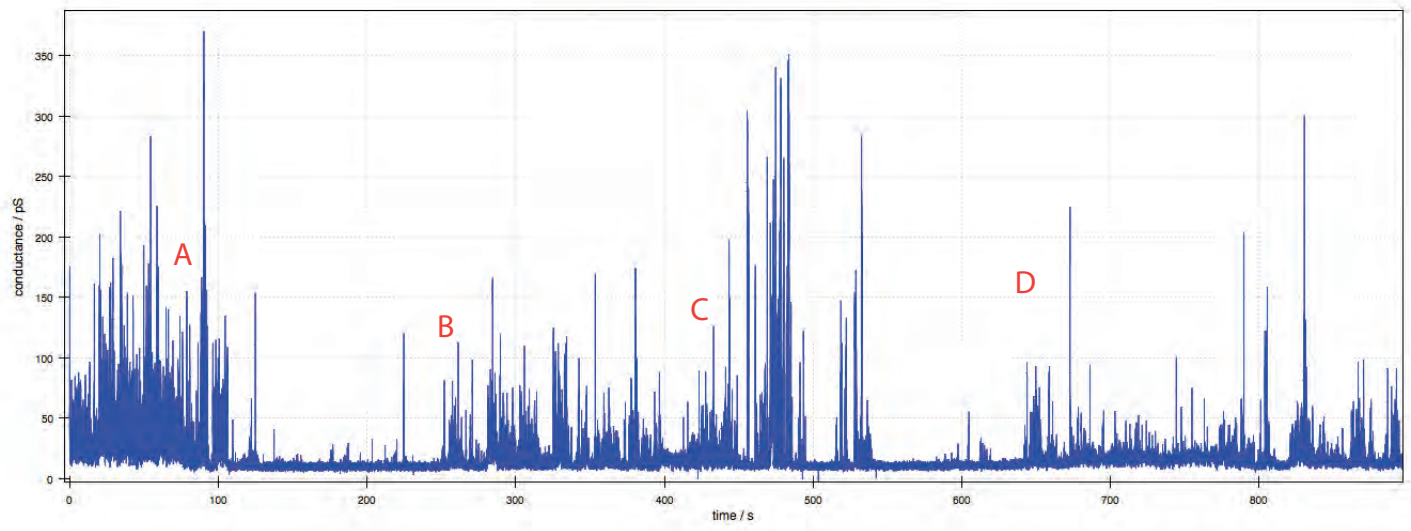
fractal?

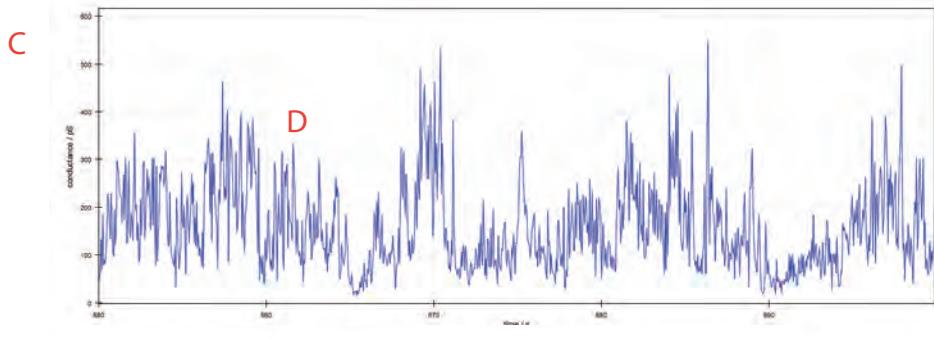
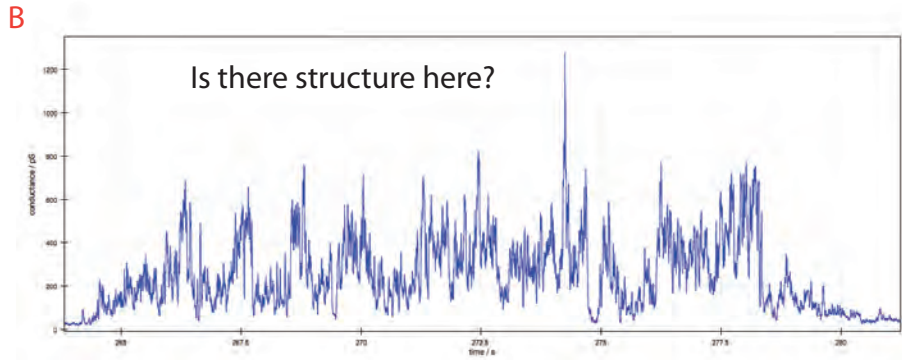
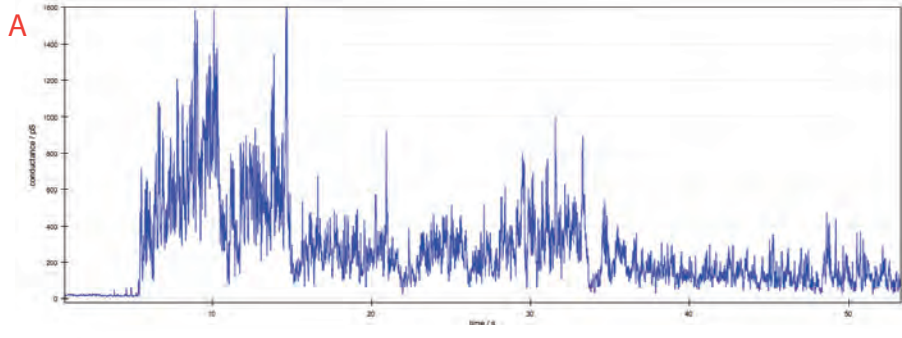
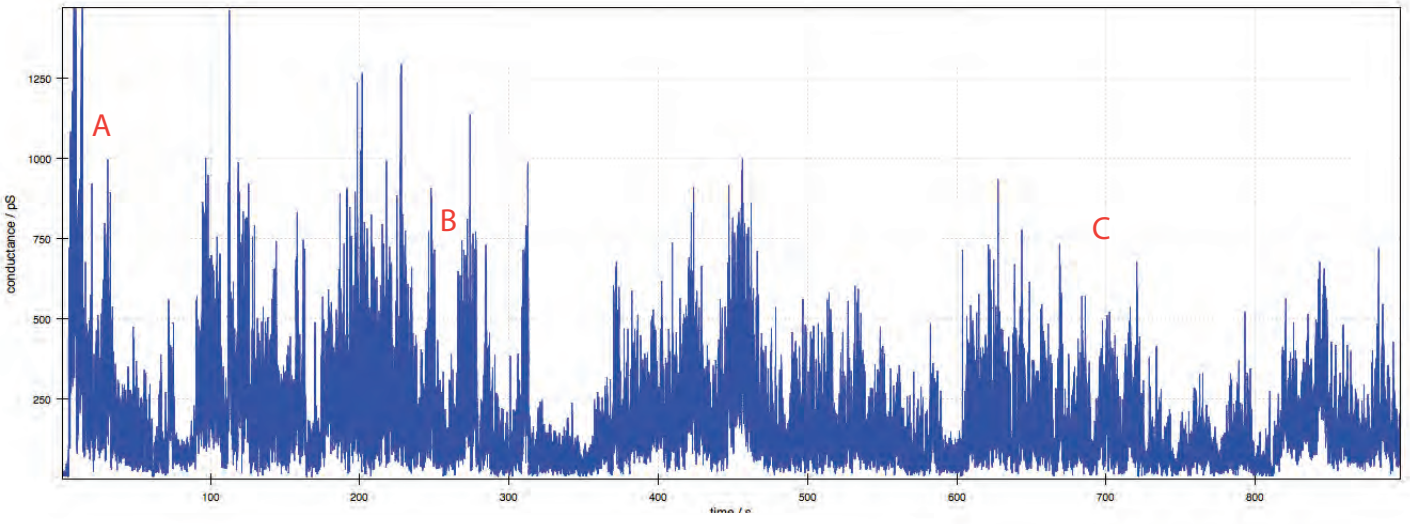
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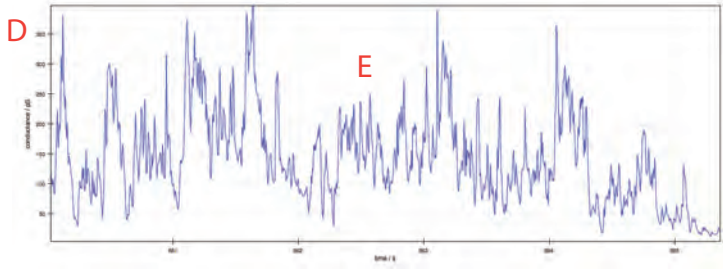


structure instable to potential changes

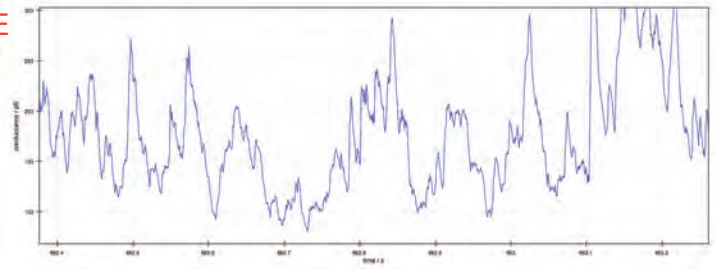




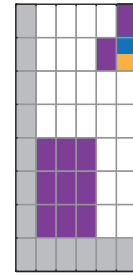
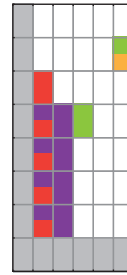
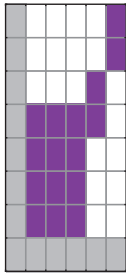
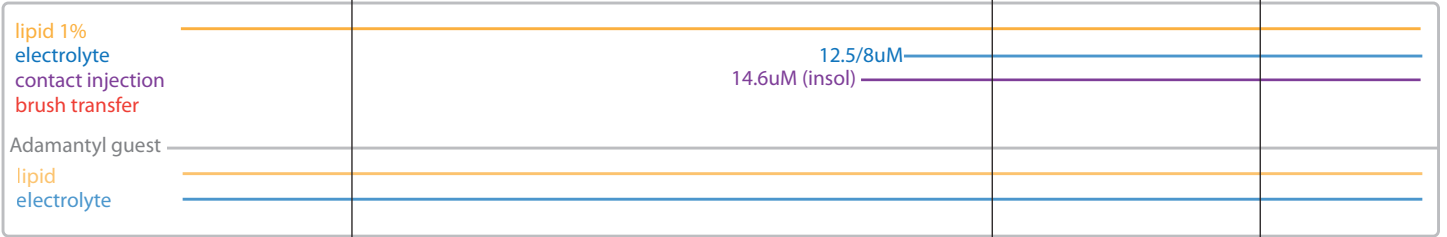
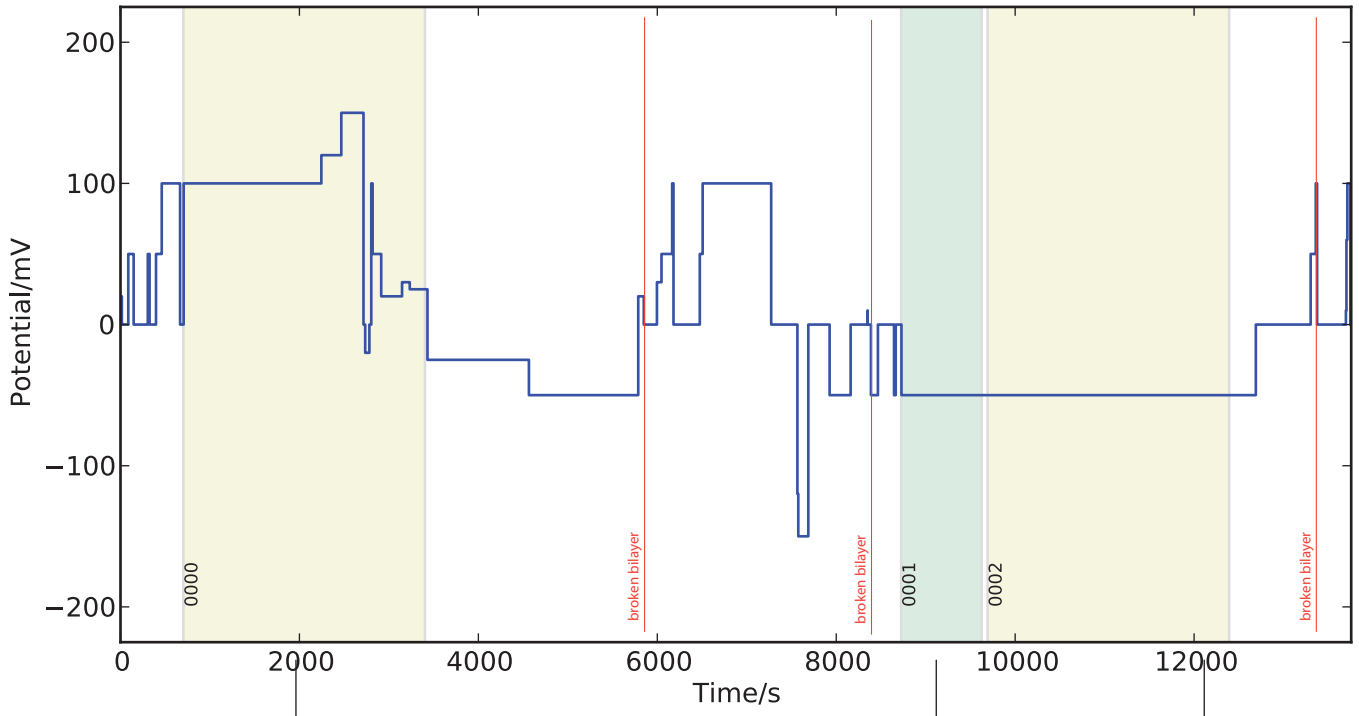
fractal?



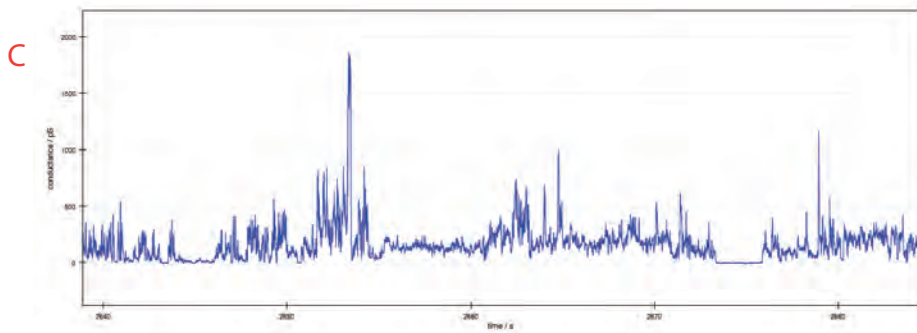
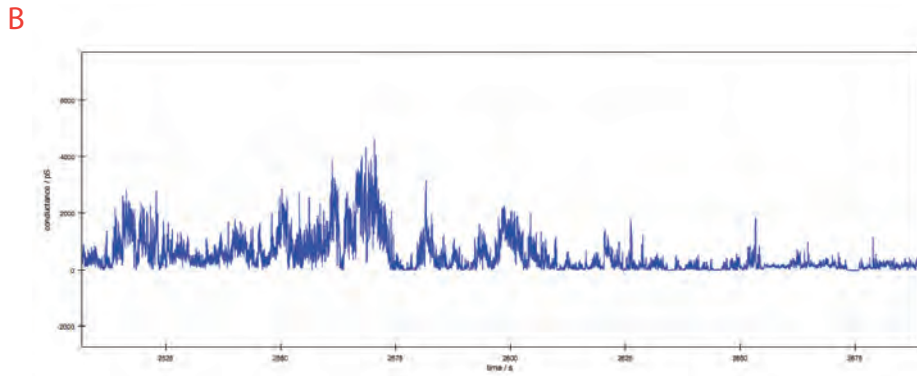
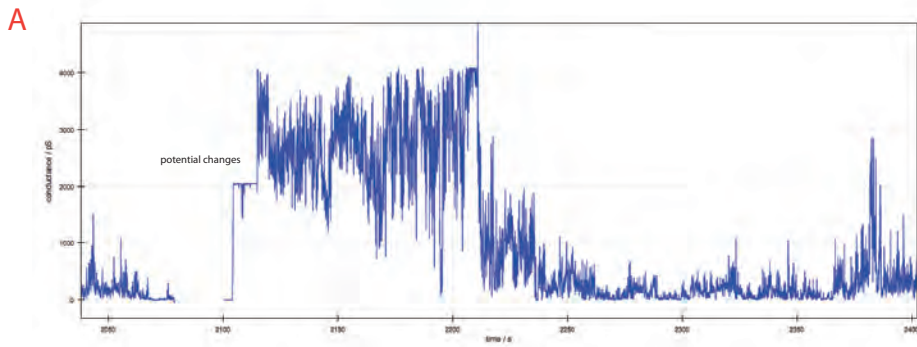
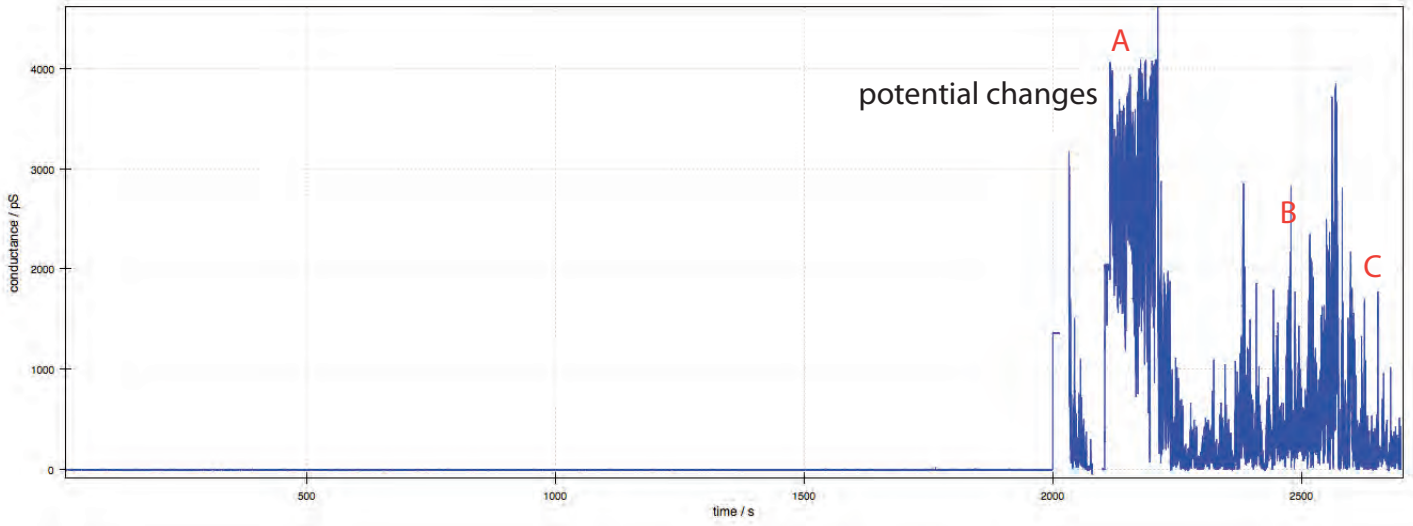
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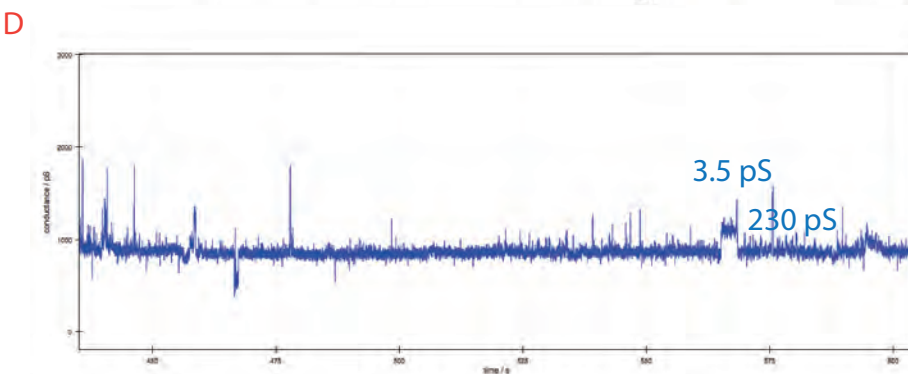
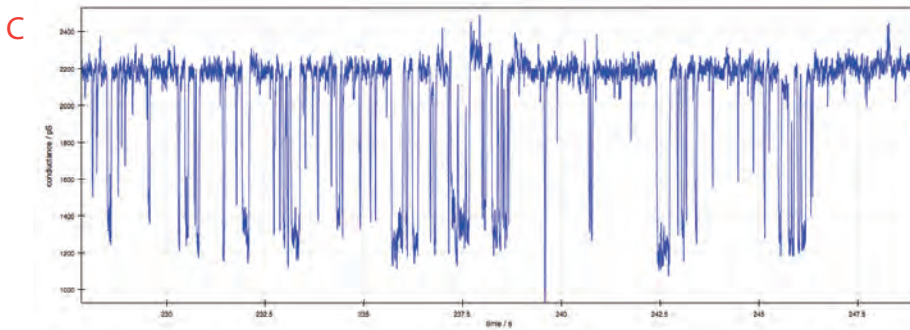
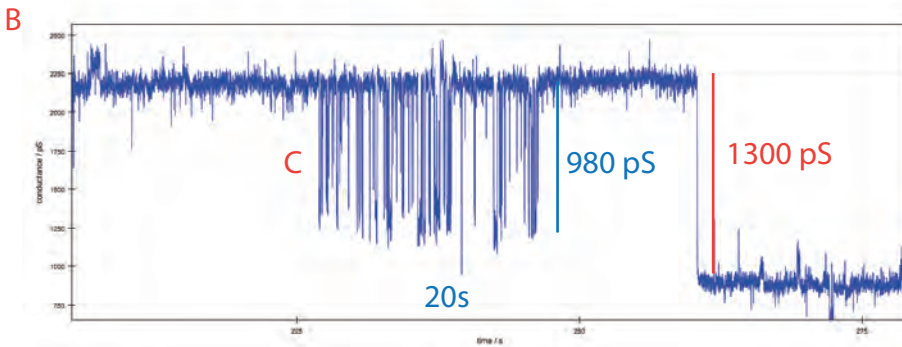
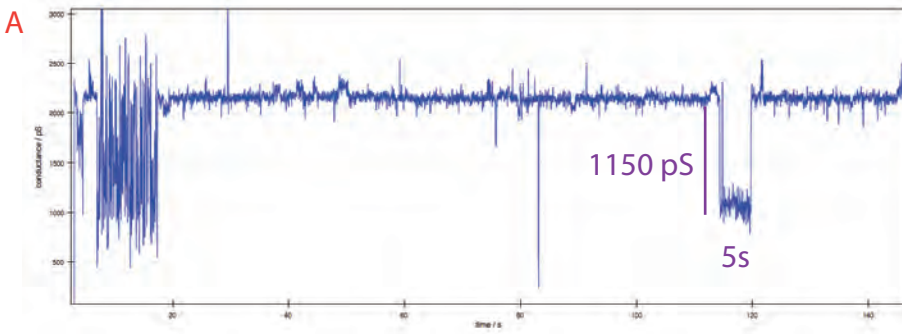
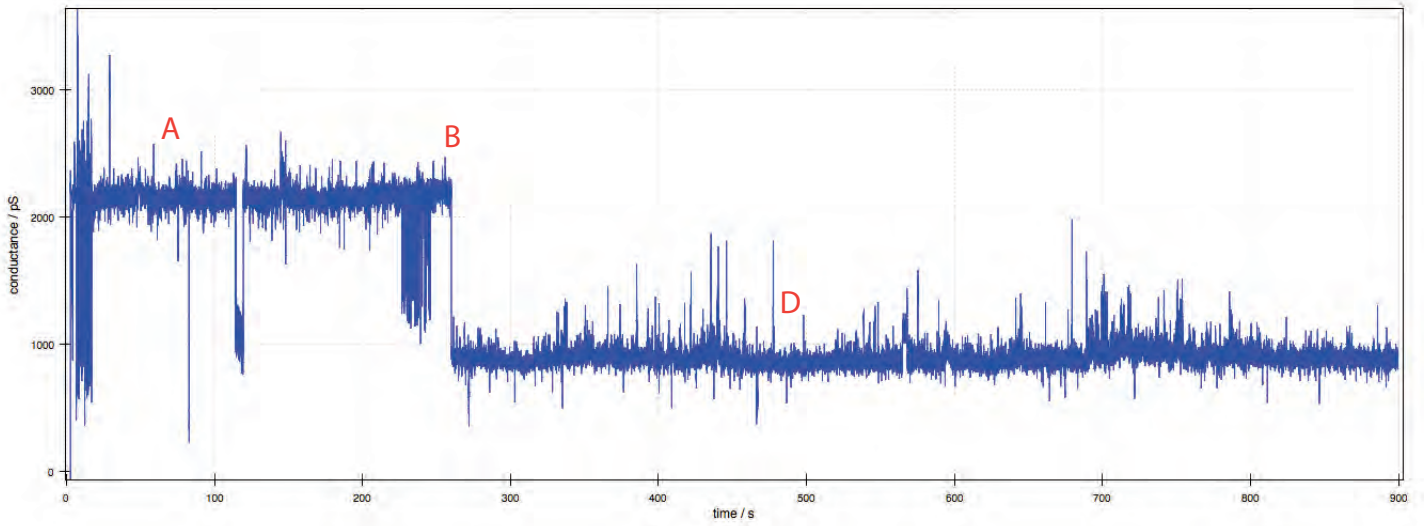


[JC-76] bCD6Es8 1M CsCl pH 7 survery run 1 perc



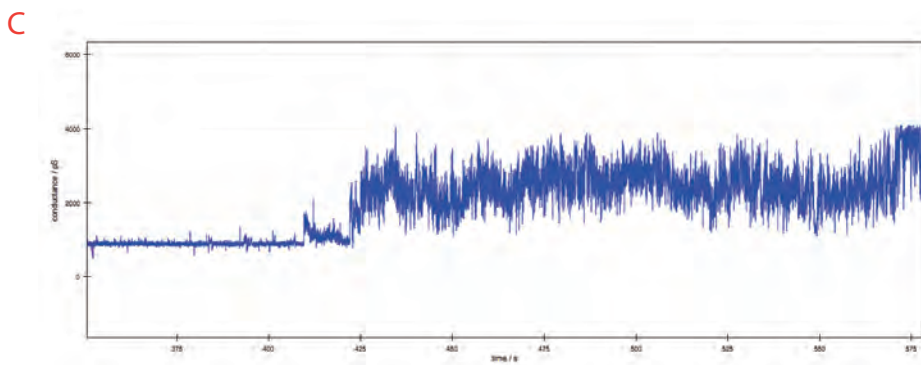
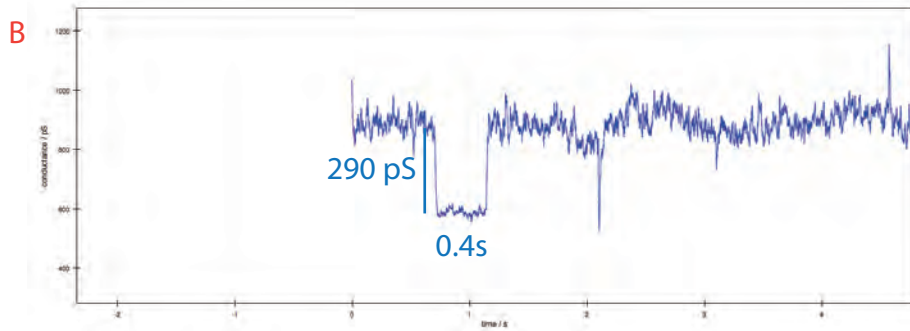
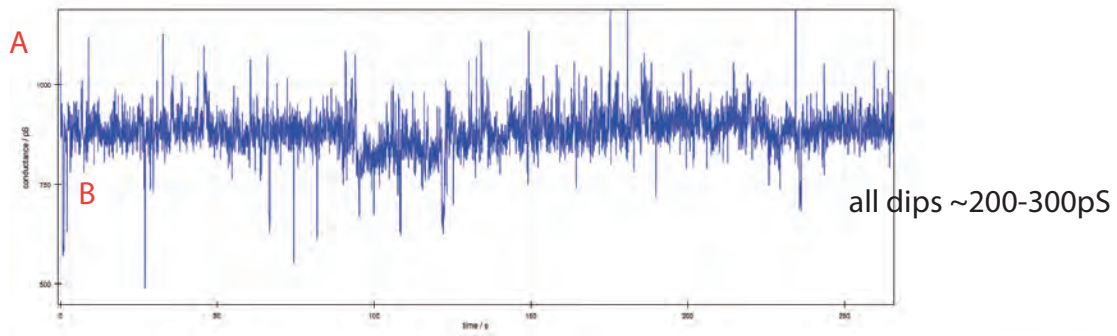
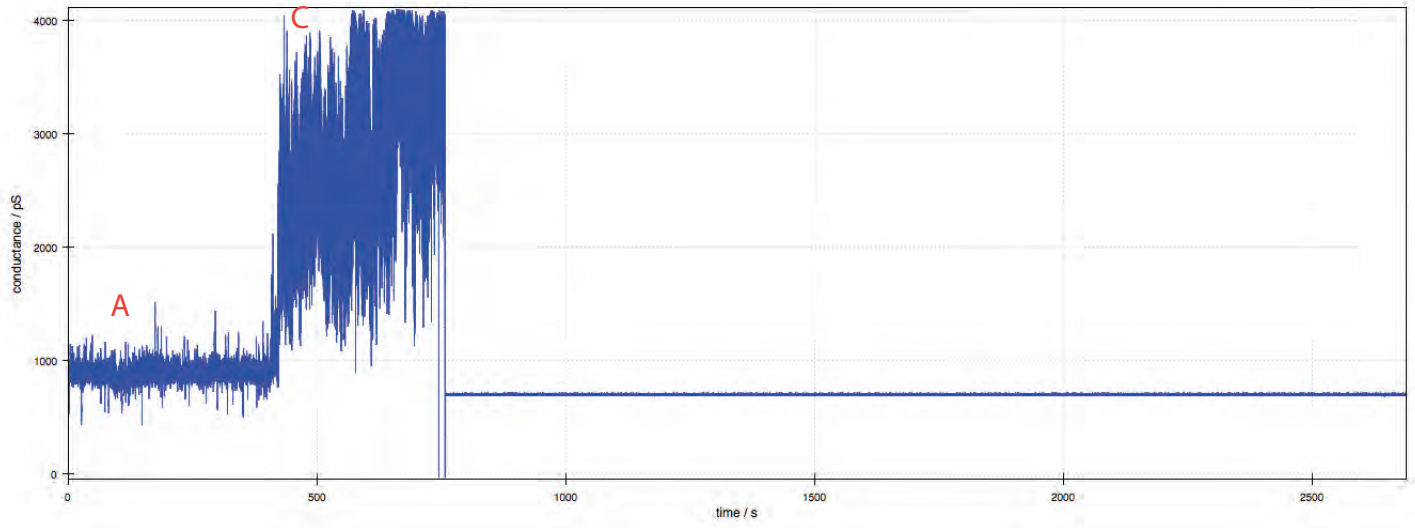
mixed with fractal-like section



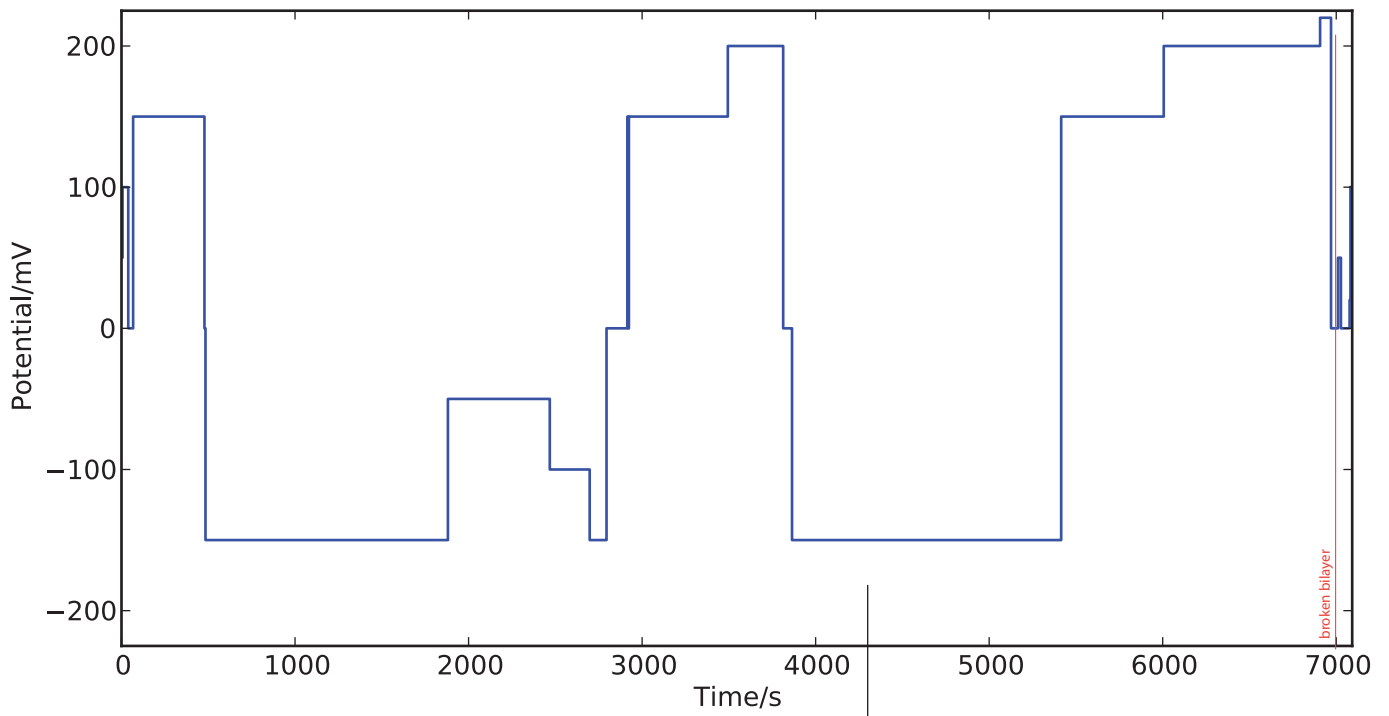


Also an open state
(see dip)
not charted here

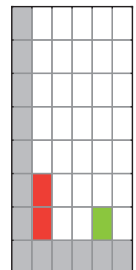
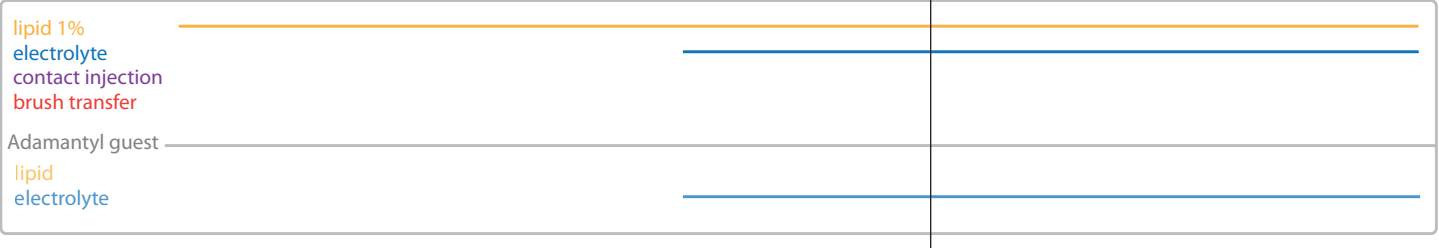
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JC-149 bCD-6Es8 1percent 1M CsCl pH 4.5

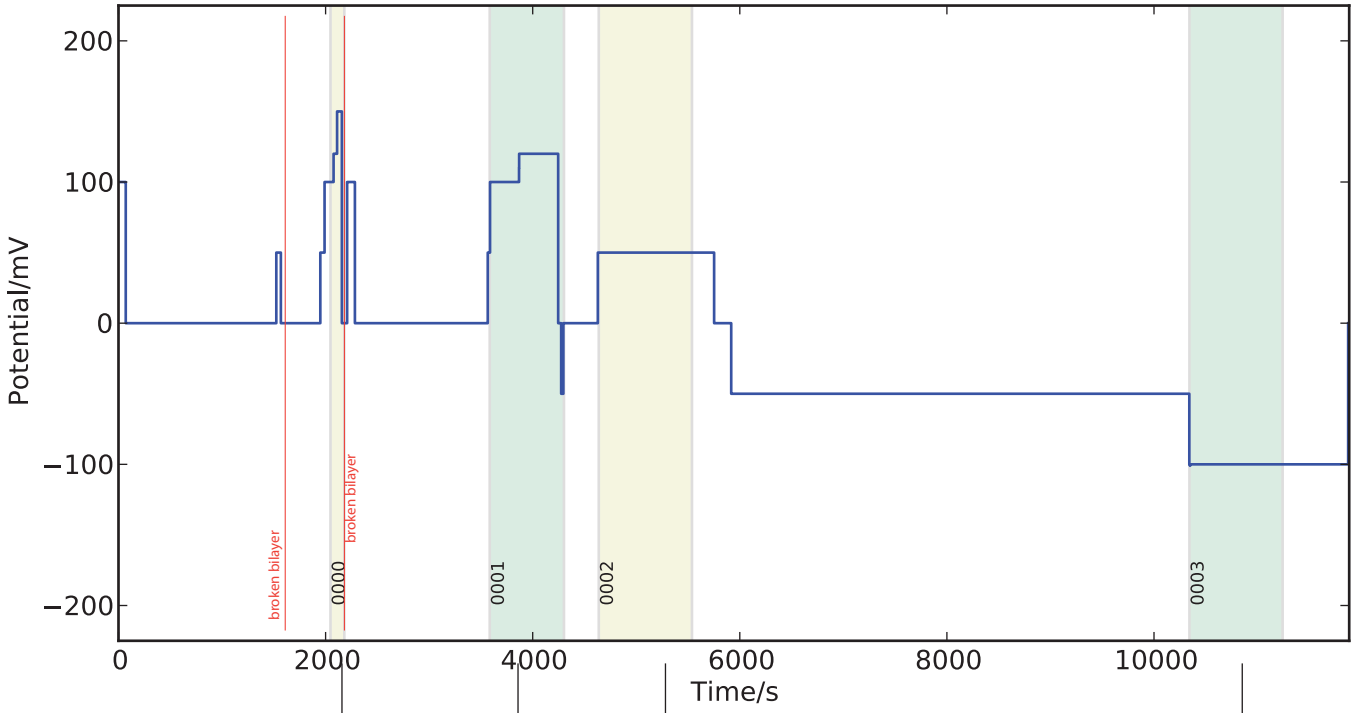


broken bilayer

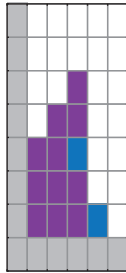
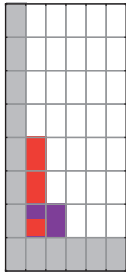


from lab book description -
no trace acquired

[JC-72] bCD-6-Es-8 1M CsCl pH 7 survey

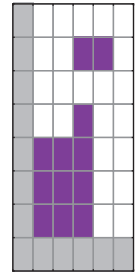


lipid
 electrolyte
 contact injection 14.6uM (insol)
 brush transfer



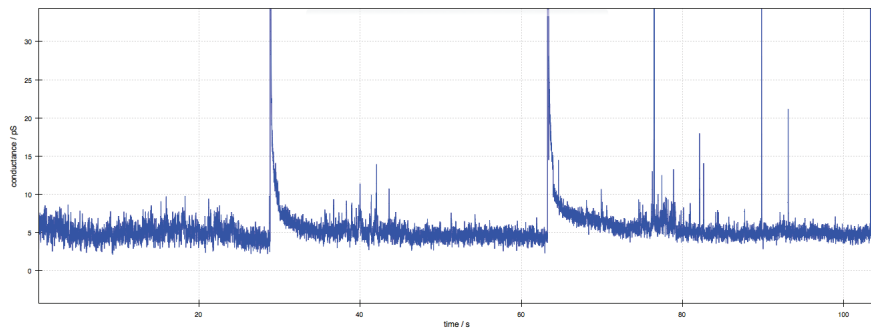
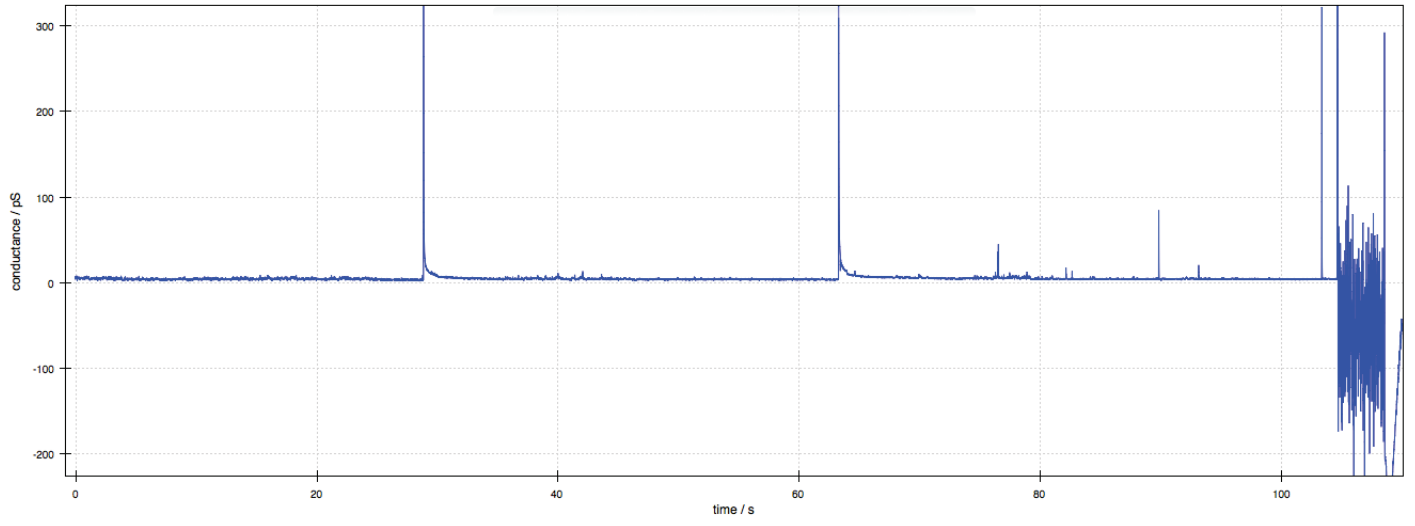
structure instable to potential changes

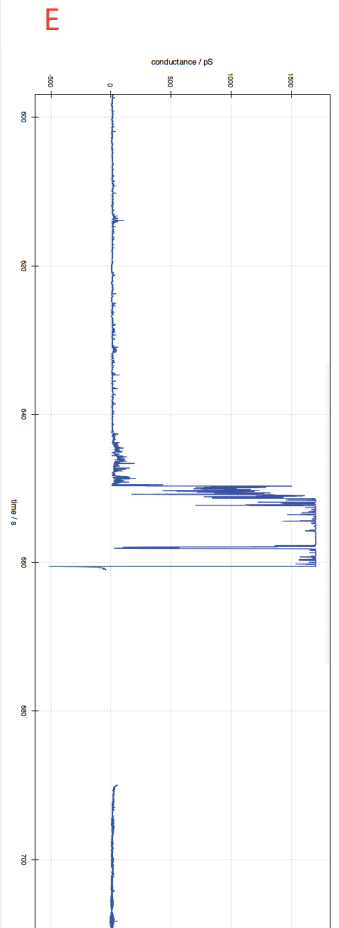
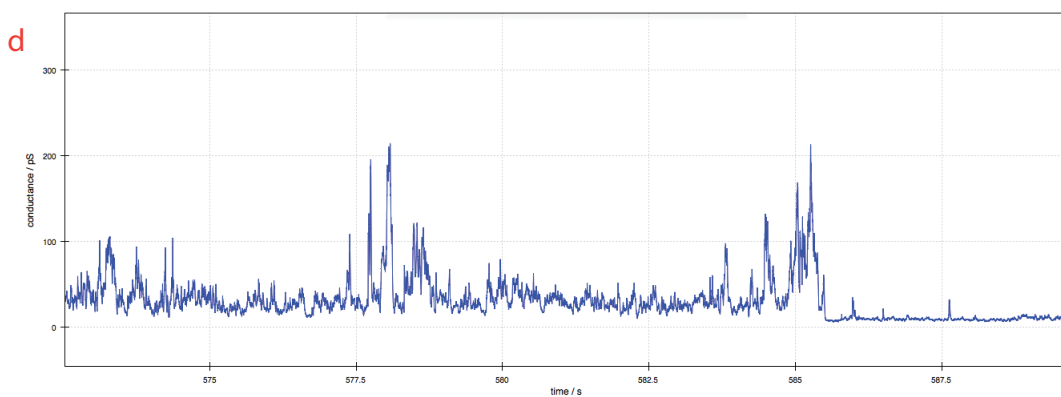
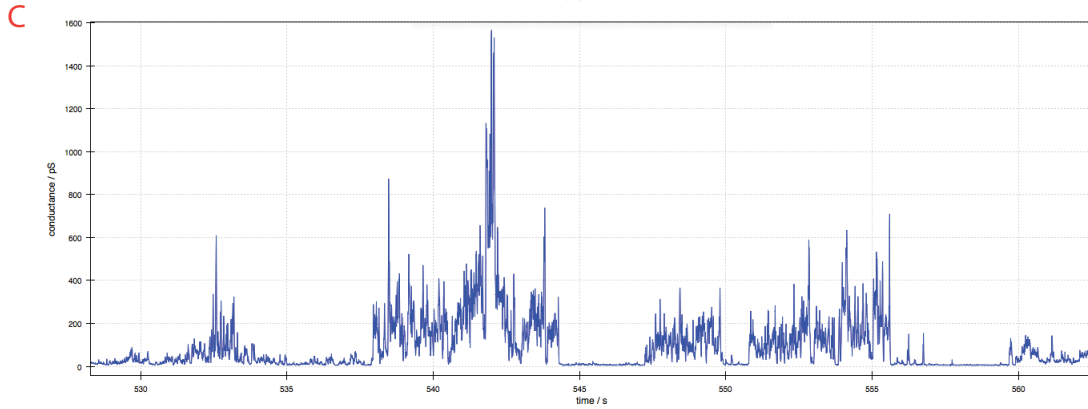
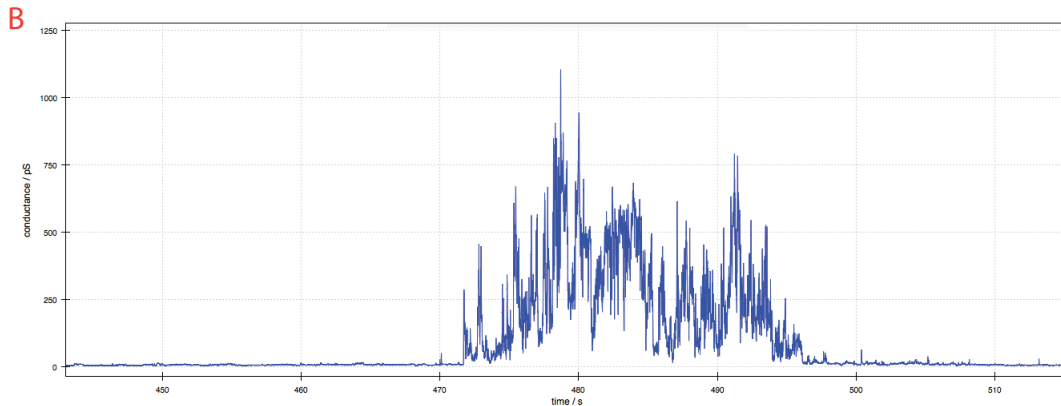
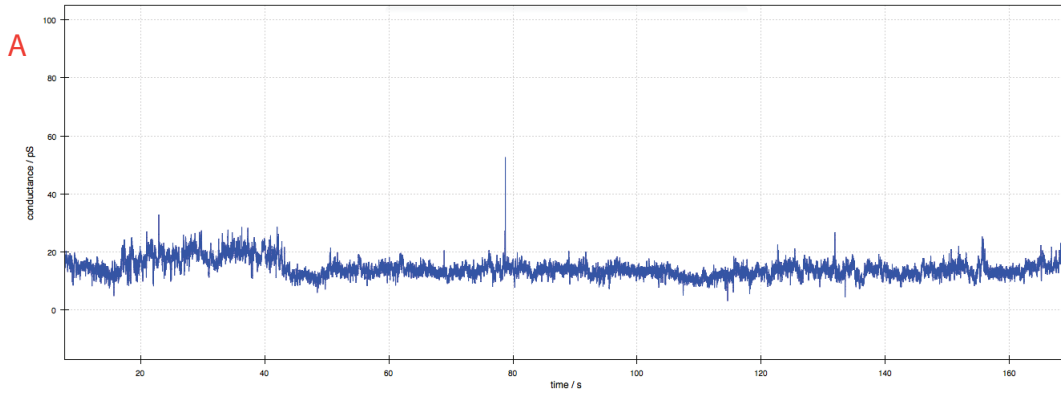
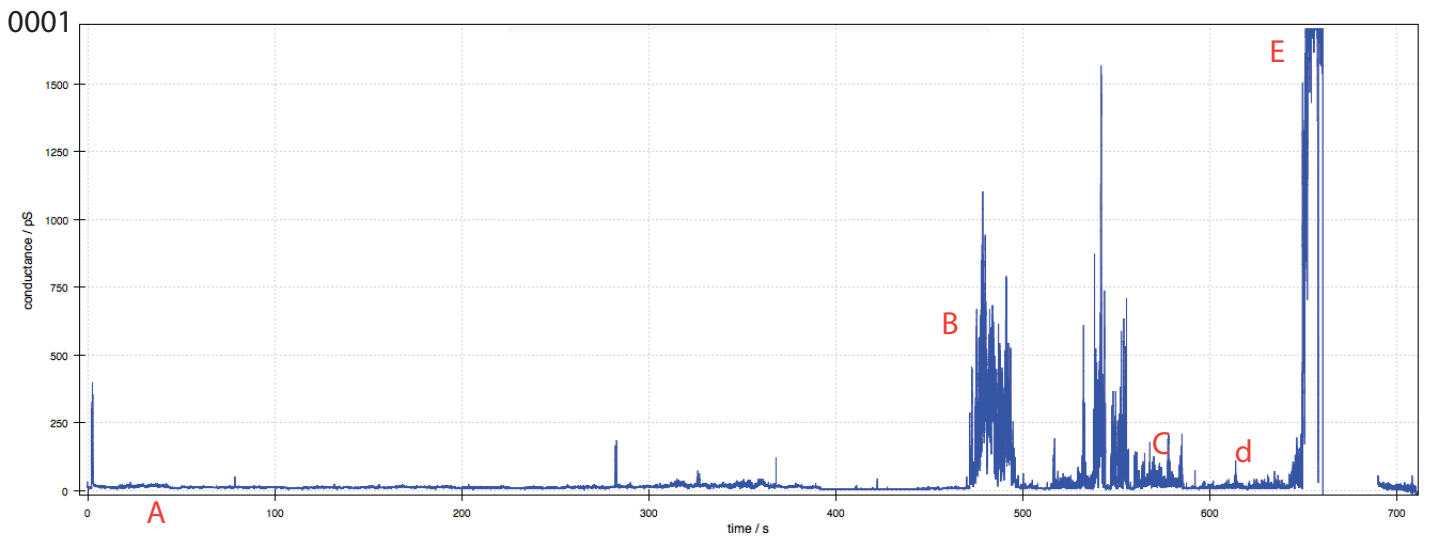
inexplicable noise
 or genuine small, frequent activity?



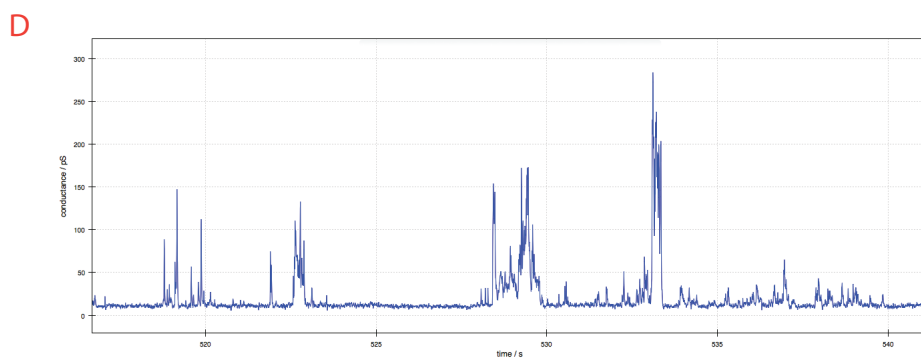
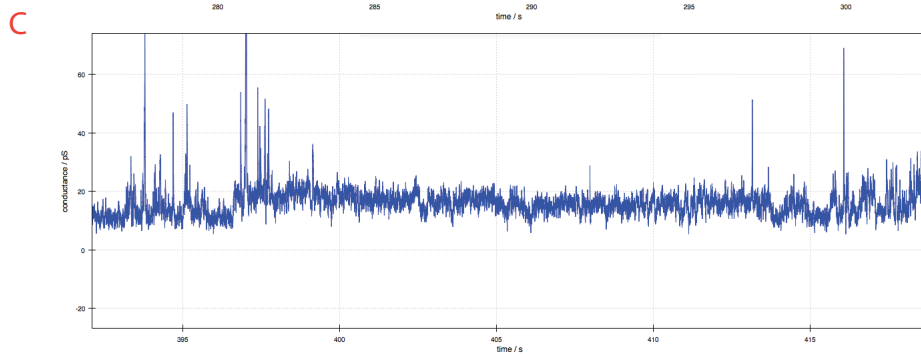
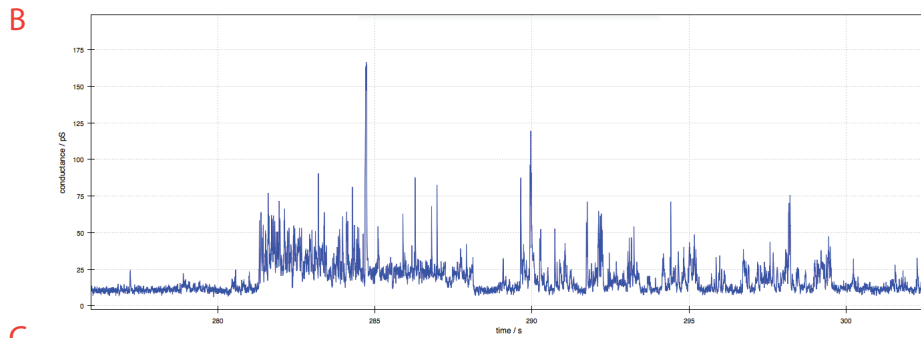
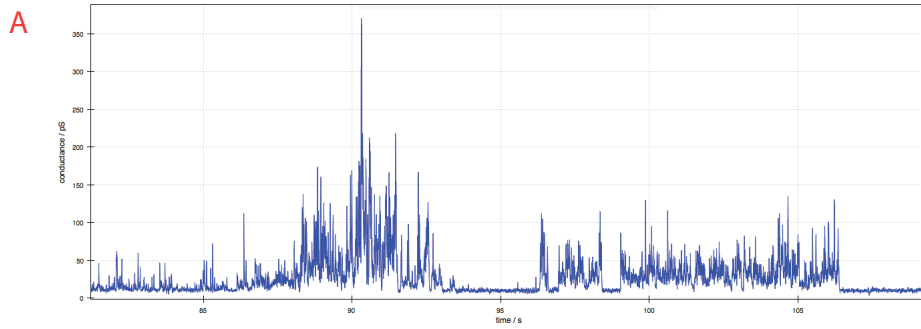
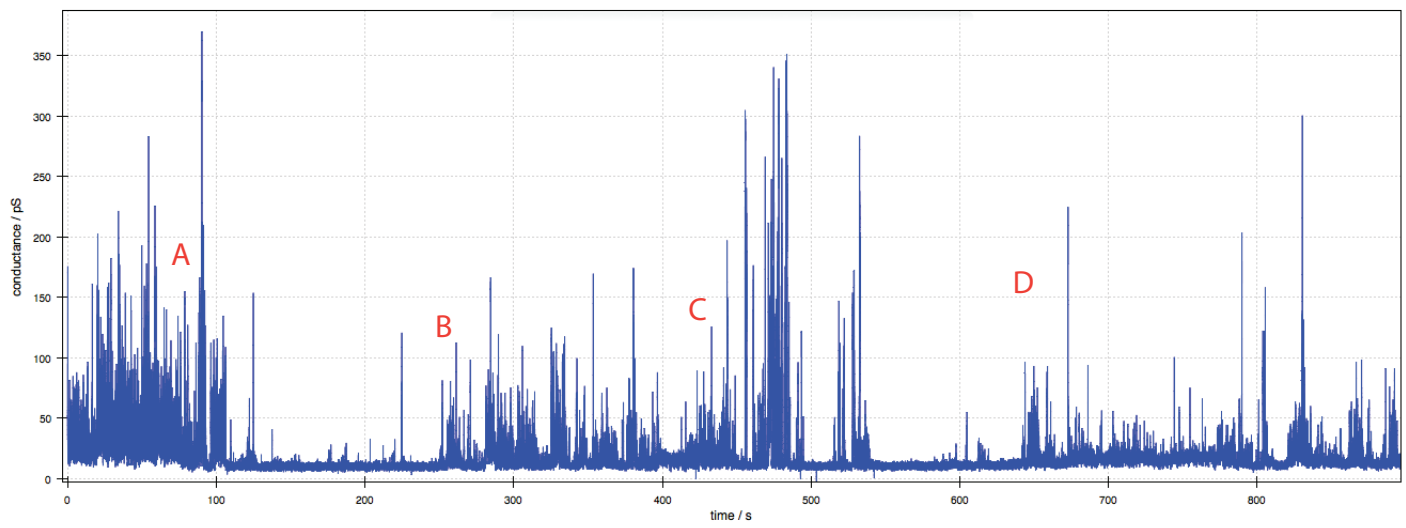
fractal?

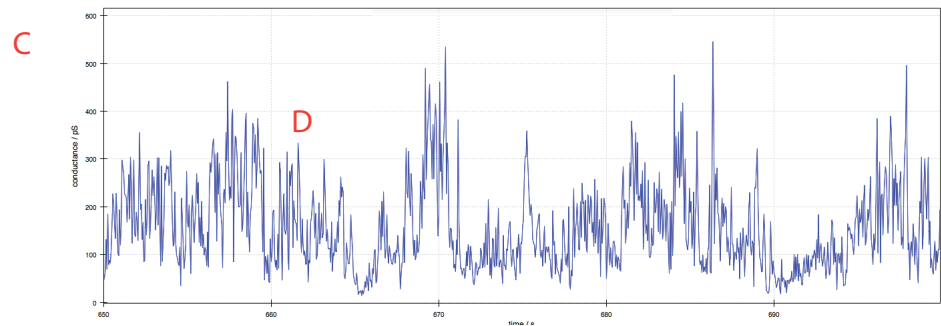
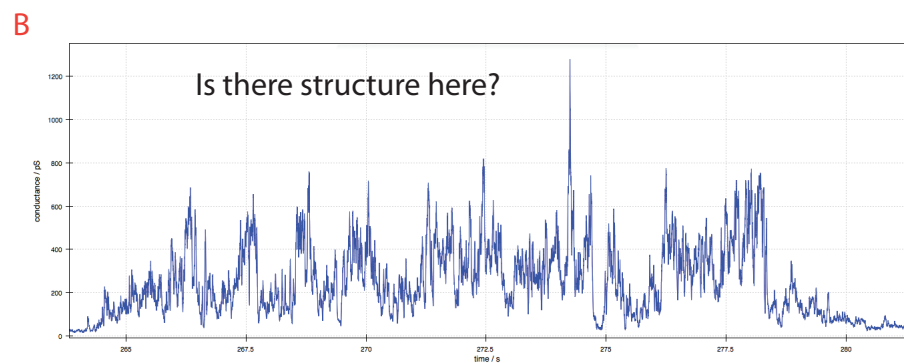
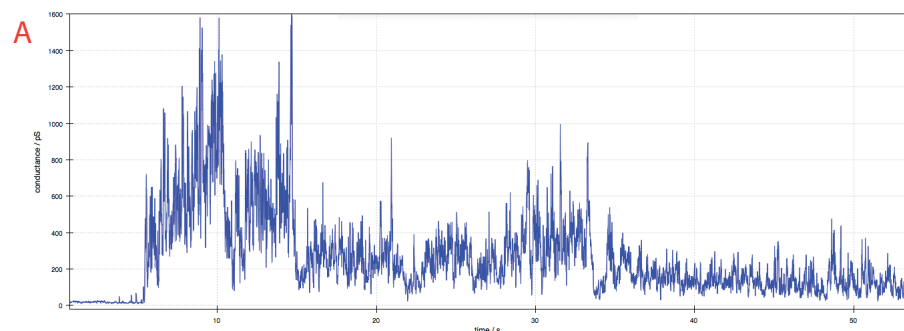
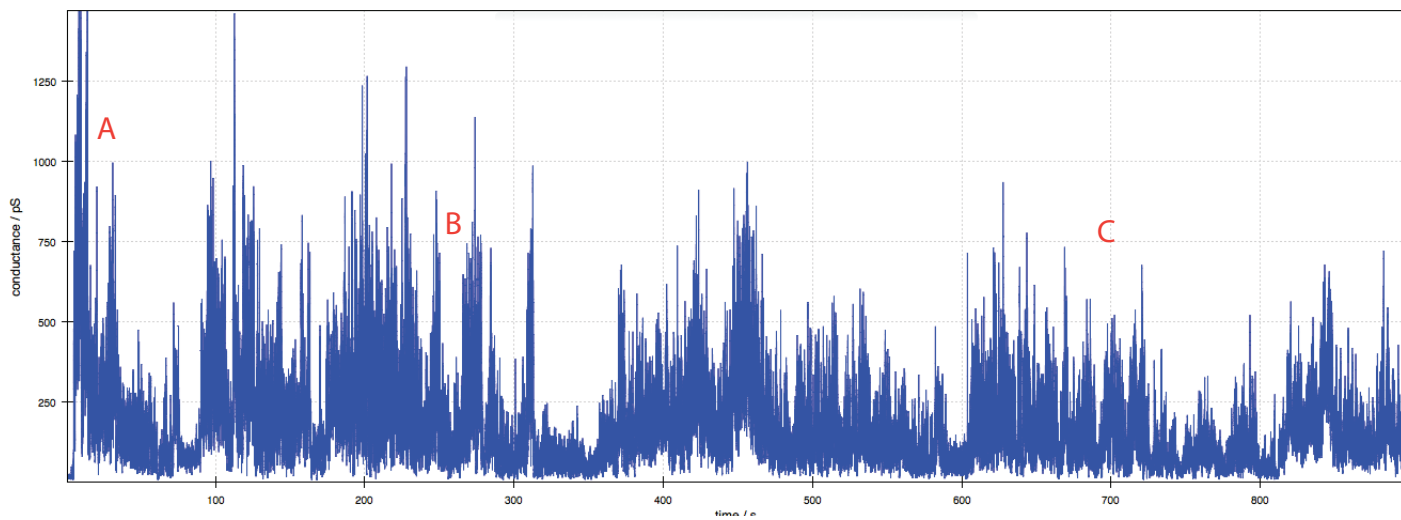
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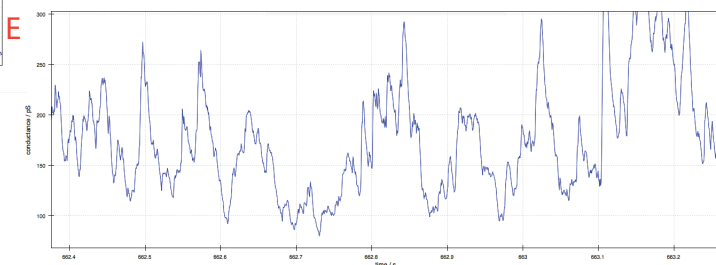
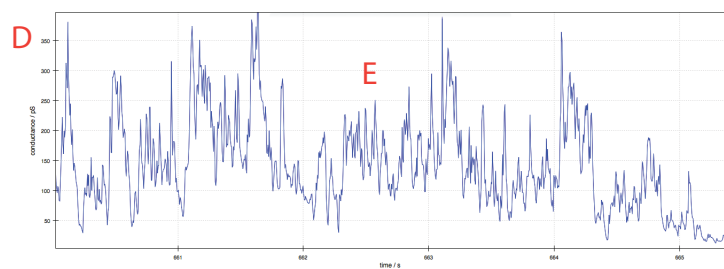


structure instable to potential changes

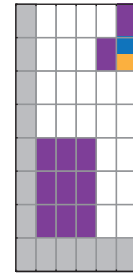
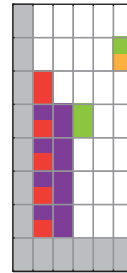
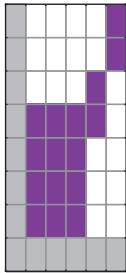
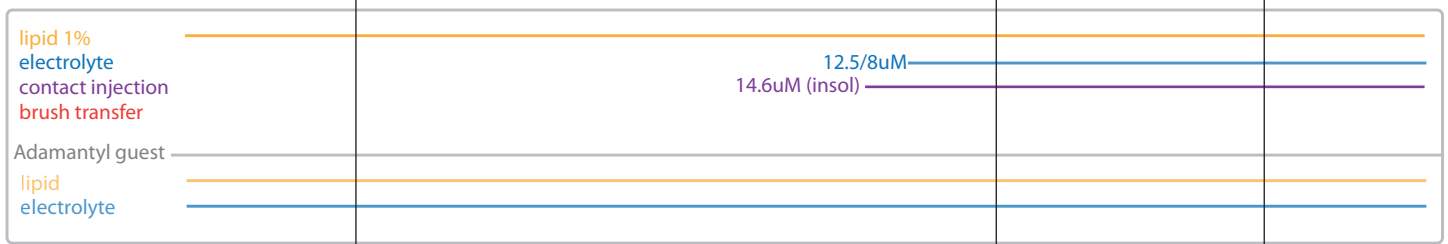
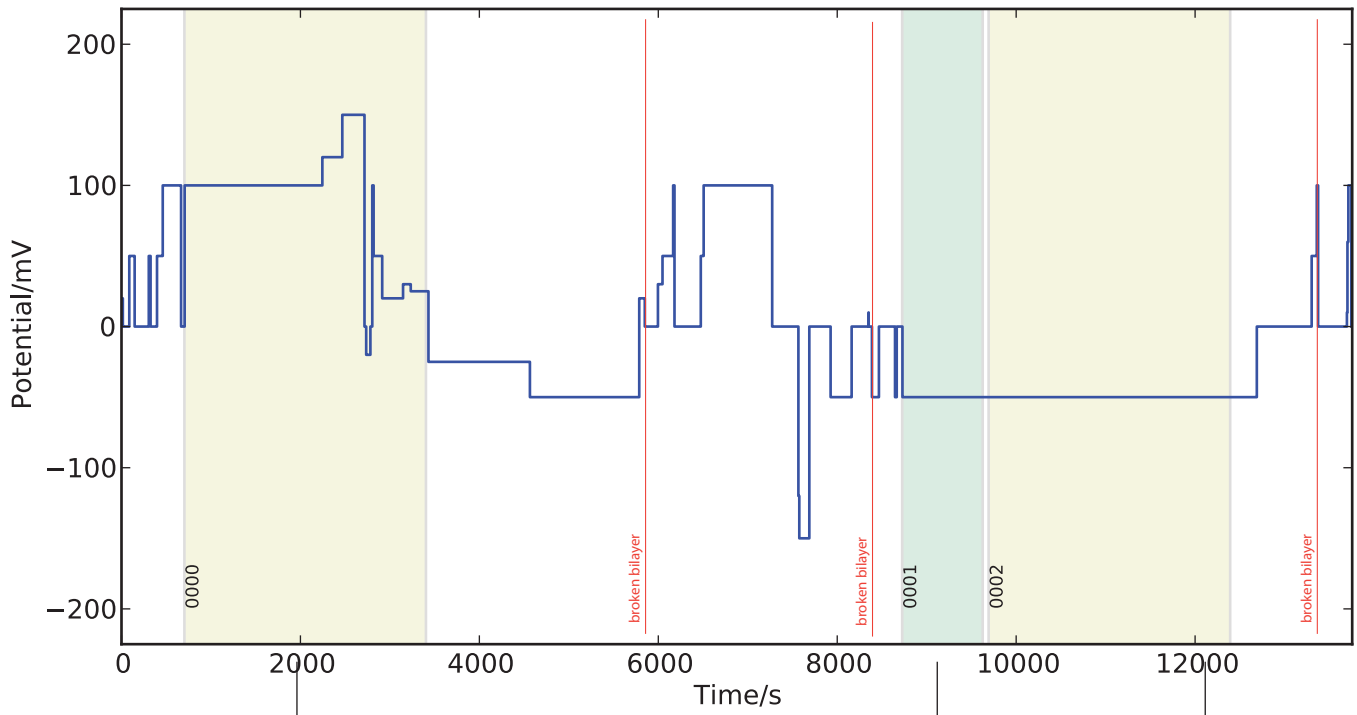




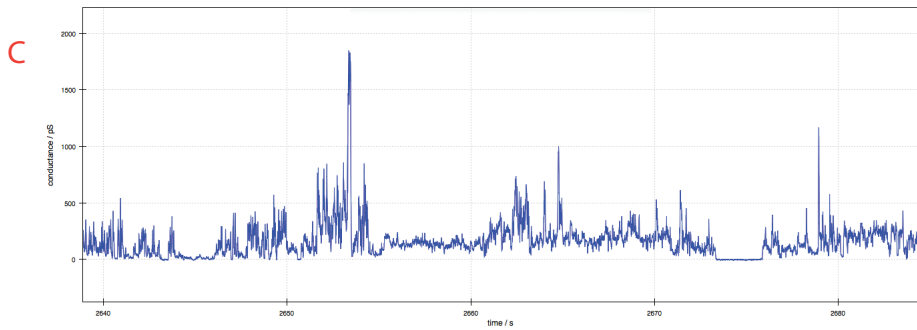
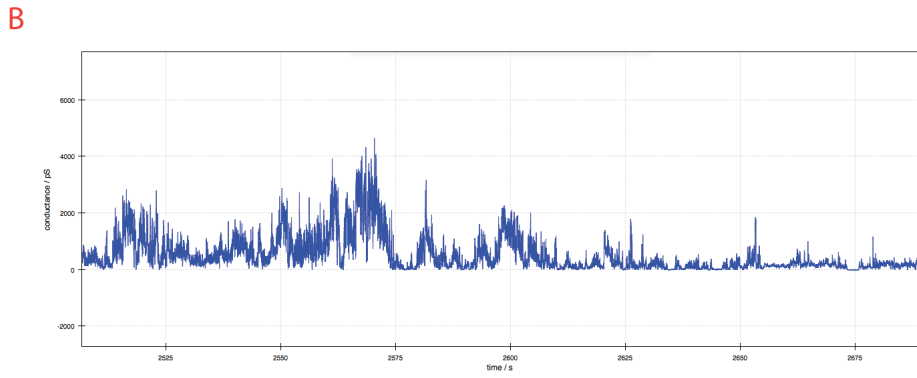
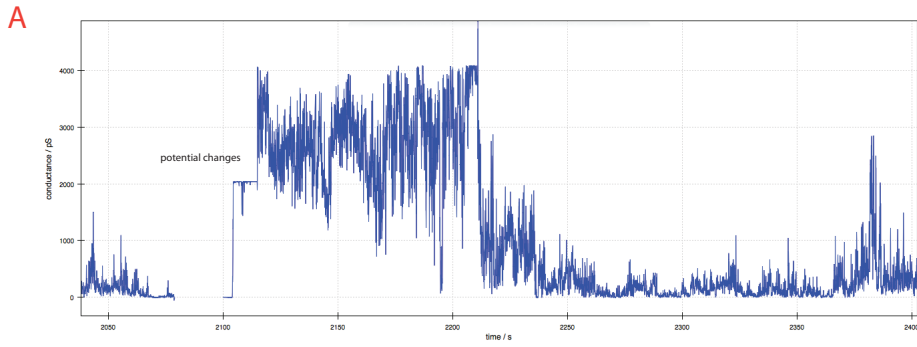
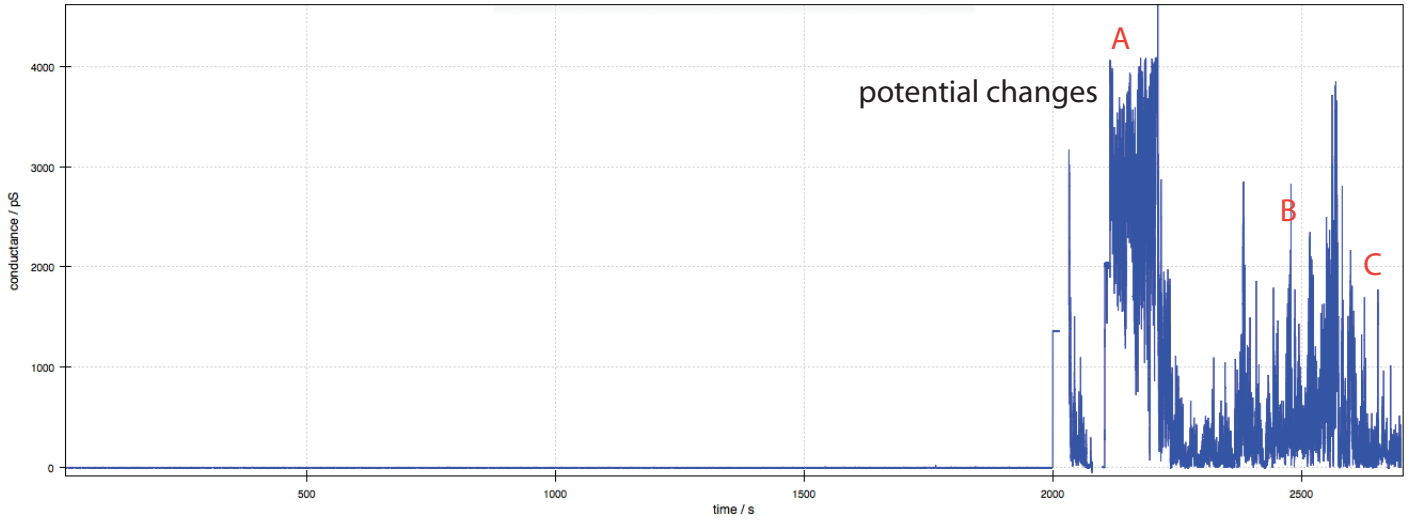
fractal?

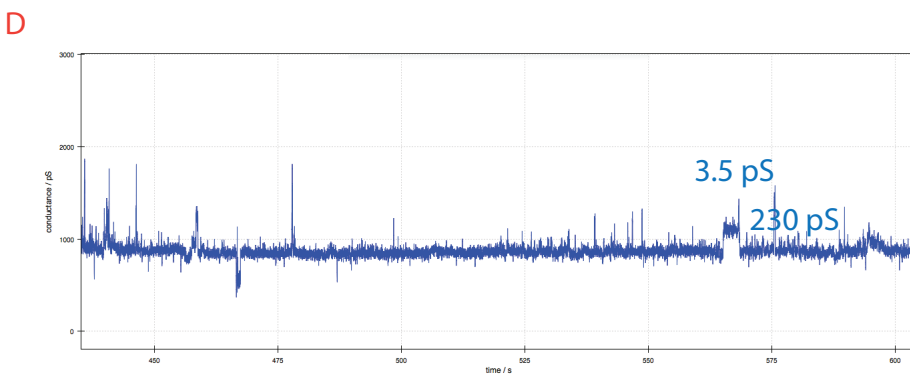
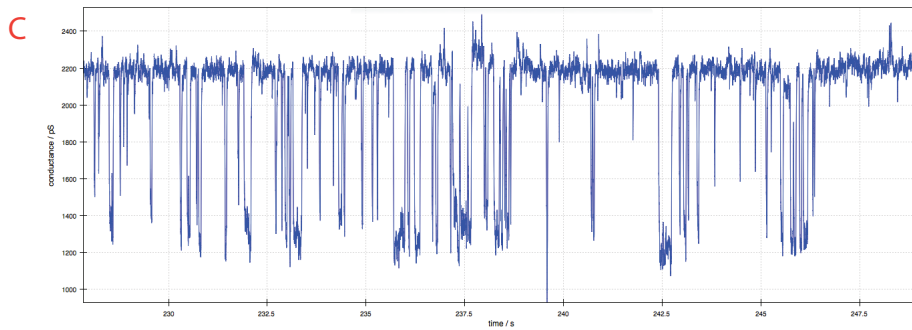
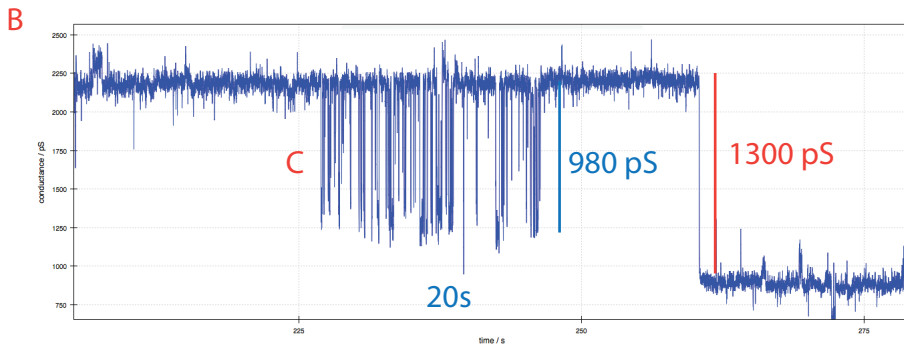
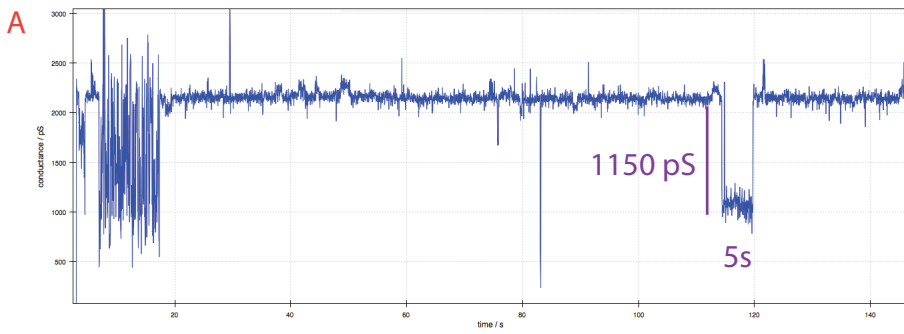
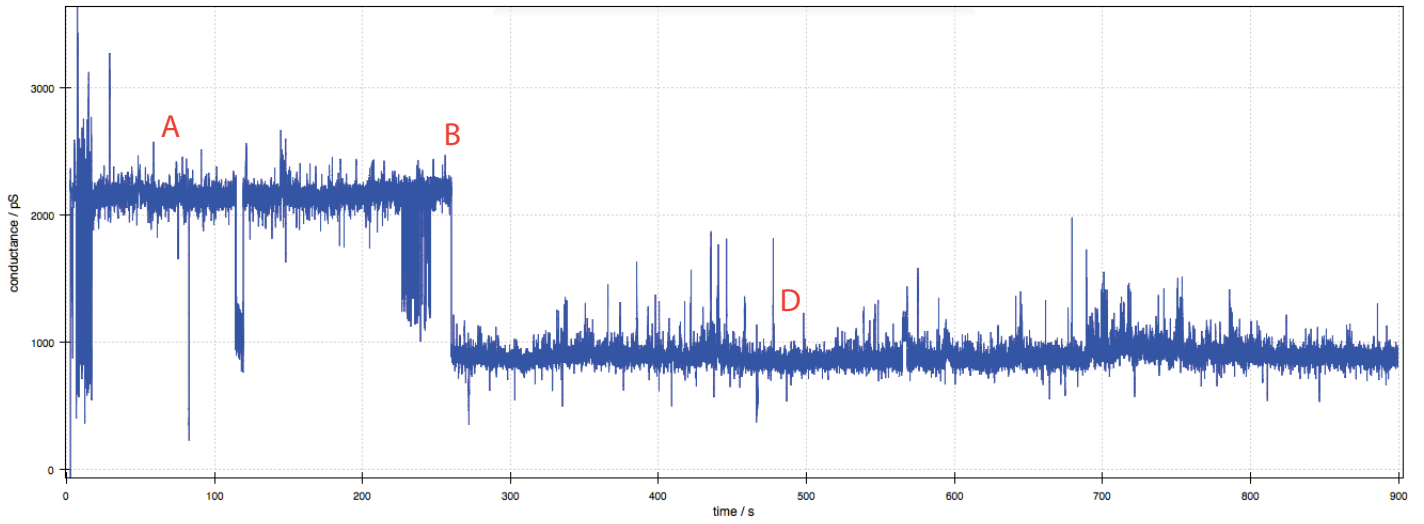


[JC-76] bCD6Es8 1M CsCl pH 7 survery run 1 perc



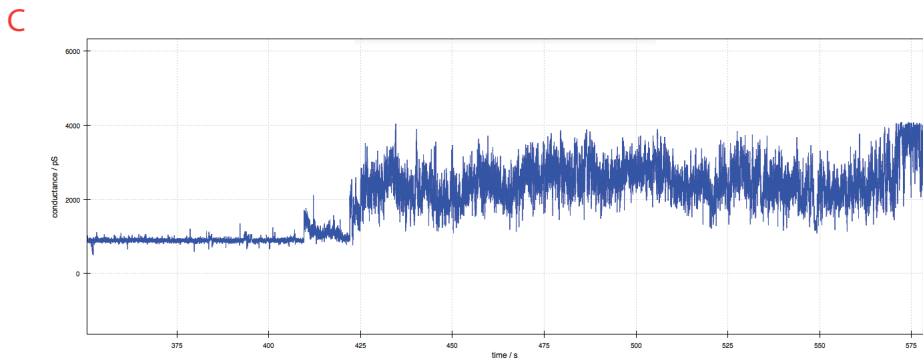
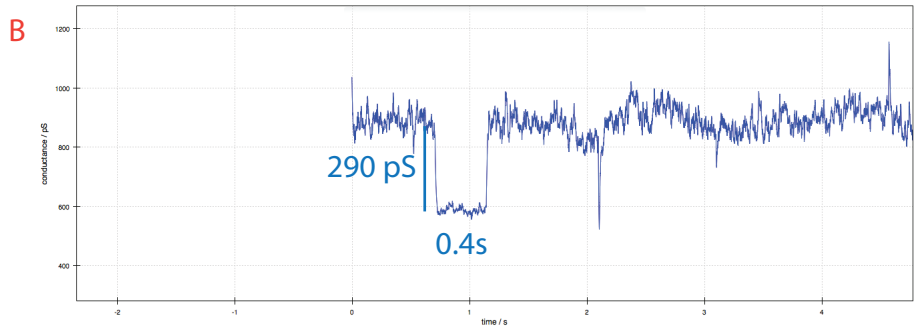
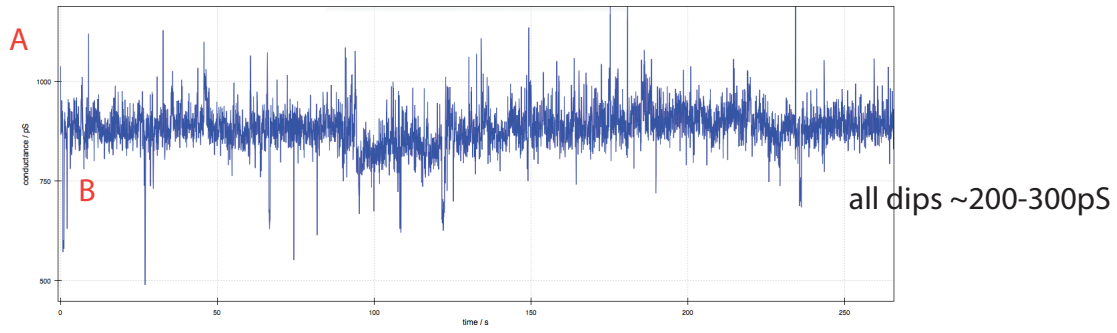
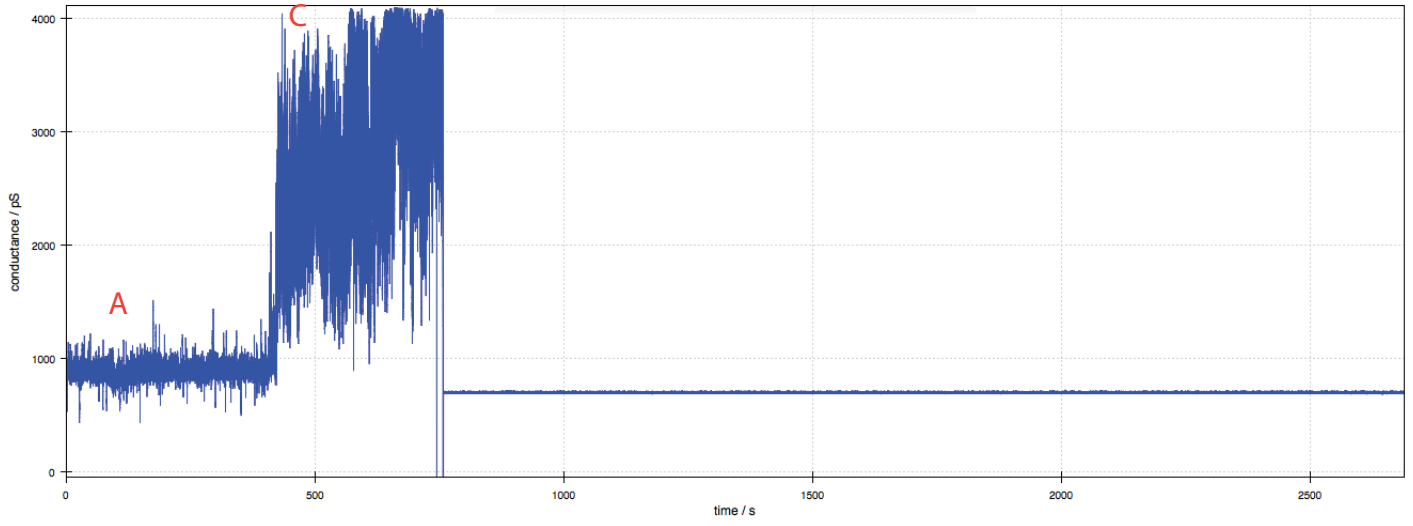
mixed with fractal-like section



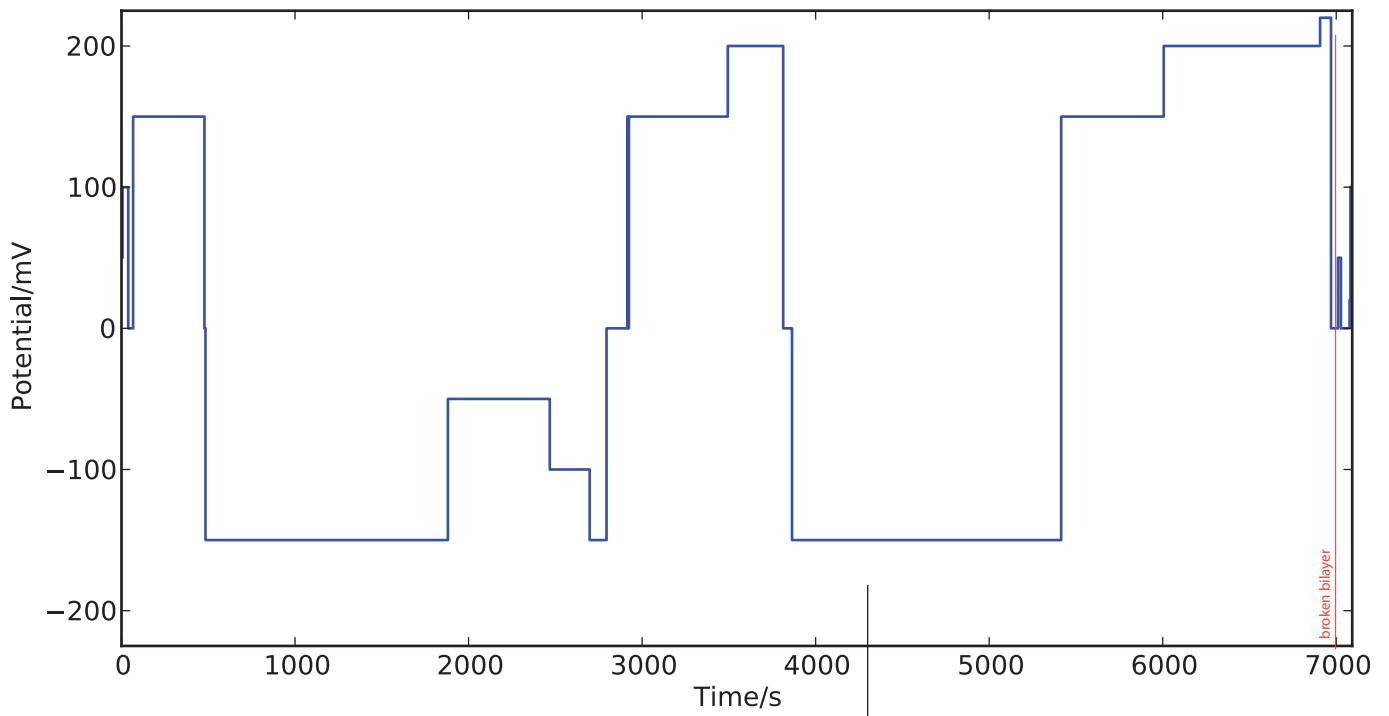


Also an open state
(see dip)
not charted here

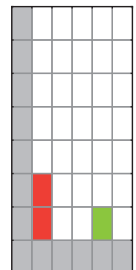
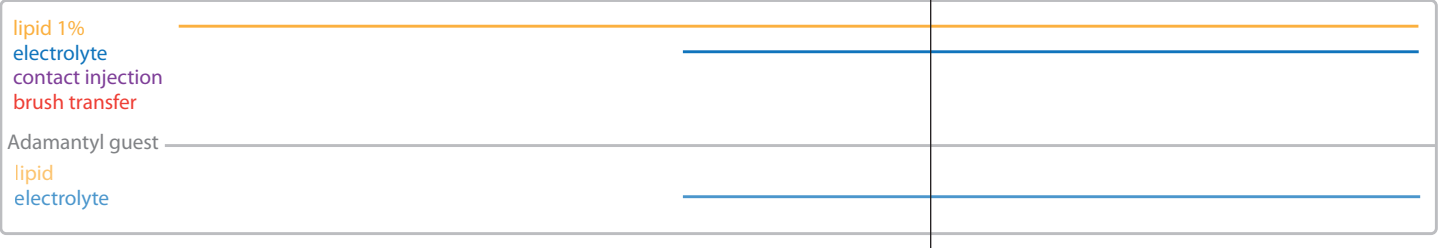
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JC-149 bCD-6Es8 1percent 1M CsCl pH 4.5

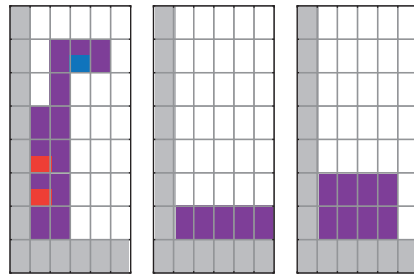
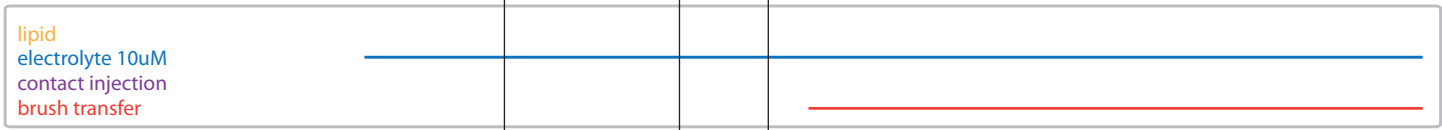
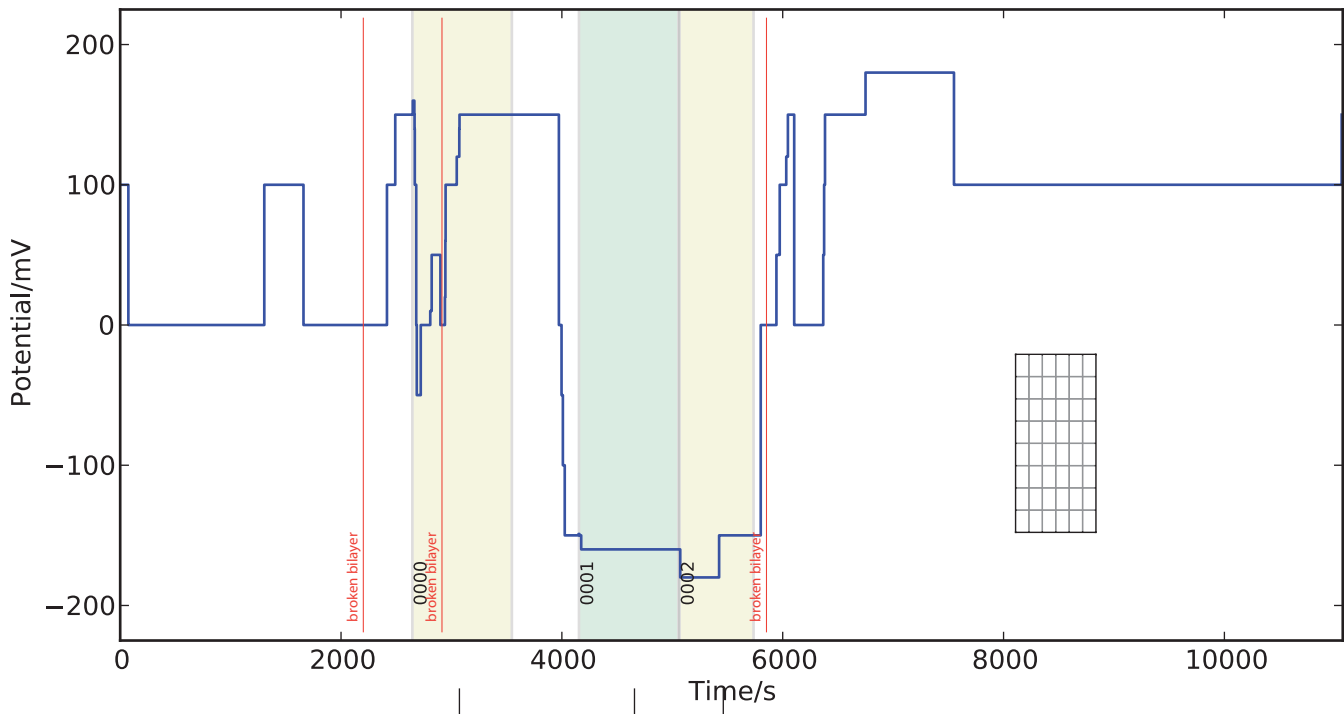


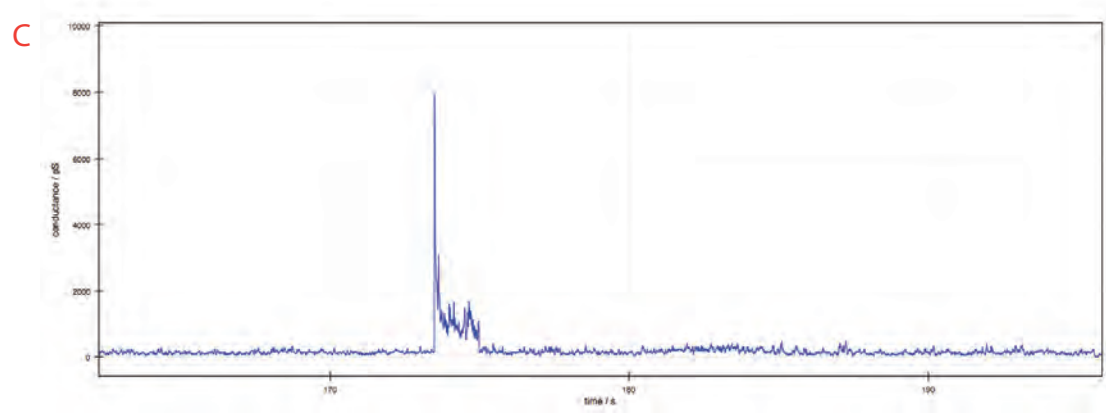
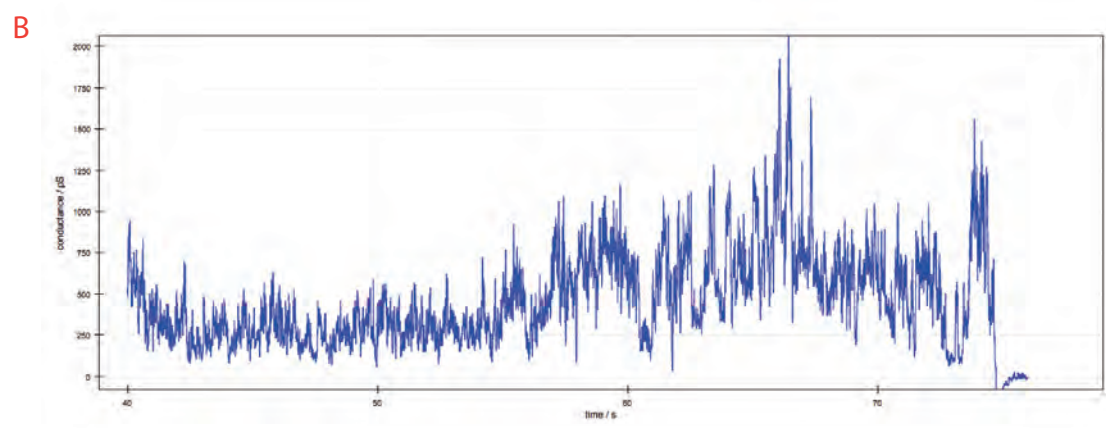
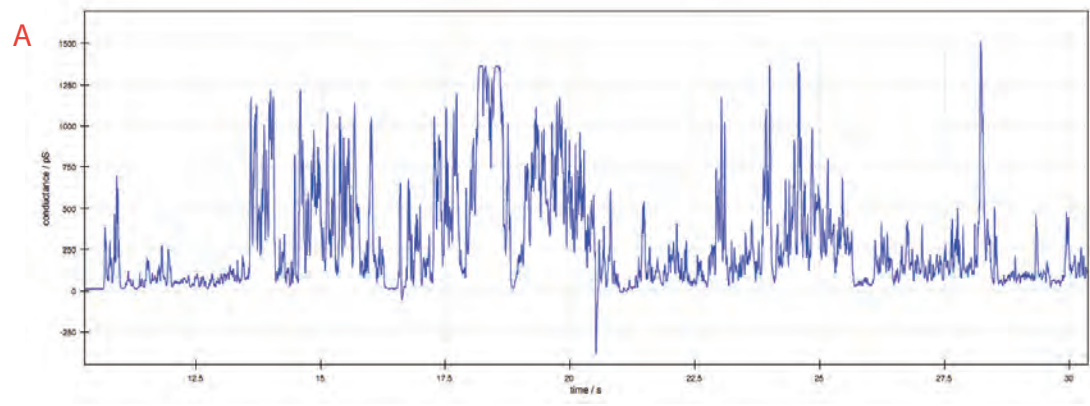
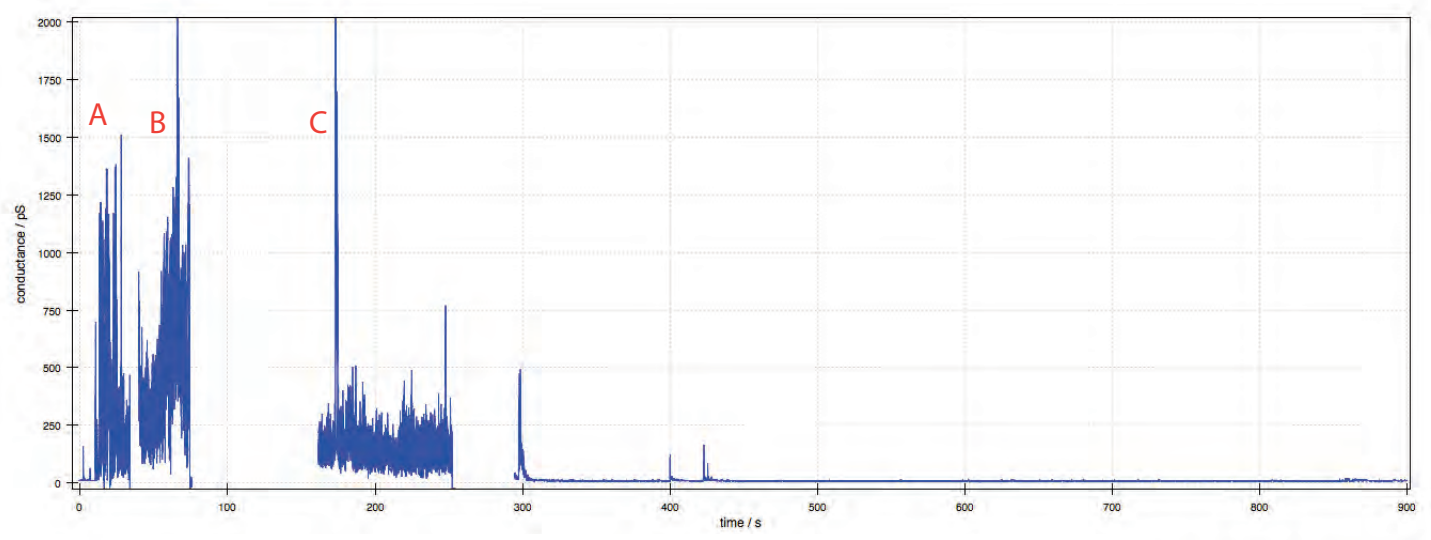
broken bilayer

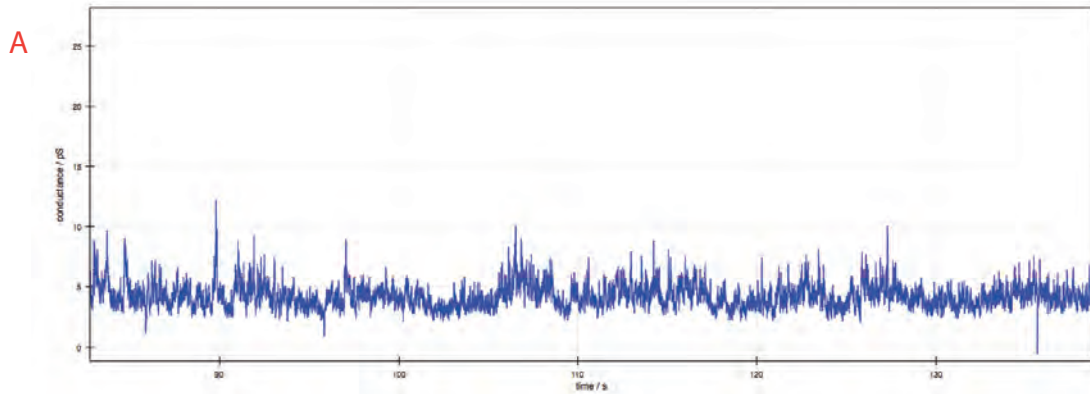
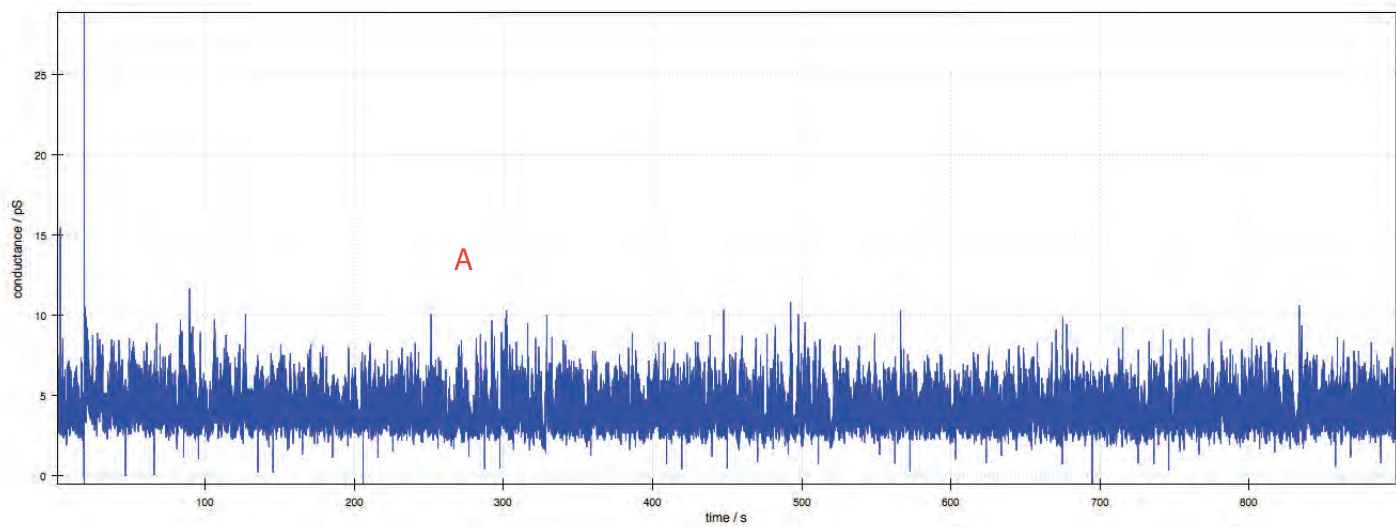


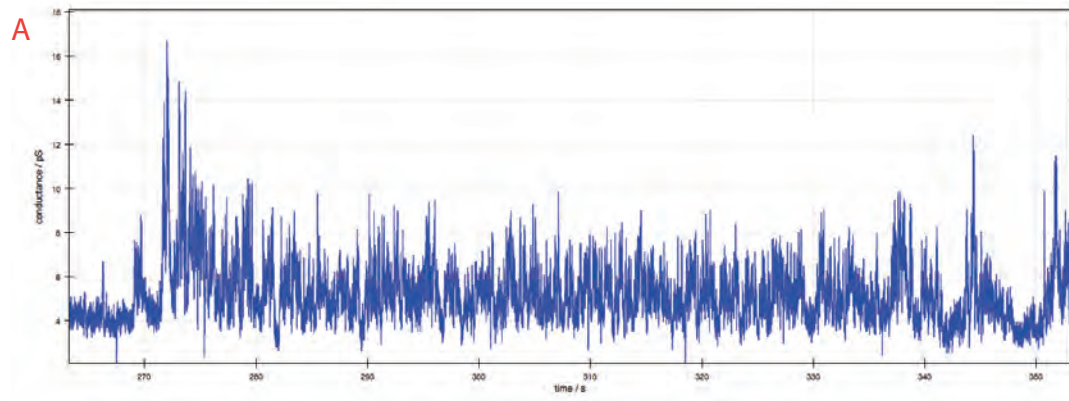
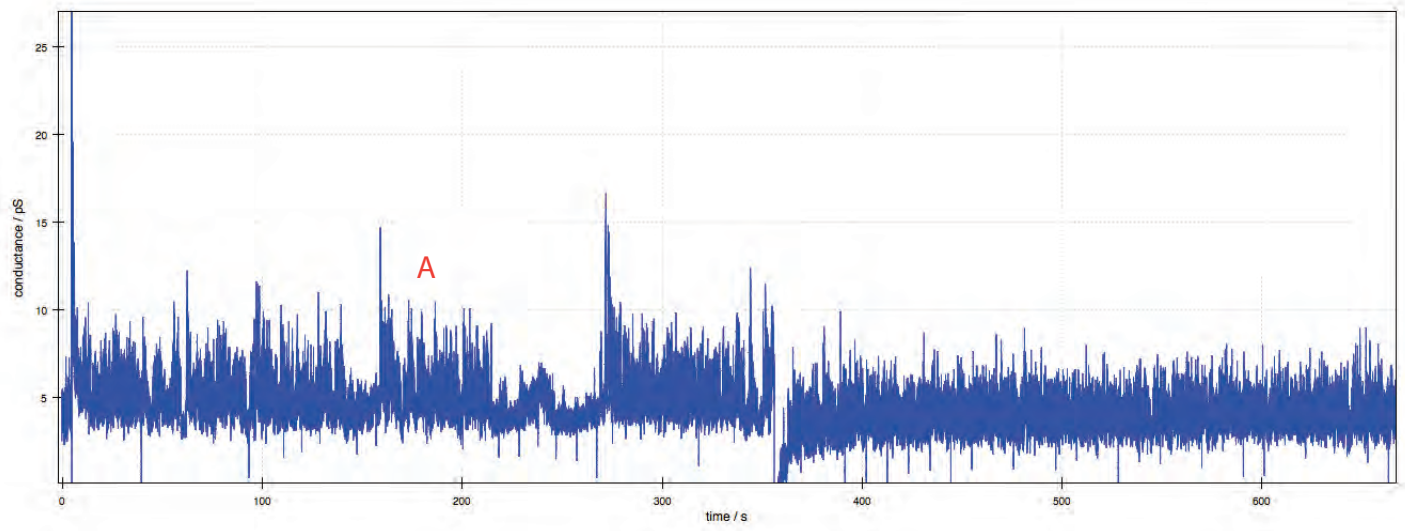
from lab book description -
no trace acquired

[JC-71] bCD-6-Am-8 1M CsCl pH 7 survey

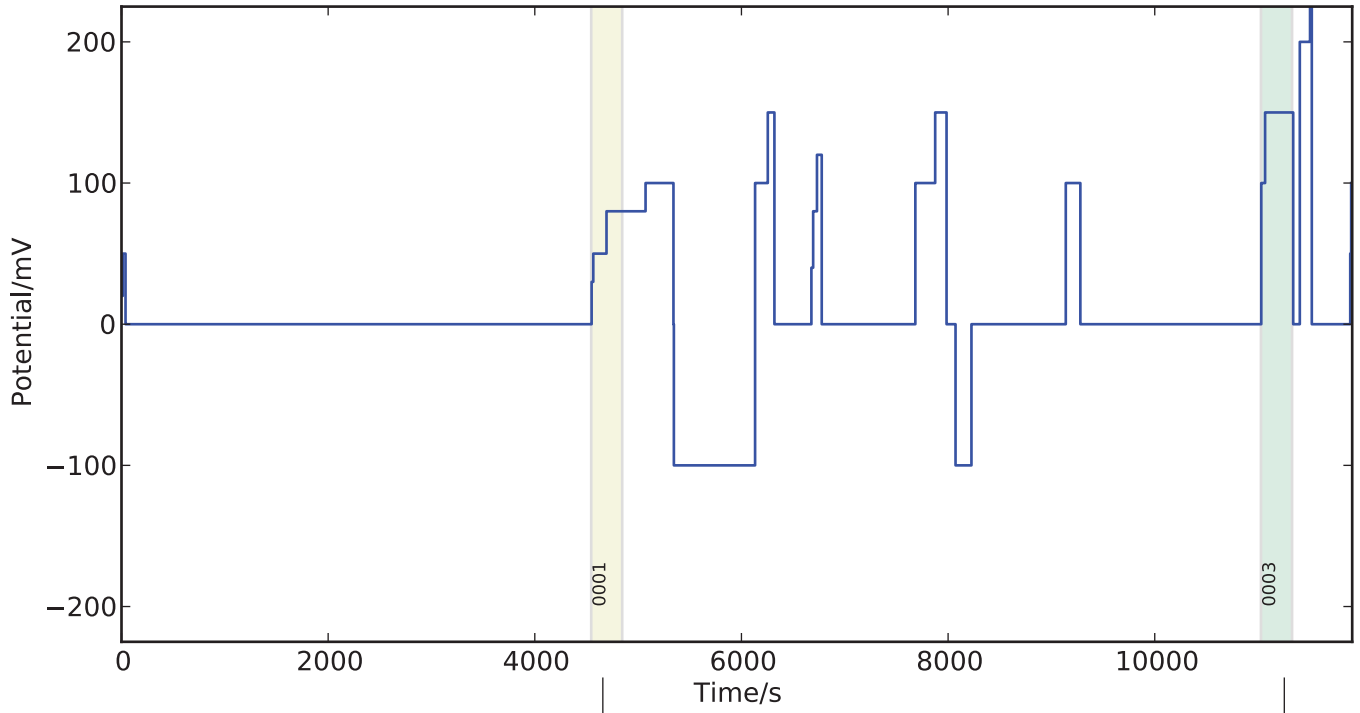




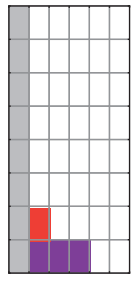
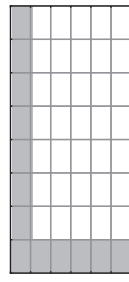


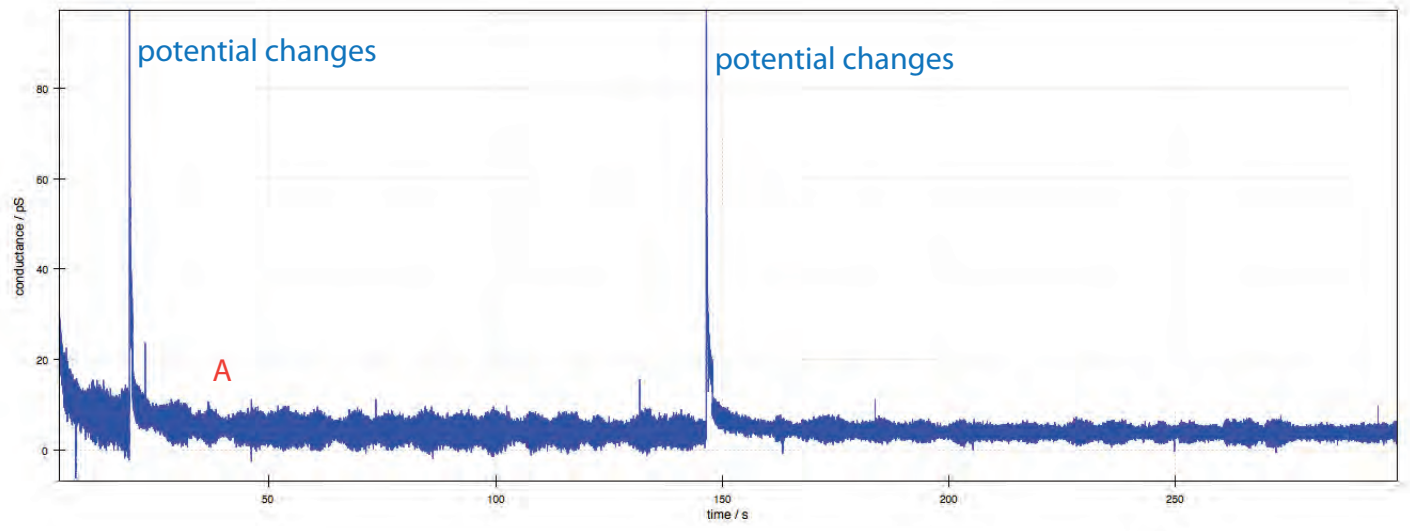


[JC-75] bCD6Am8 1M CsCl pH 7 survery run 1 perc

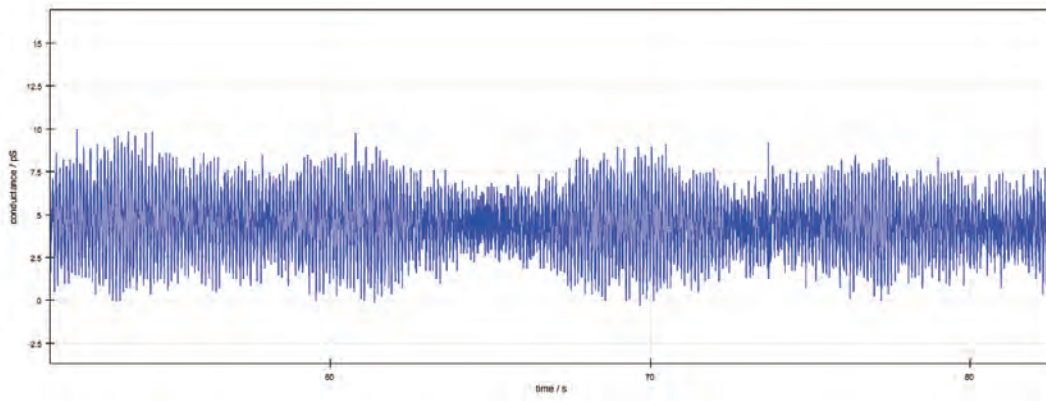


lipid 1%
electrolyte
contact injection
brush transfer

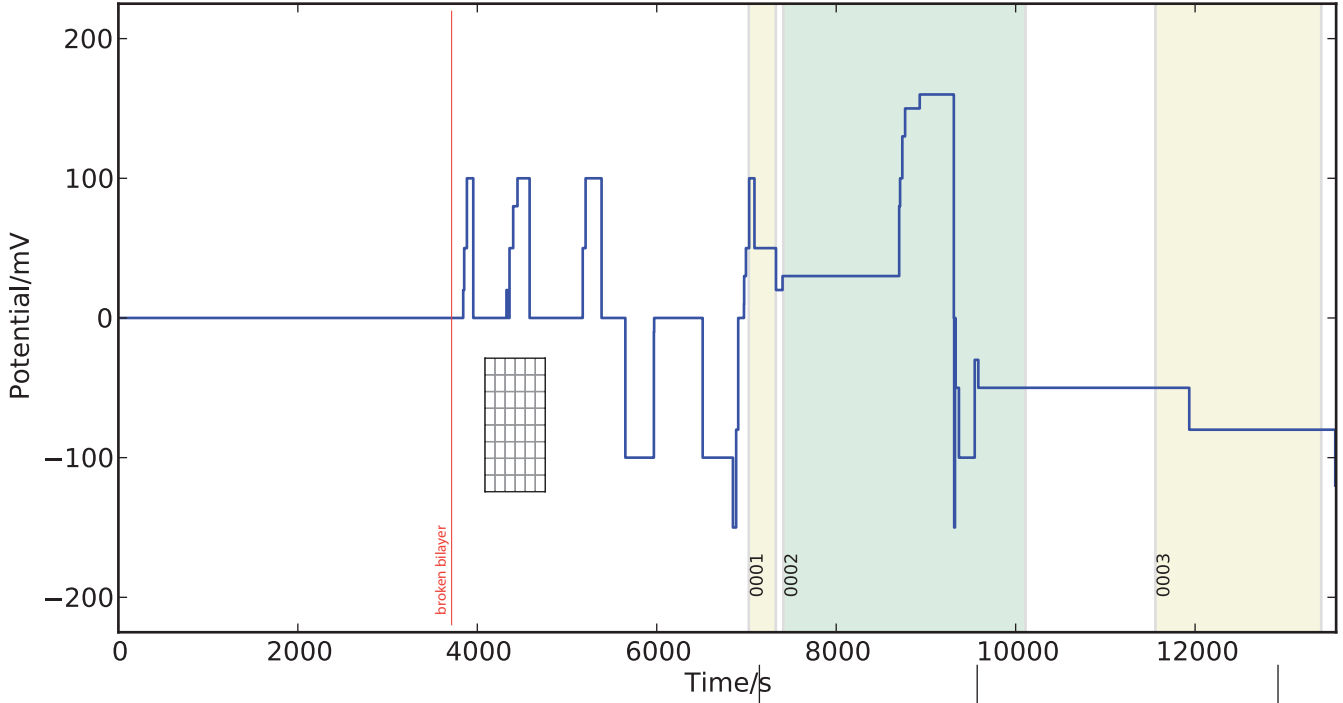




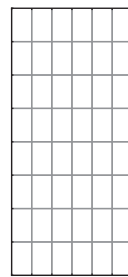
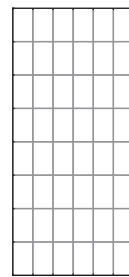
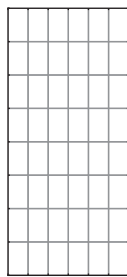
A



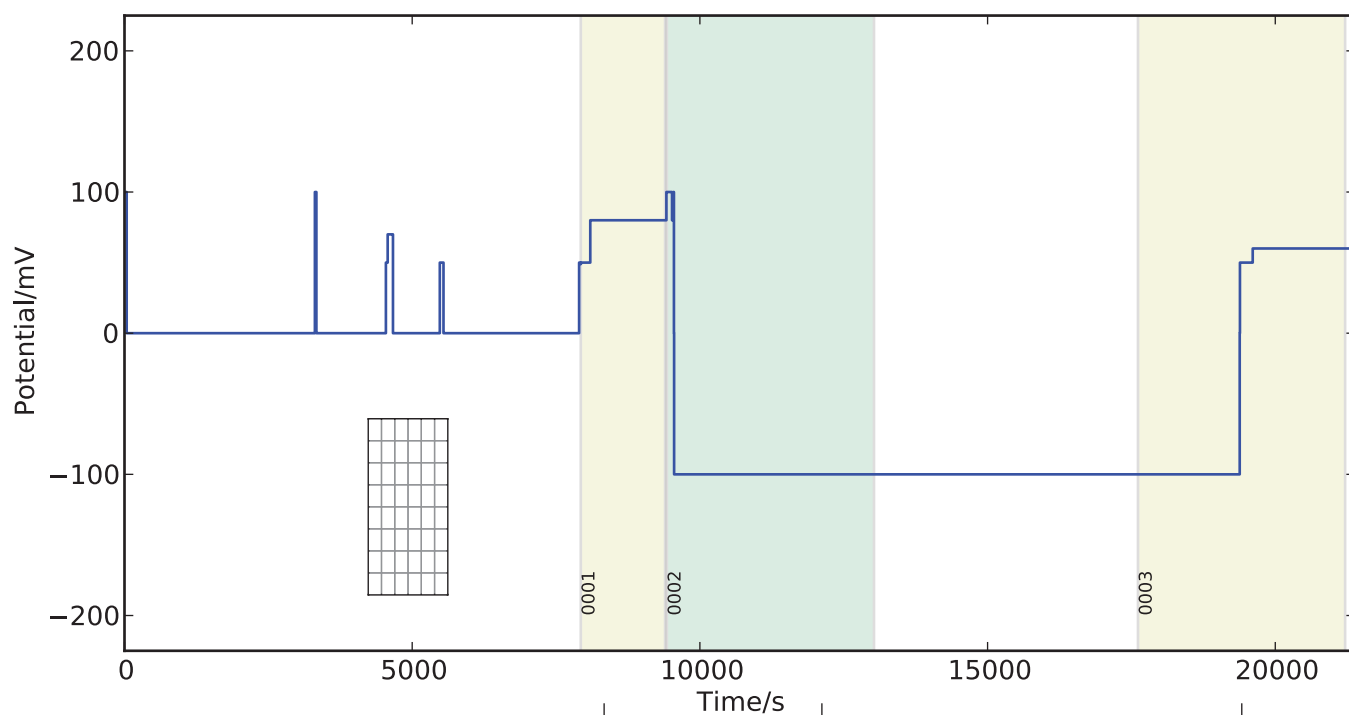
[JC-77] bCD6Am8 1M CsCl pH 7 homoAdd



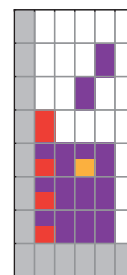
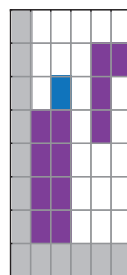
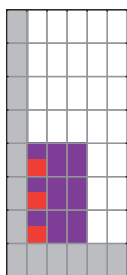
lipid
electrolyte 6.4/9.6uM
contact injection
brush transfer

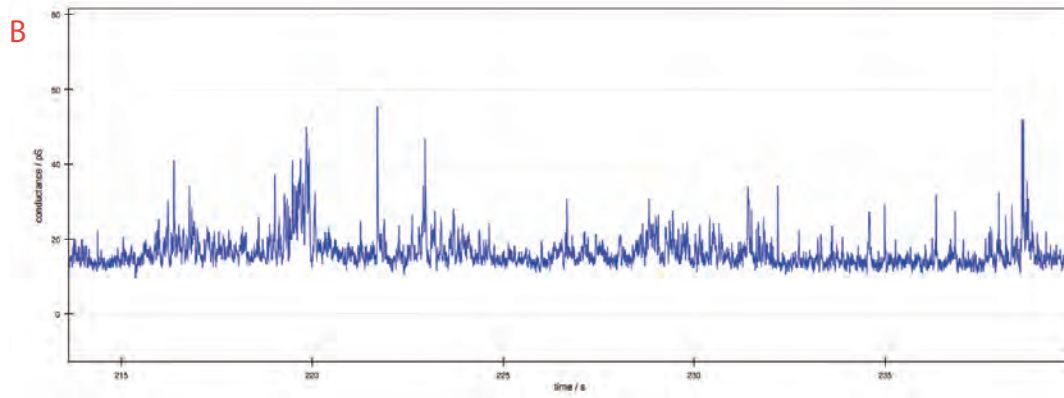
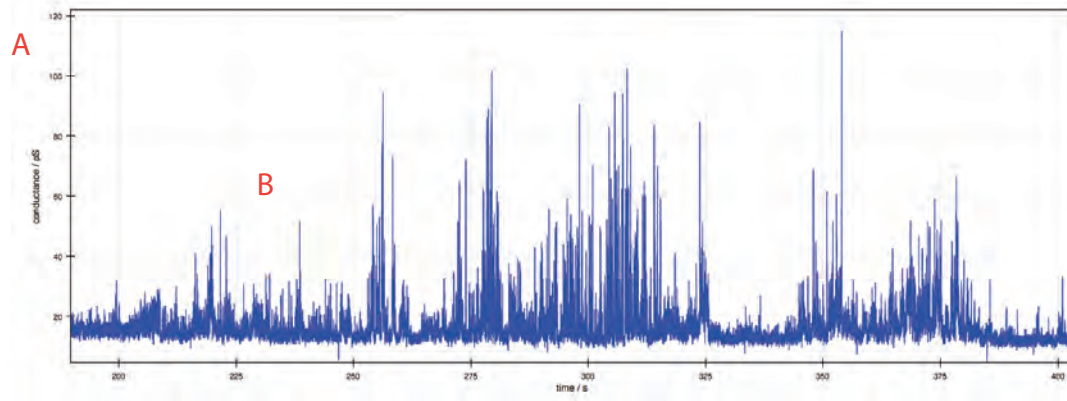
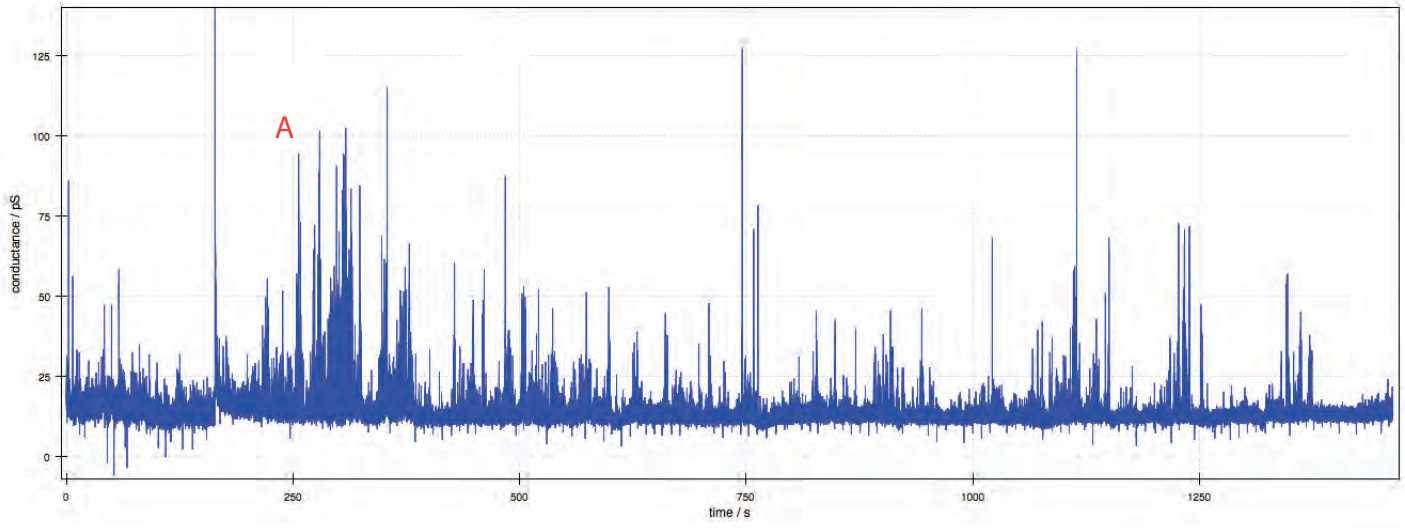


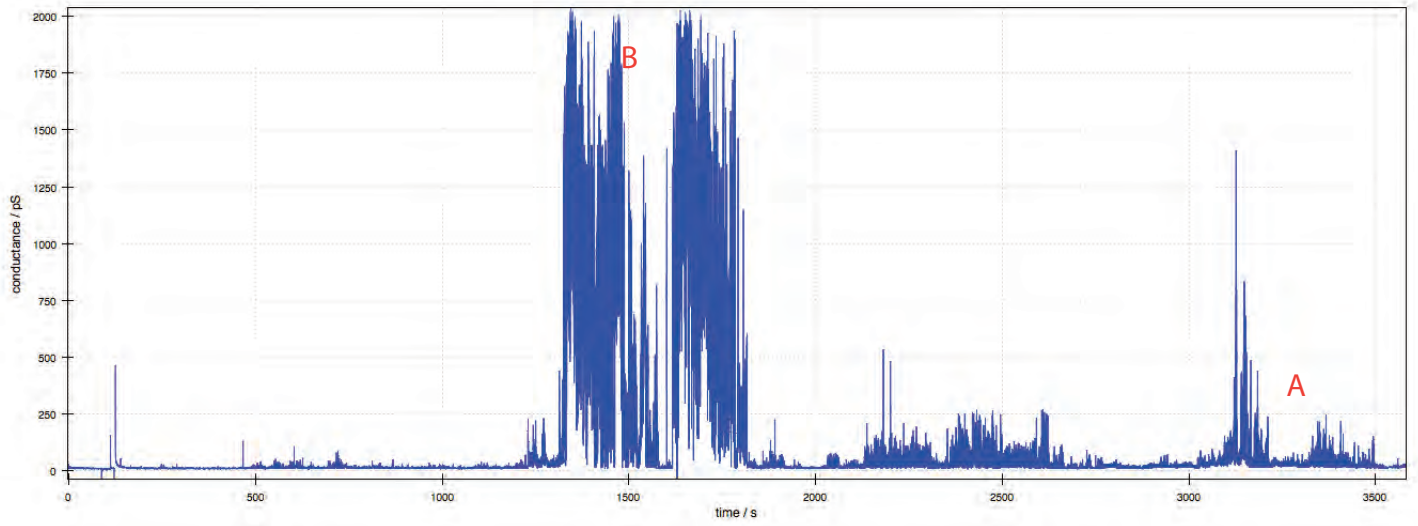
[JC-79] bCD6Am8 1M CsCl pH 7 homoAdd (2)



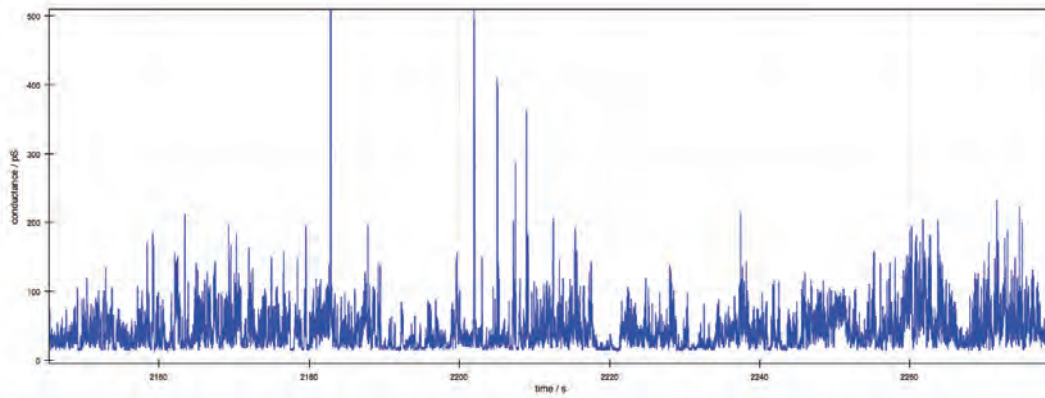
lipid
electrolyte 10/16uM
contact injection
brush transfer



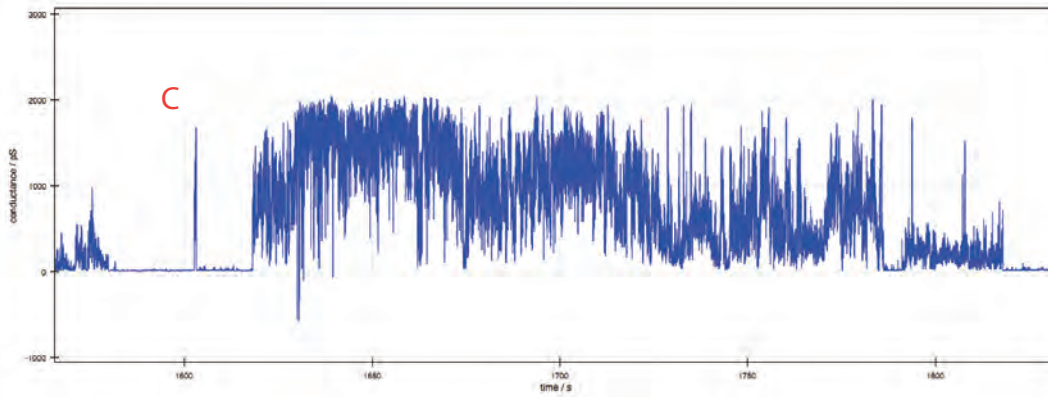




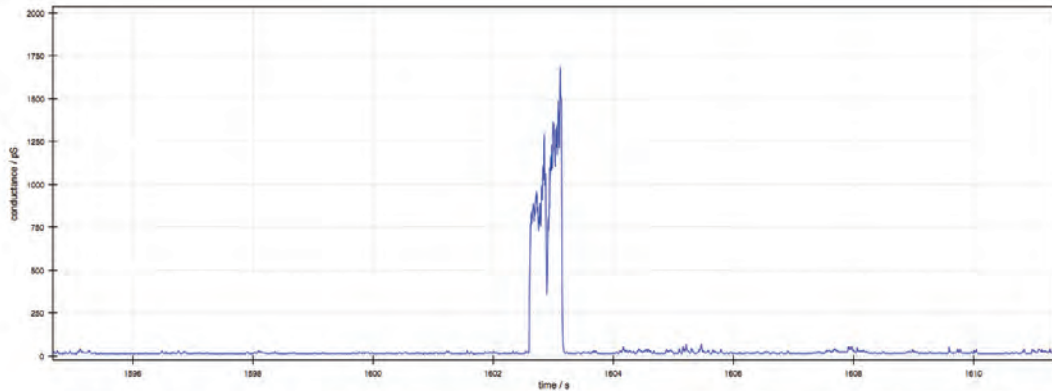
A

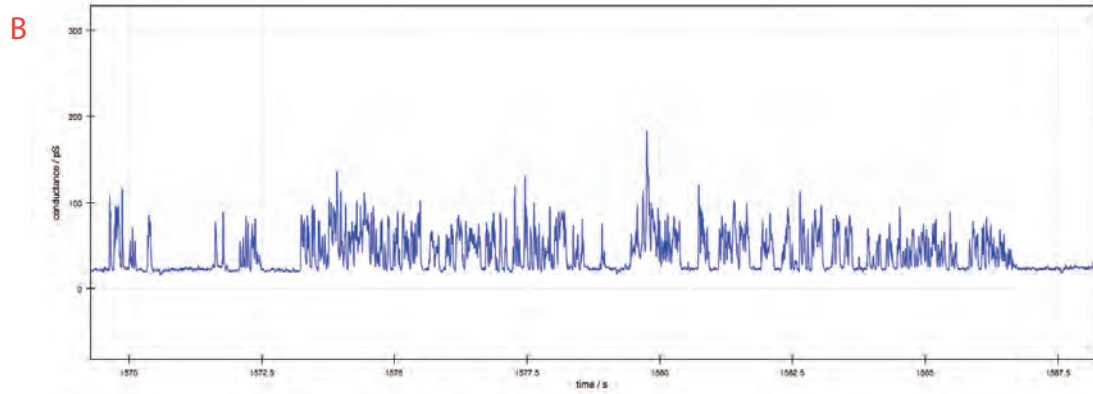
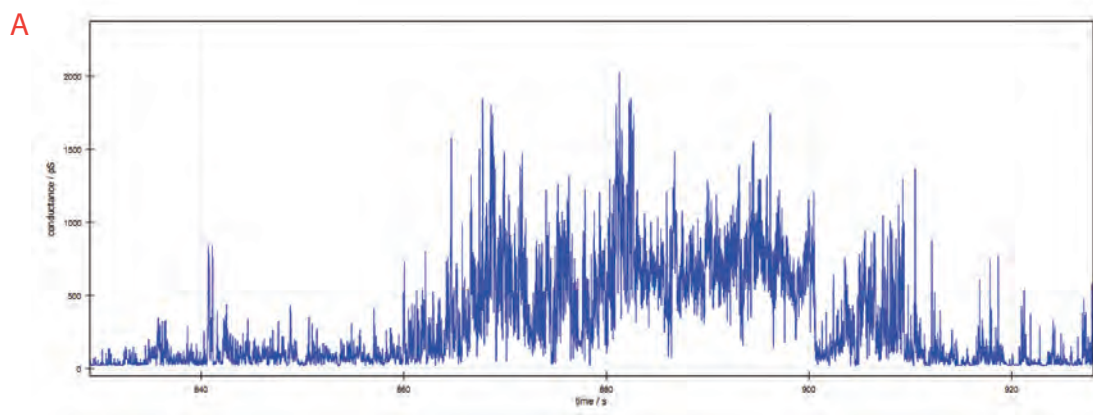
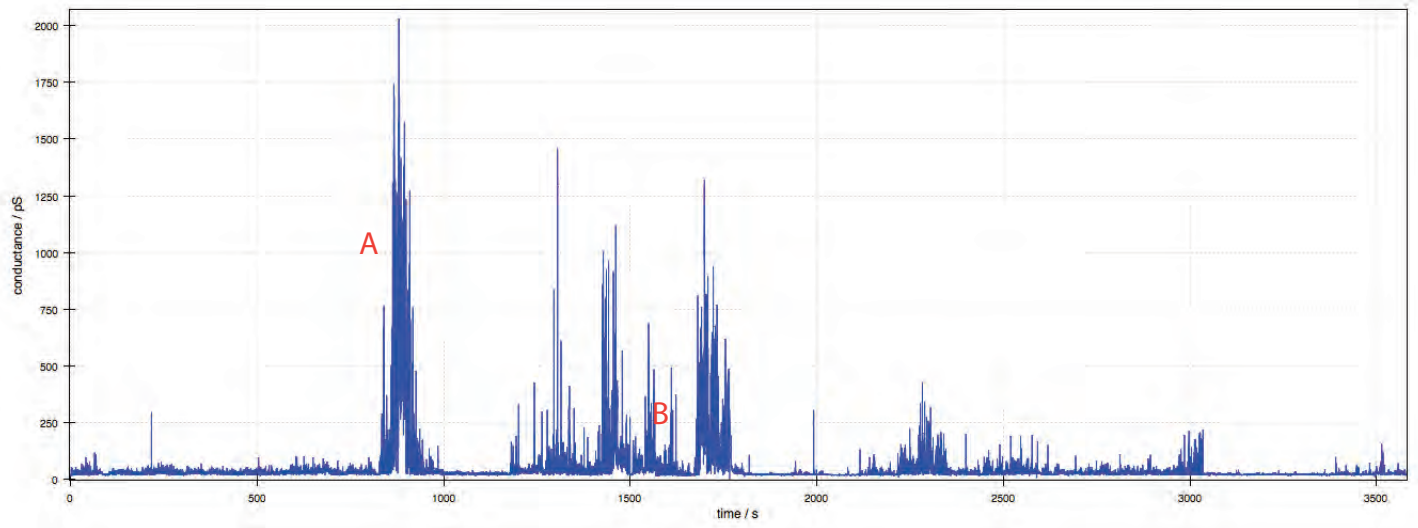


B

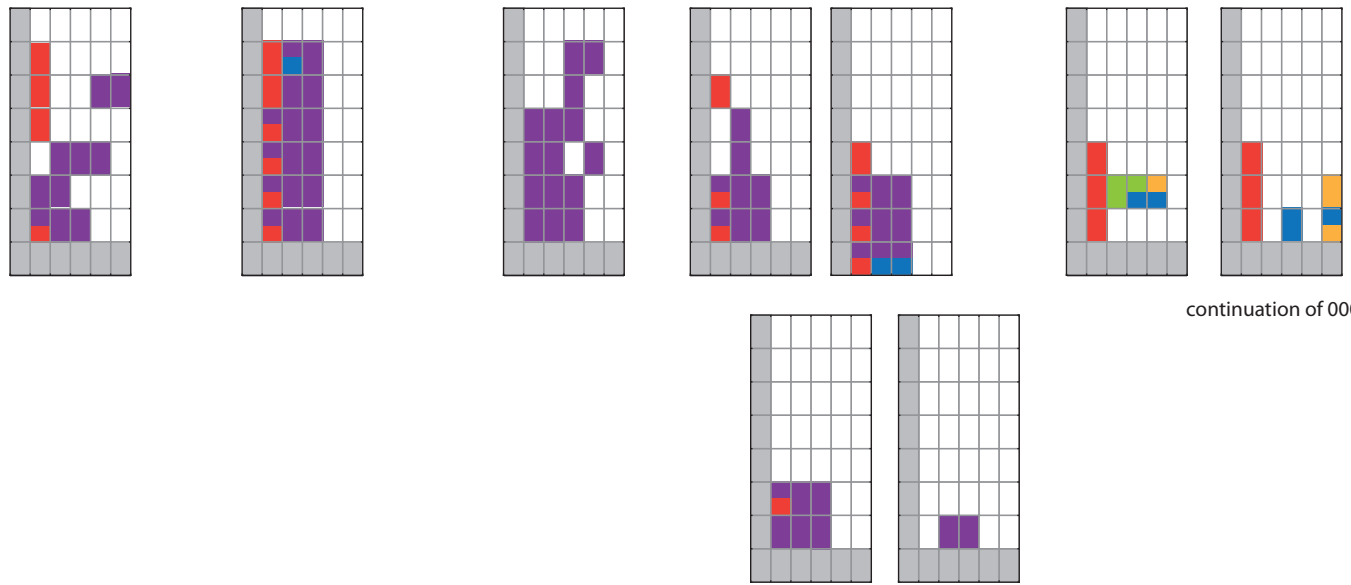
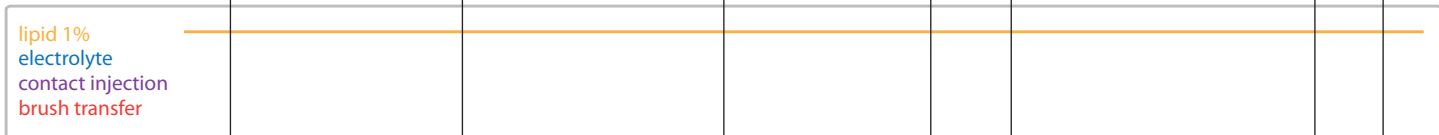
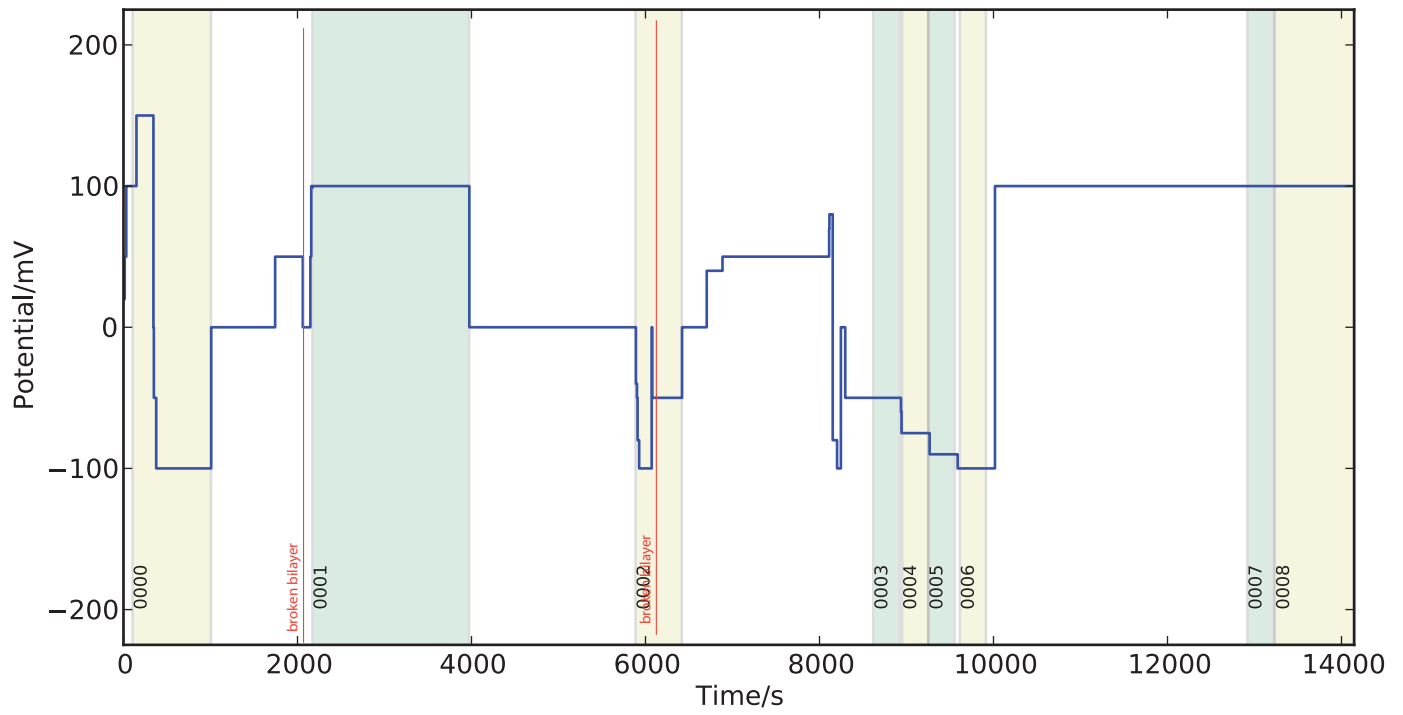


C

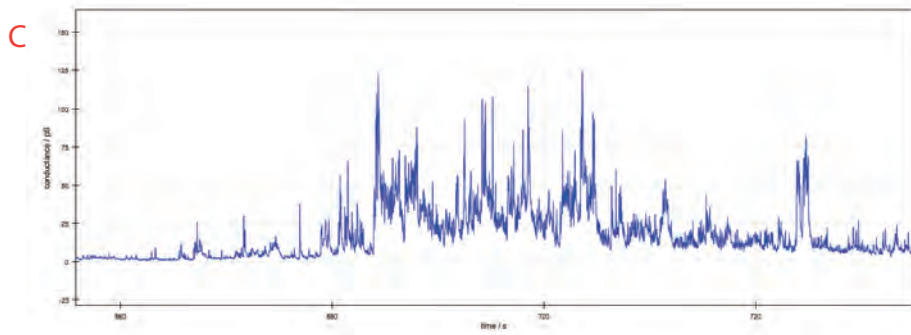
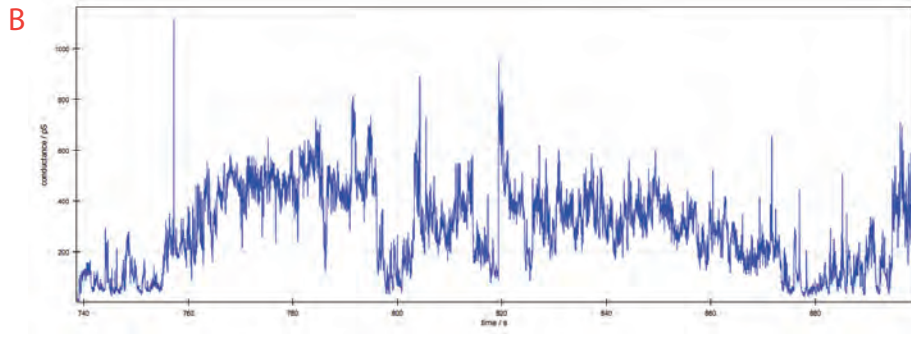
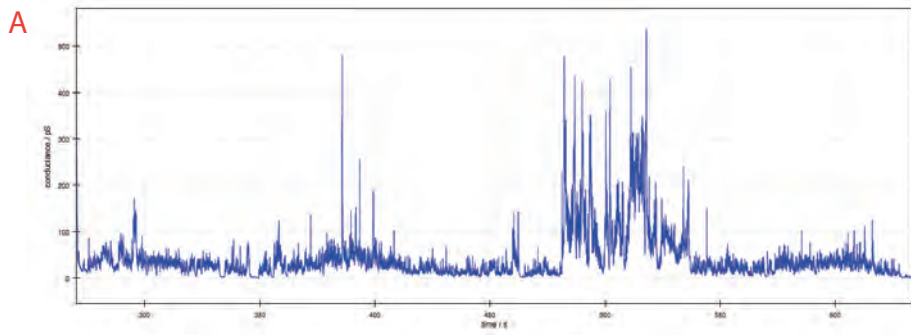
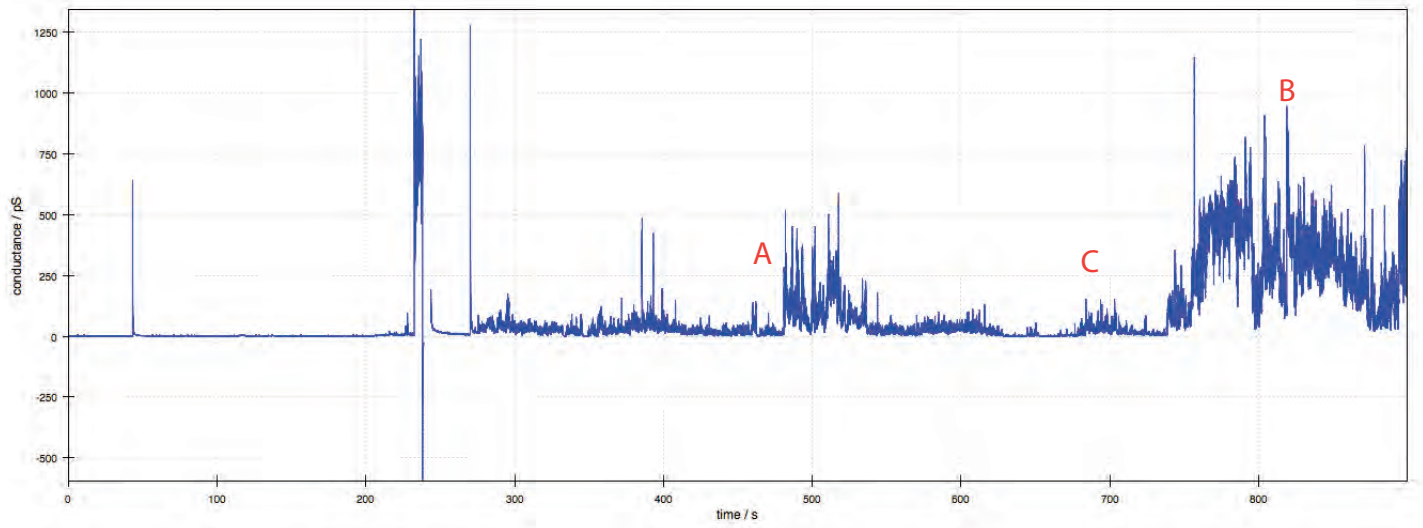


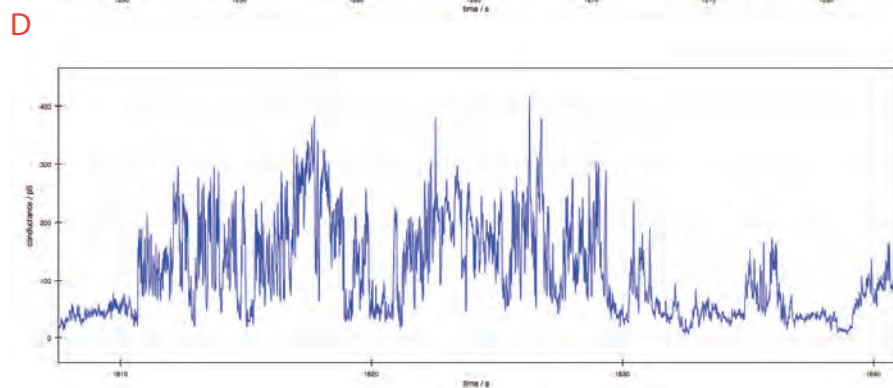
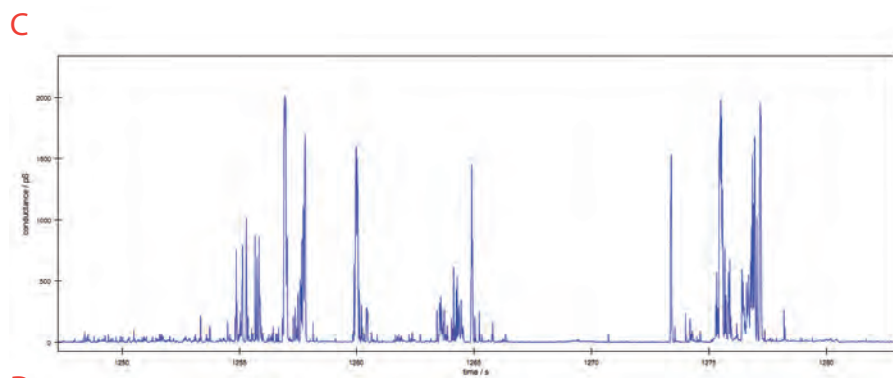
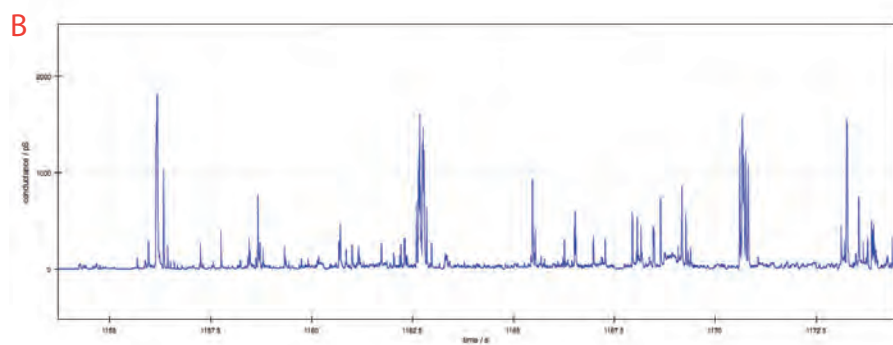
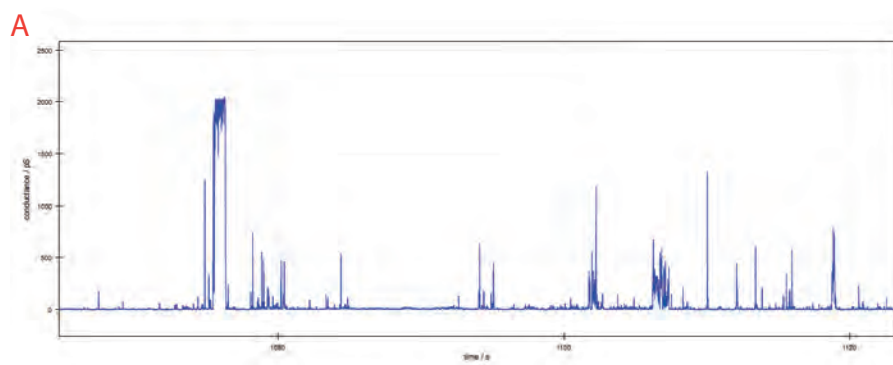
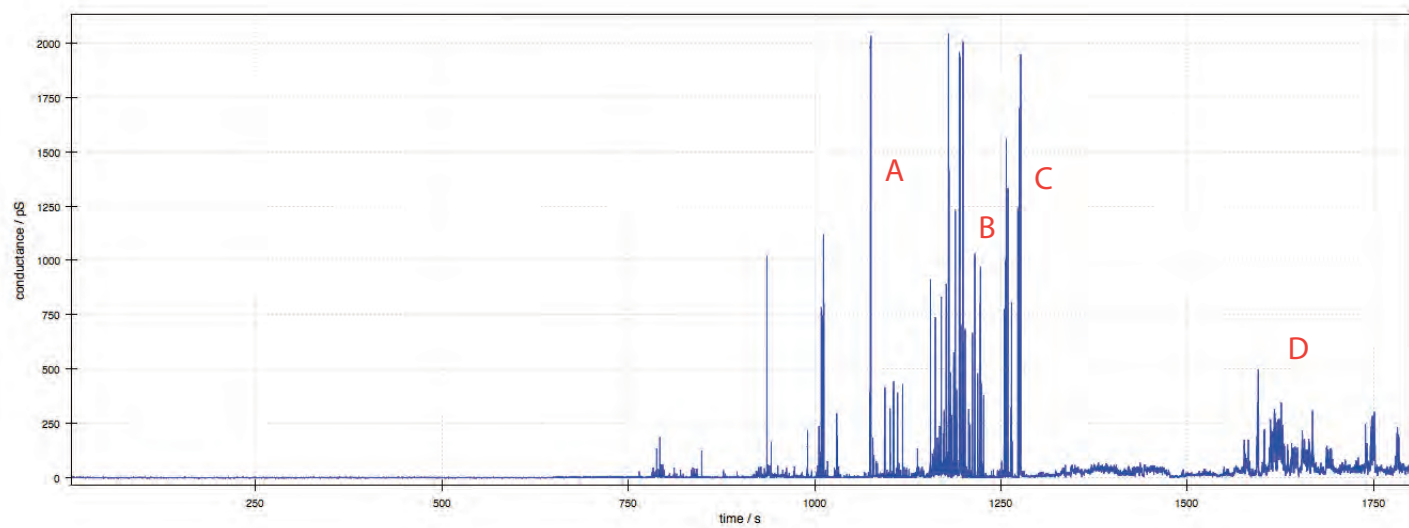


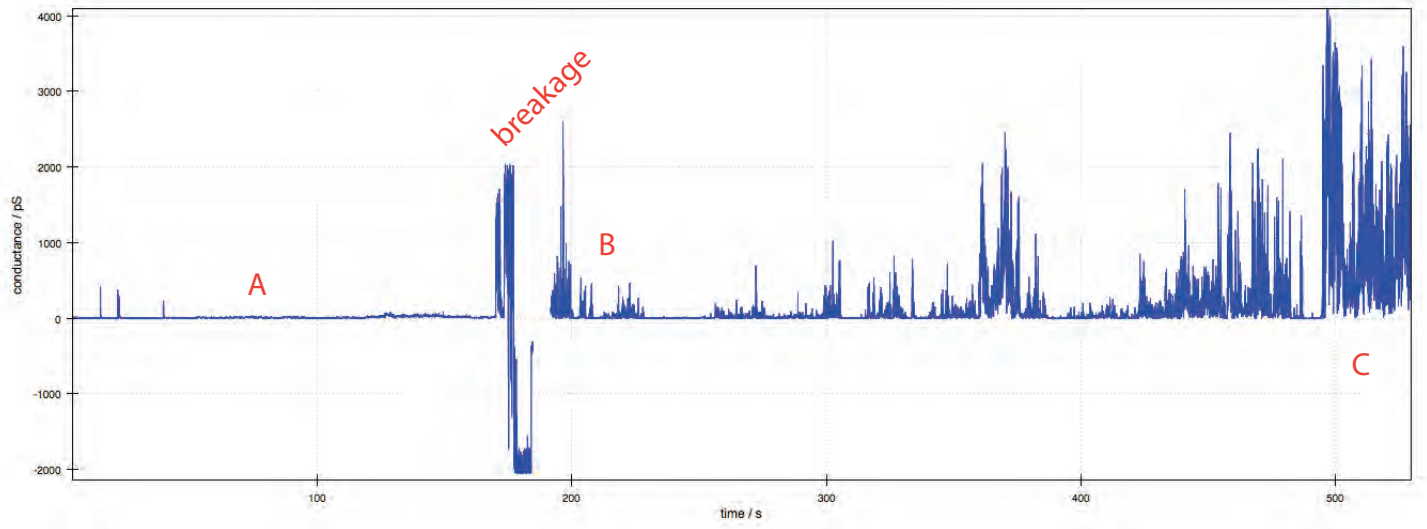
[JC-73] bCD6Ur8 1M CsCl pH 7 survery run 1 perc



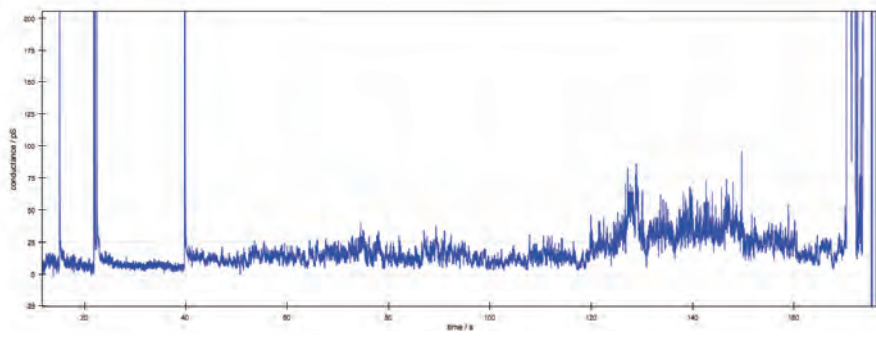
continuation of 0007



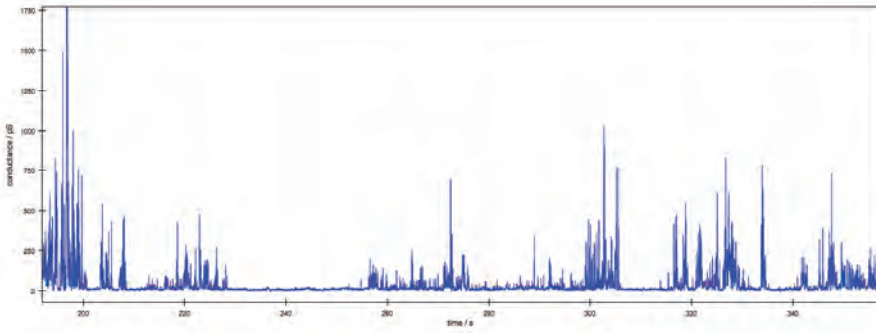




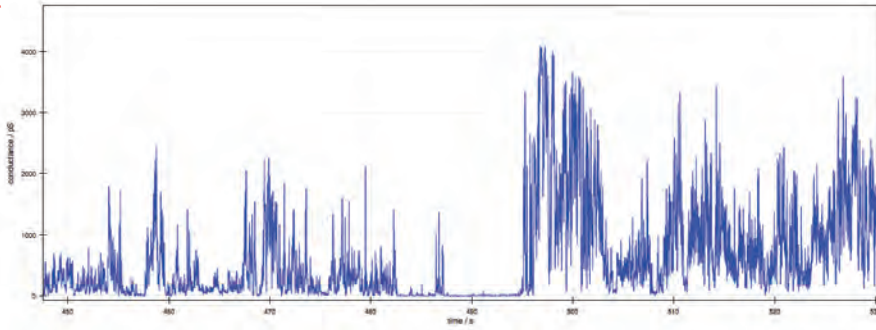
A

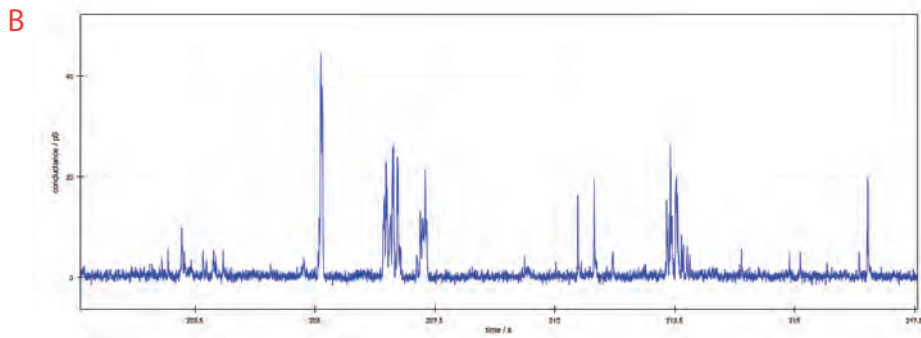
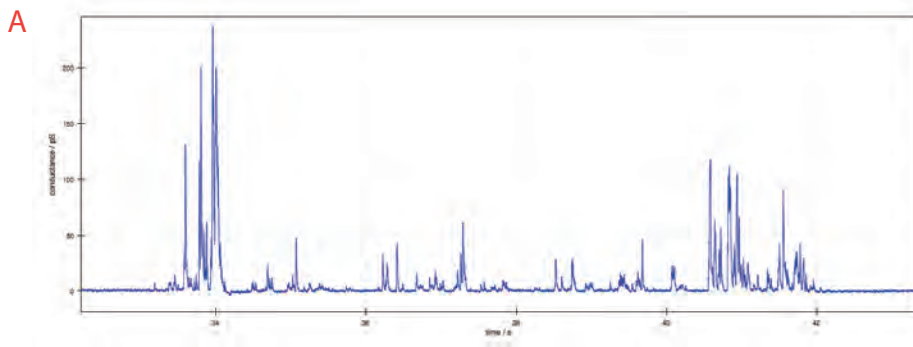
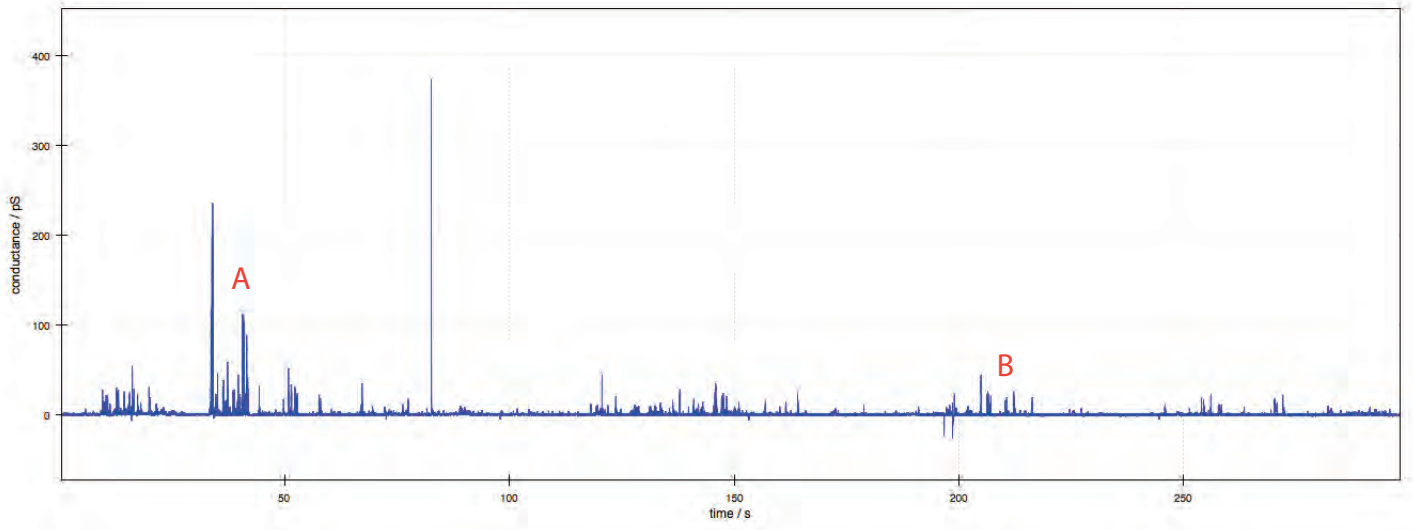


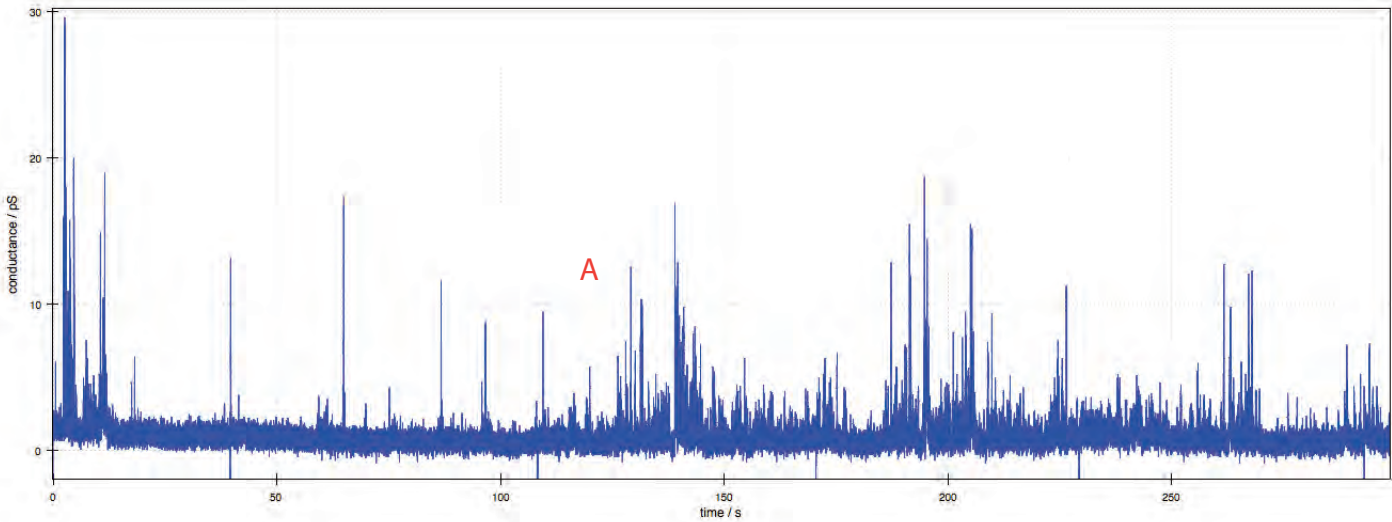
B



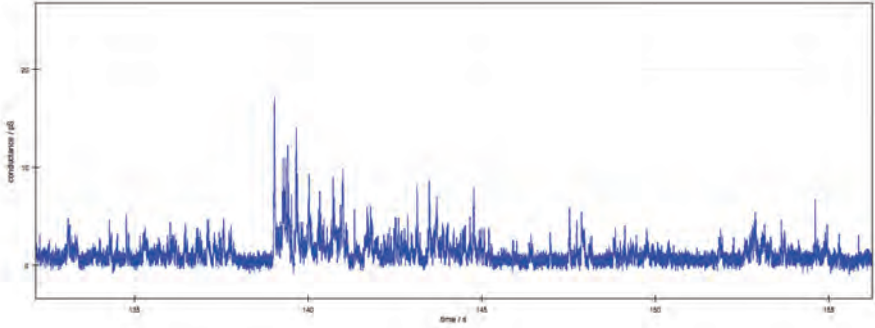
C

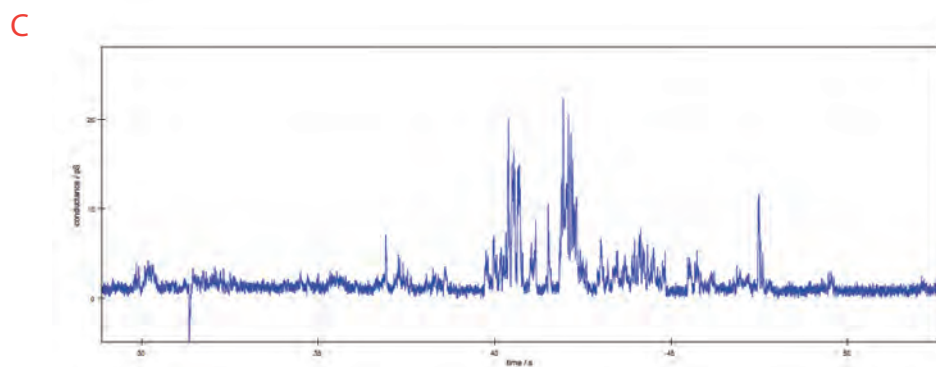
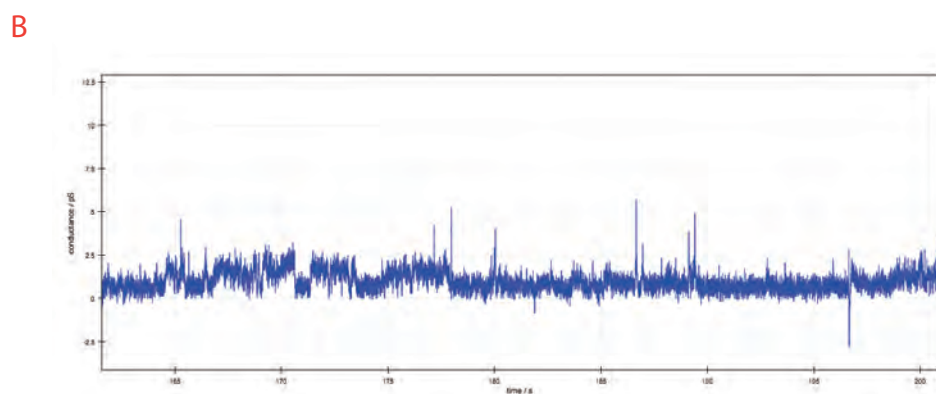
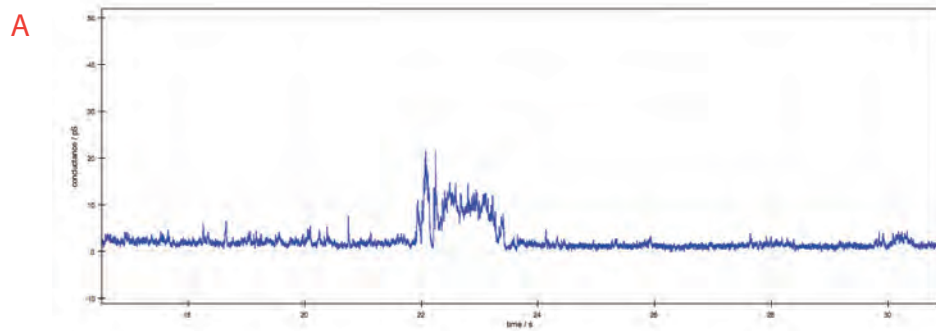
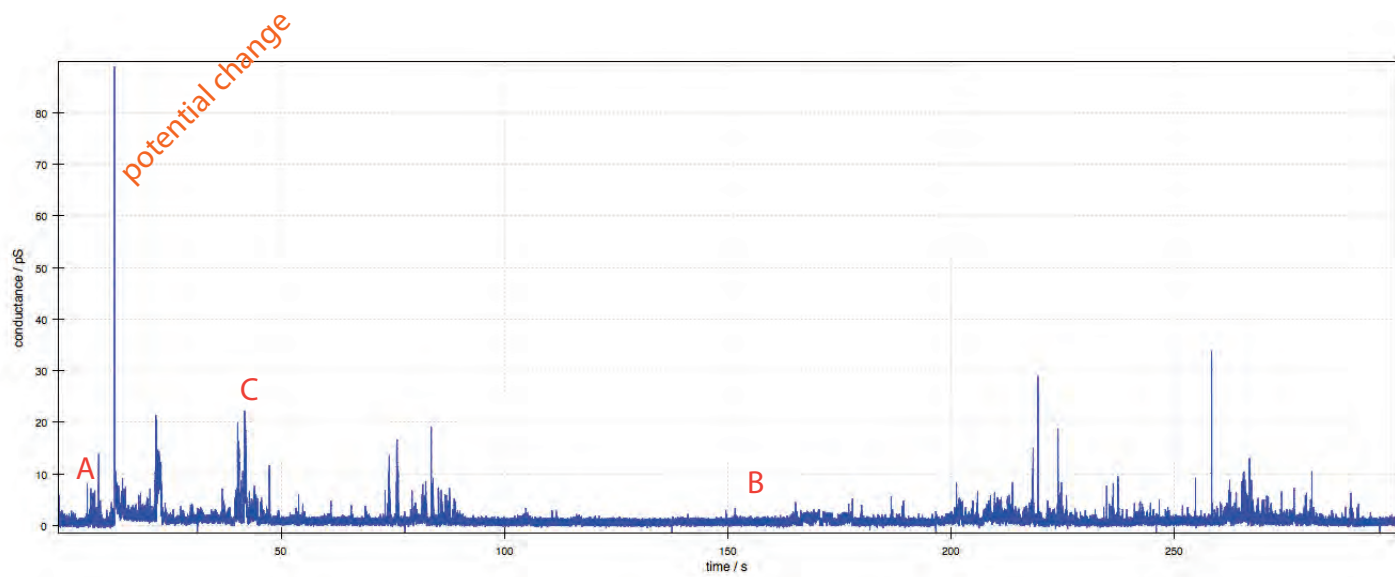


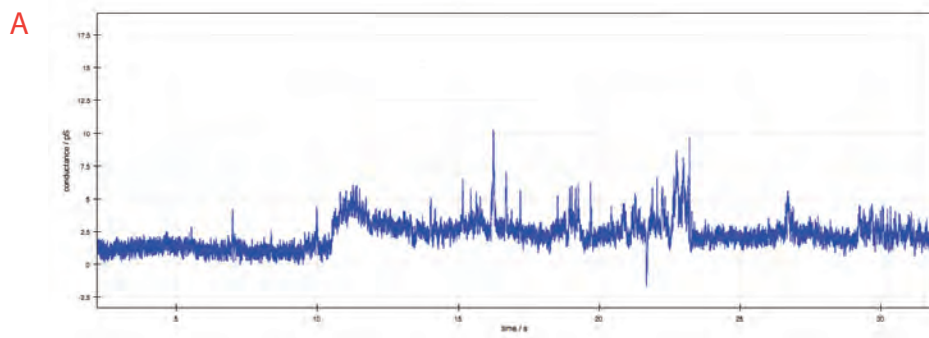
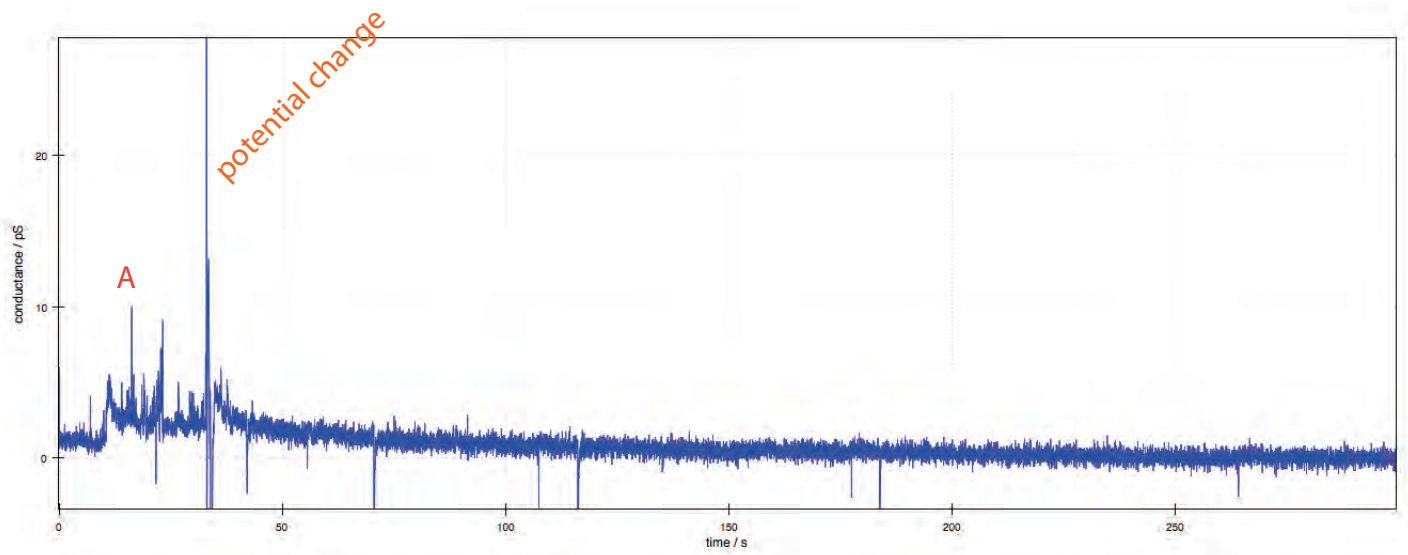


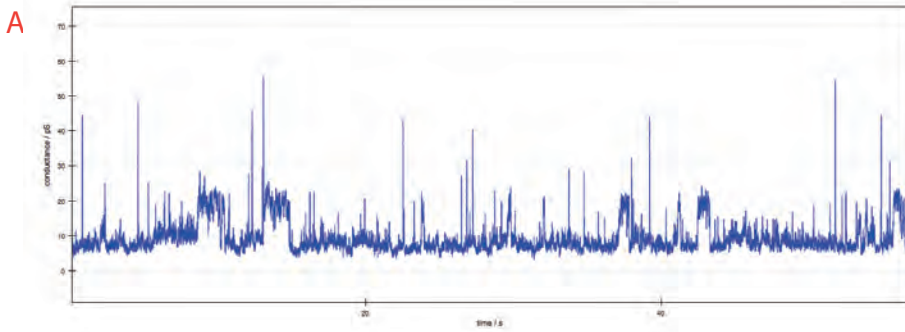
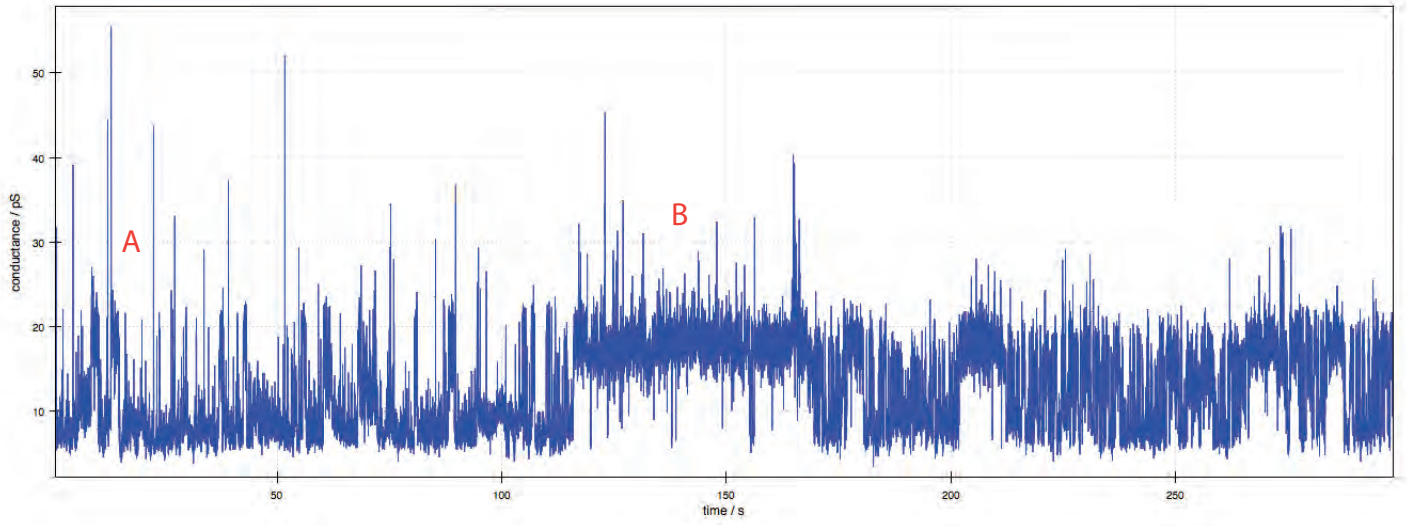


A

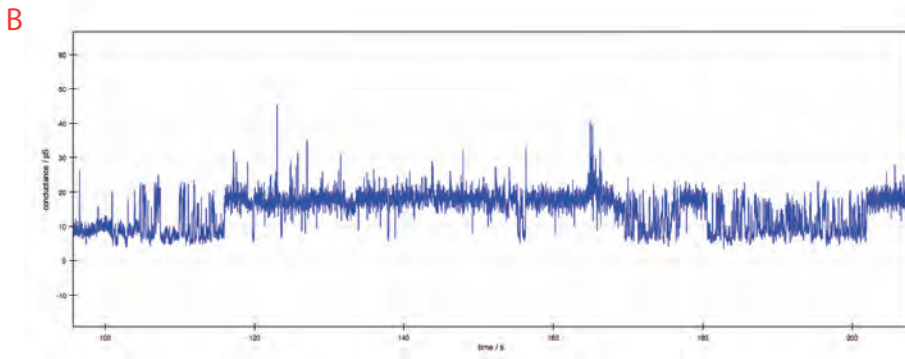


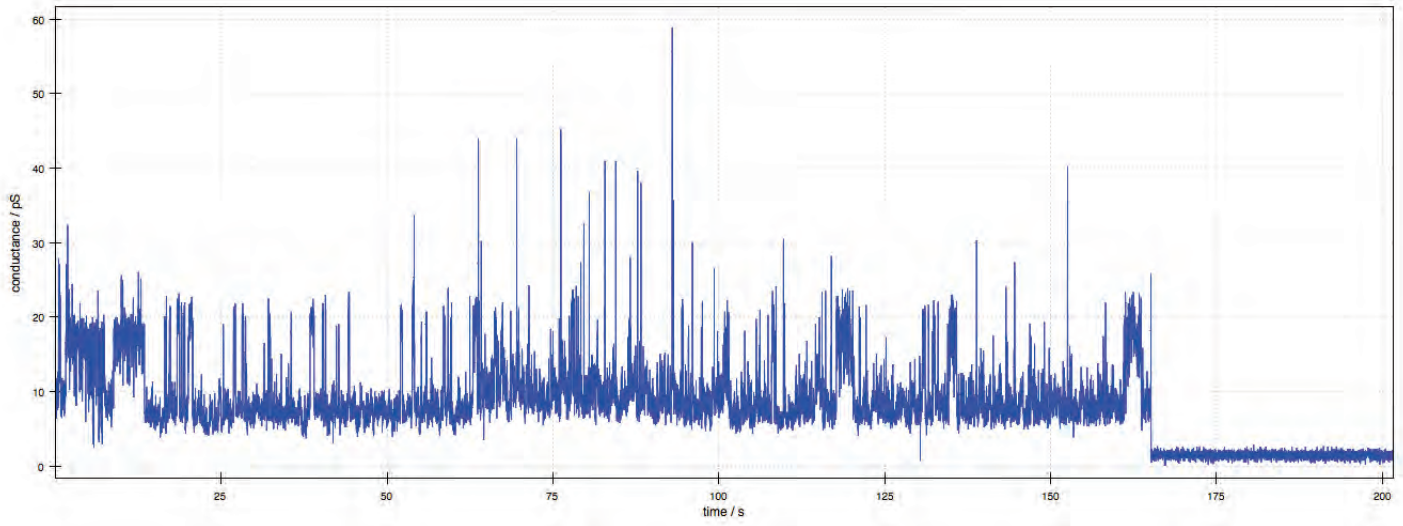






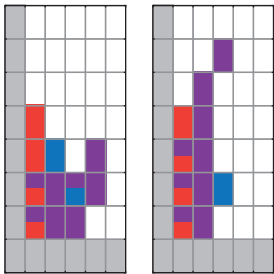
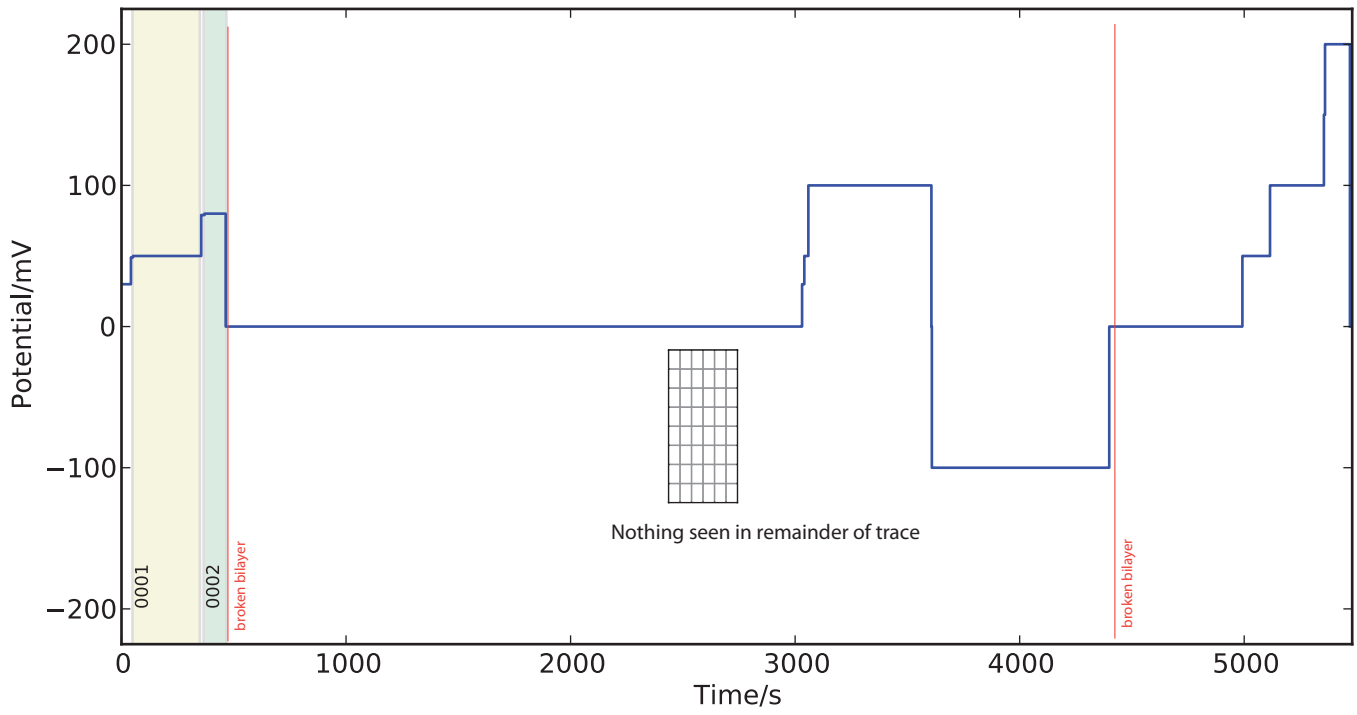
This is a very good illustration of flicker/inverse flicker

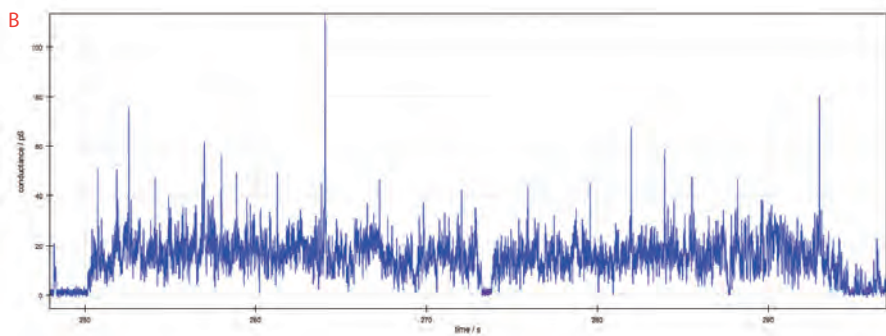
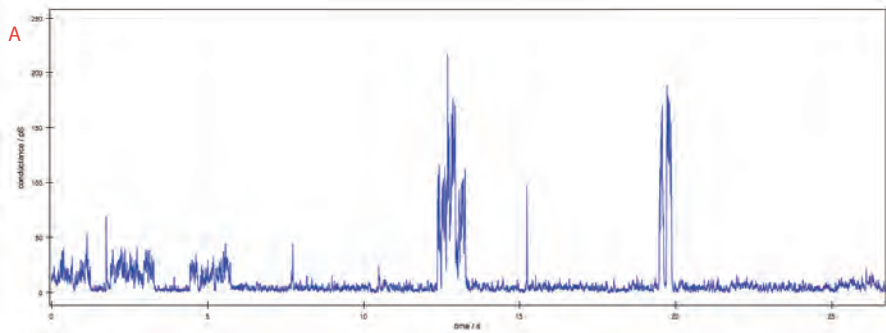
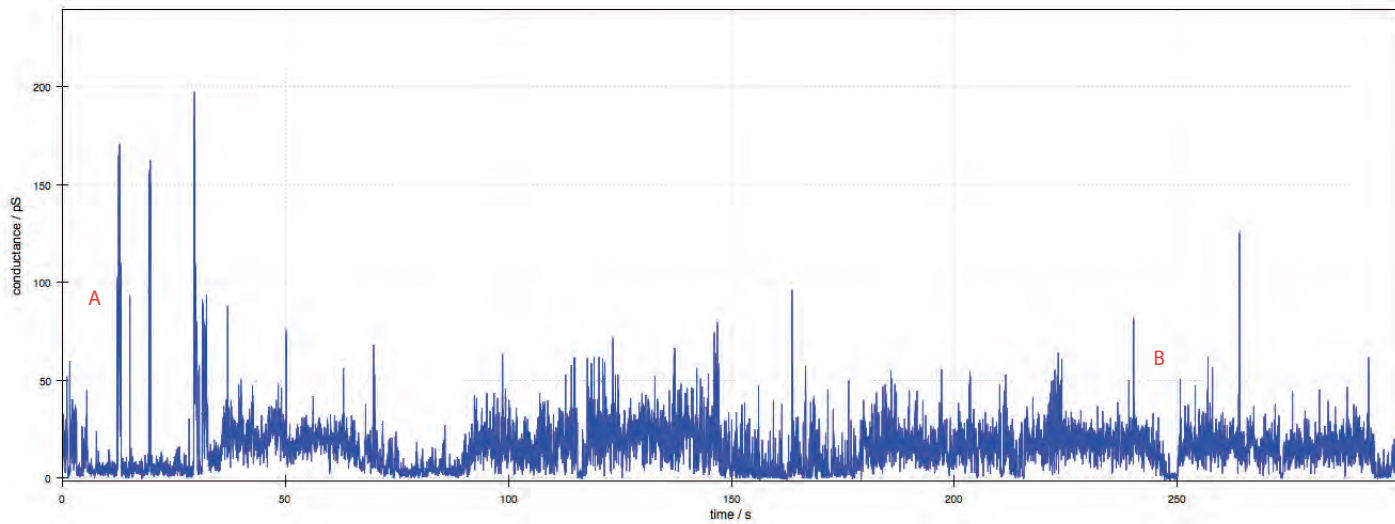


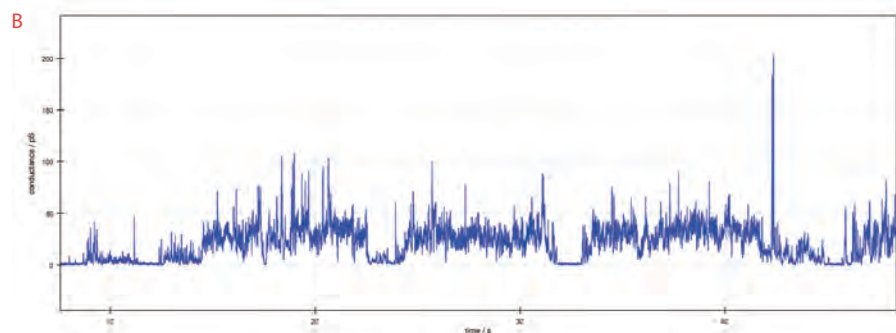
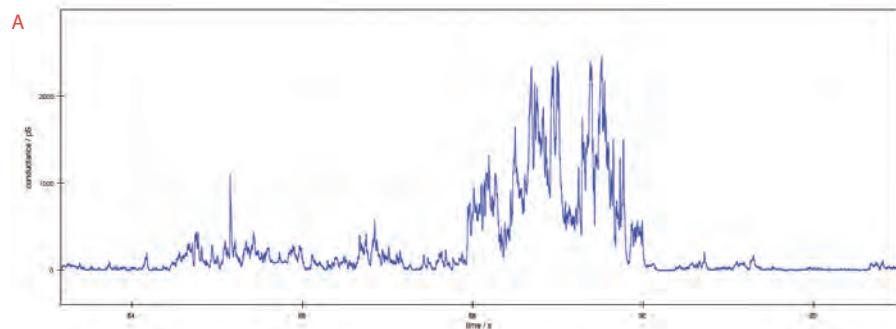
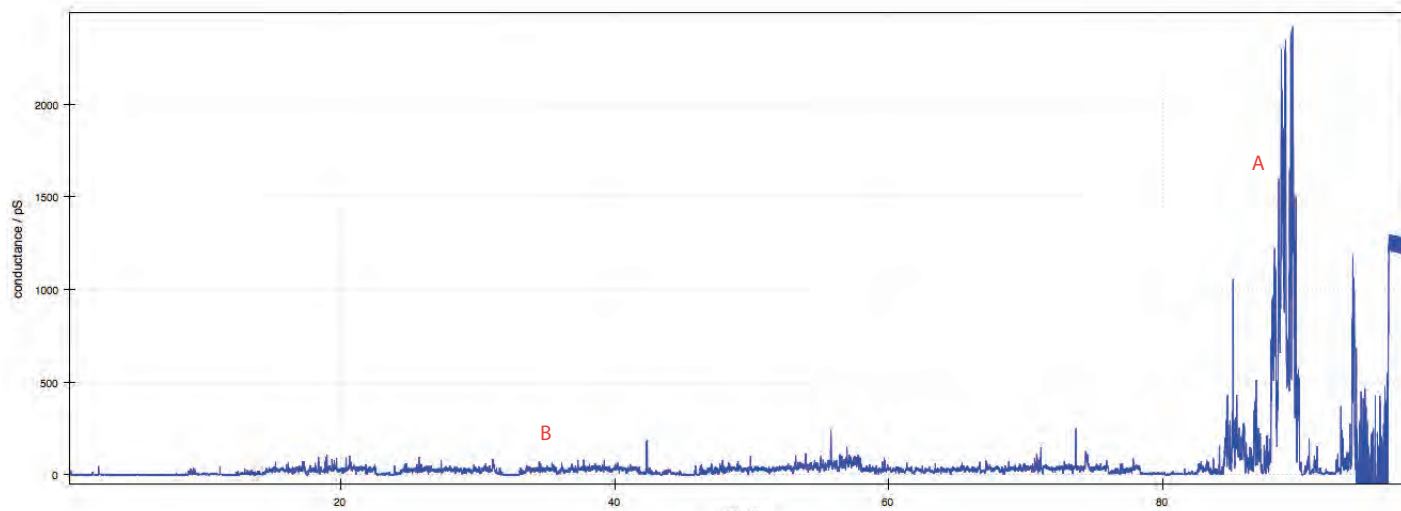


This is a very good illustration of flicker/inverse flicker Continuation from 0007.

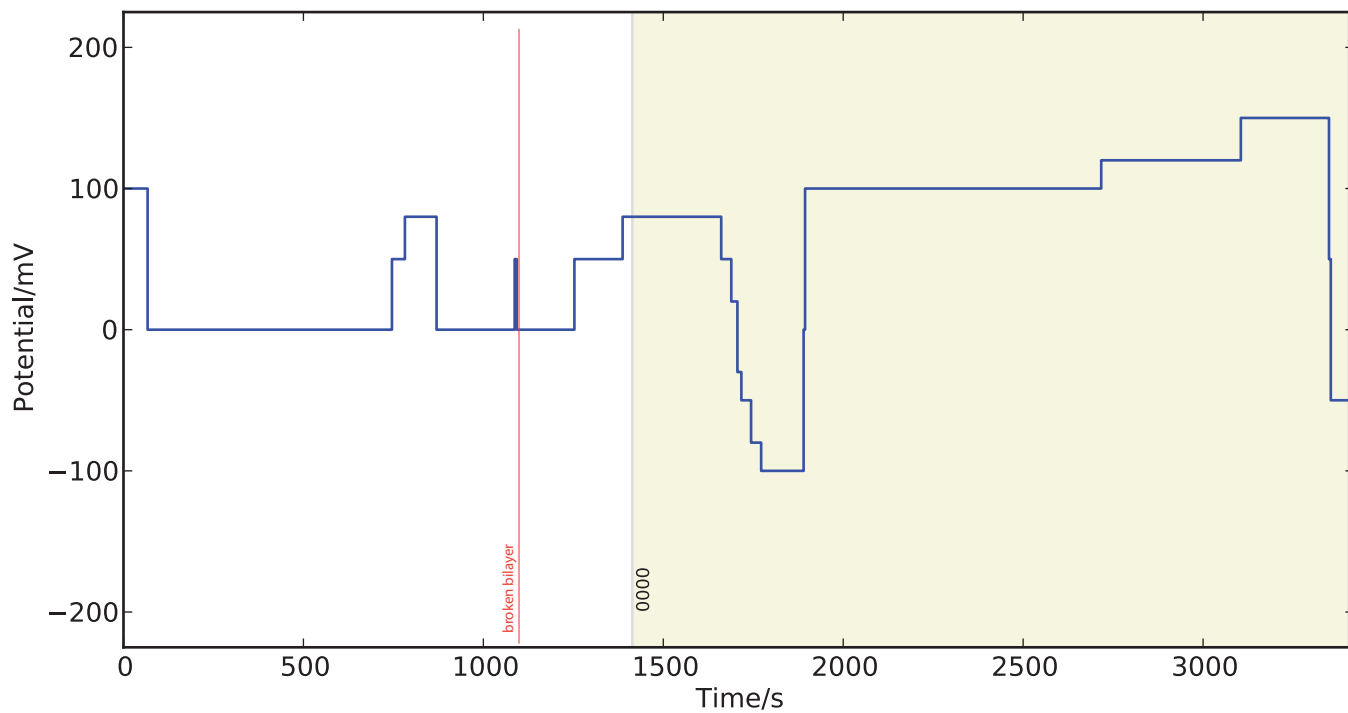
[JC-74] bCD6Ur8 1M CsCl pH 7 survery run 1 perc (2)



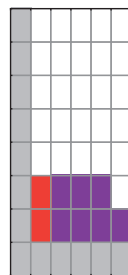


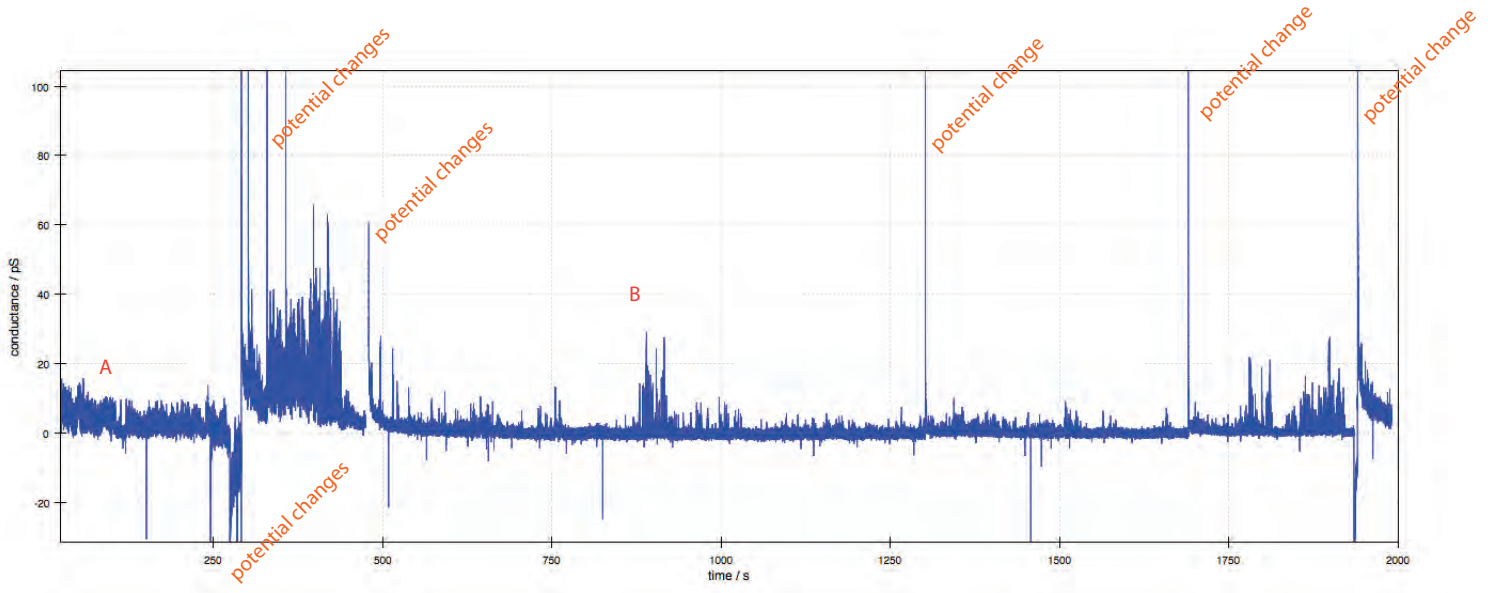


[JC-82] bCD6Ur8 1M CsCl pH 7 homoAdd

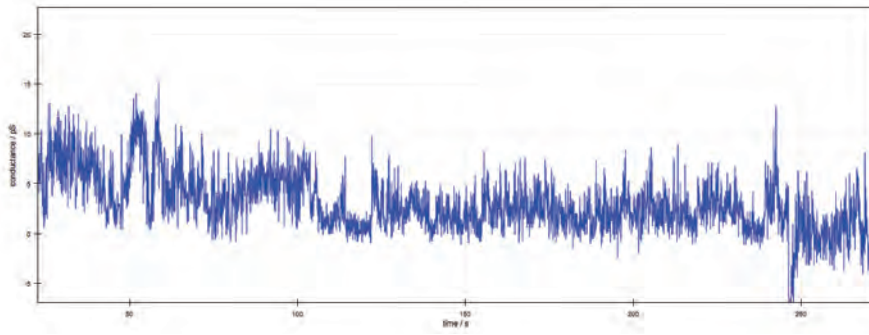


lipid
electrolyte 30/20uM
contact injection
brush transfer

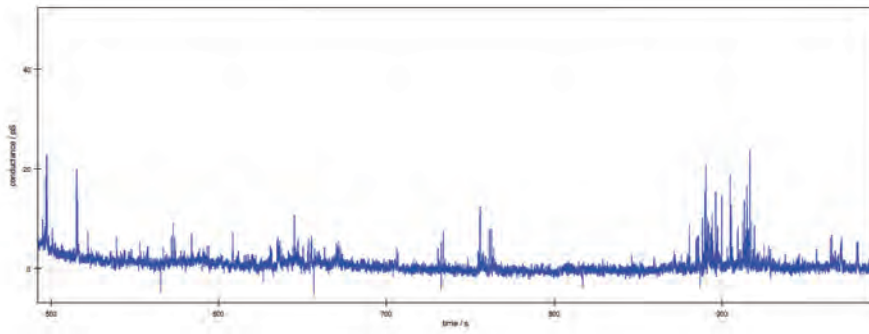




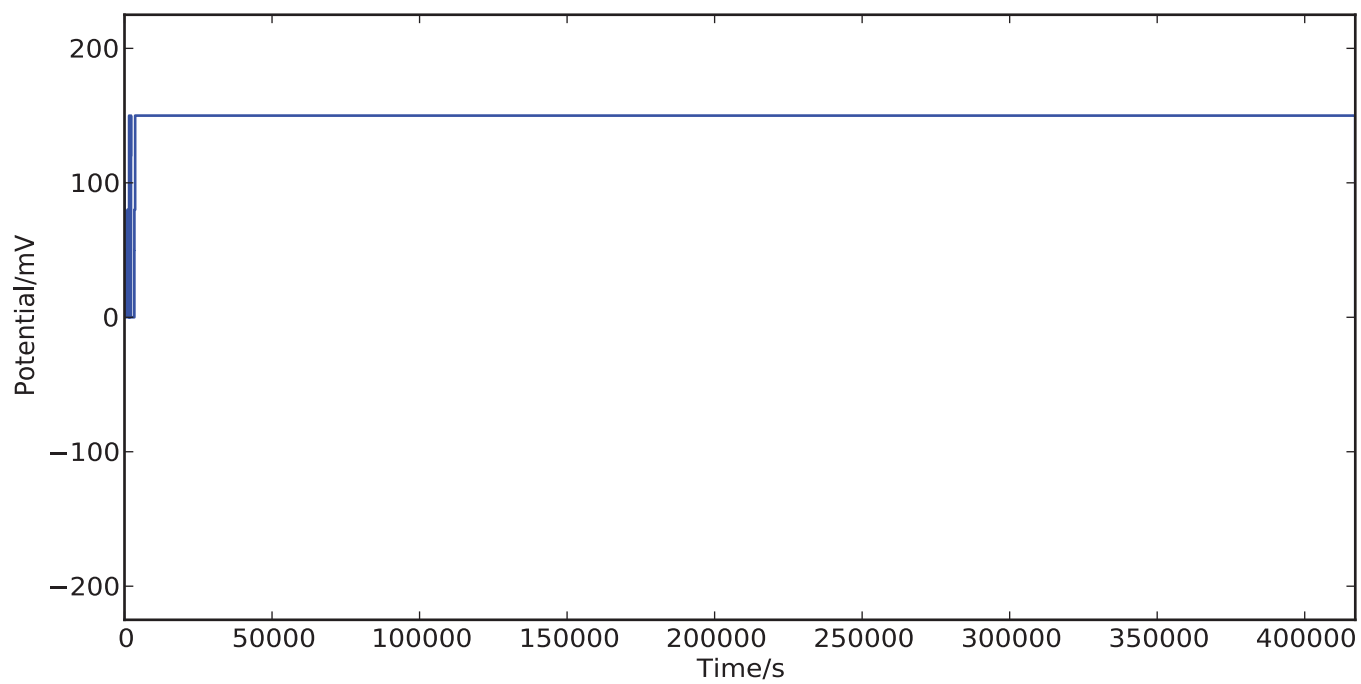
A



B



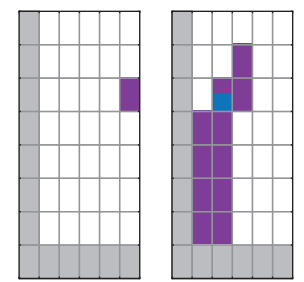
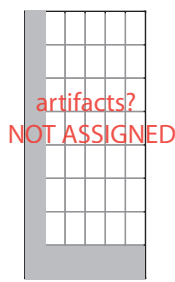
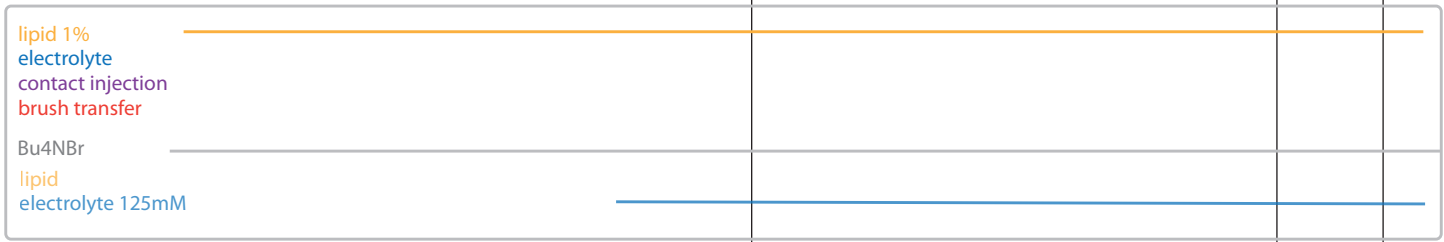
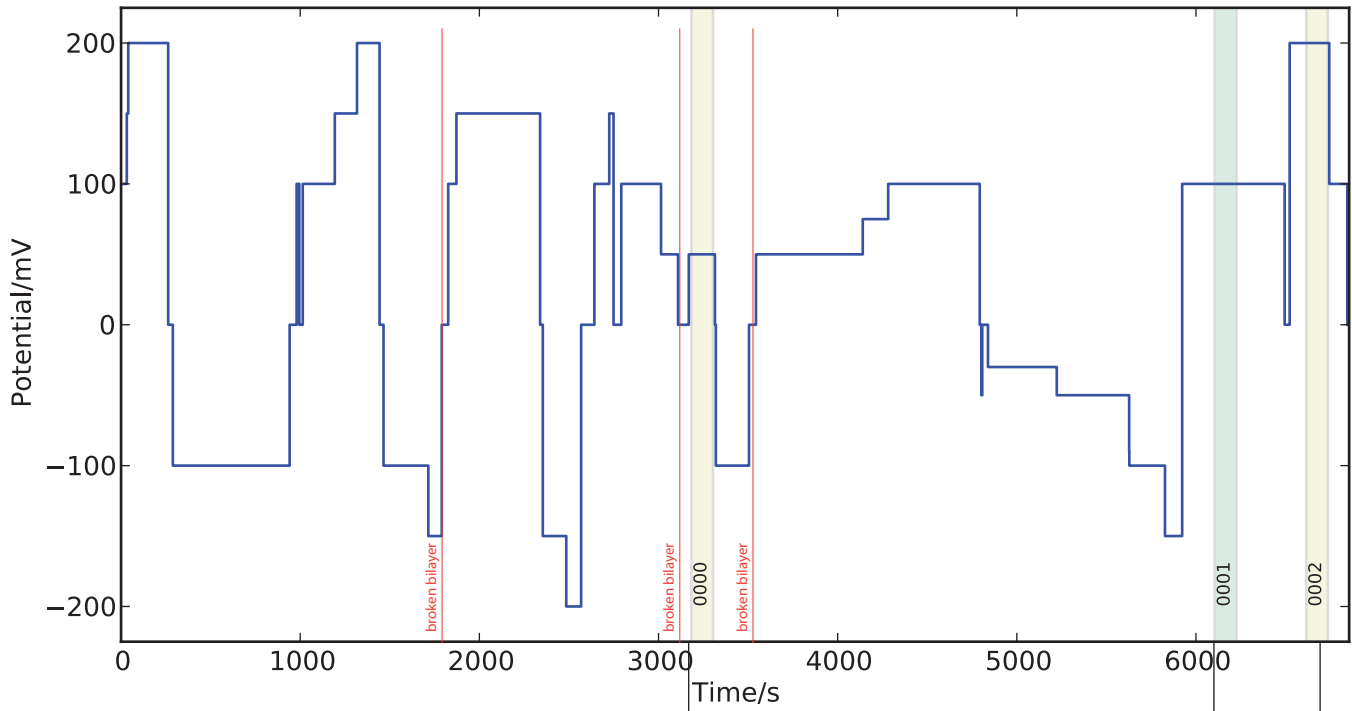
[JC-86] bCD6Ur8 1M CsCl pH 7 homoAdd (2)



lipid
electrolyte 30/20uM
contact injection
brush transfer

It is not clear what I saw in this experiment

JC-141 JC-T-20-II bCD-6Ur8 1percent 1M KCl pH 5



noisy looking,
I feel this is
too regular
to be fractal

