

## Supporting information for: *Cyclodextrin Ion Channels*

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### *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  $\mu\text{m}$  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  $\text{KNO}_3$  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 described<sup>1</sup>. 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  $\mu\text{L}$  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  $\text{CDCl}_3$  or  $\text{MeOH-d}_4$ ) was added to the diPhyPC/ $\text{CHCl}_3$  solution, and solvent removed with a stream of  $\text{N}_2$ , 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,  $\alpha$  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.

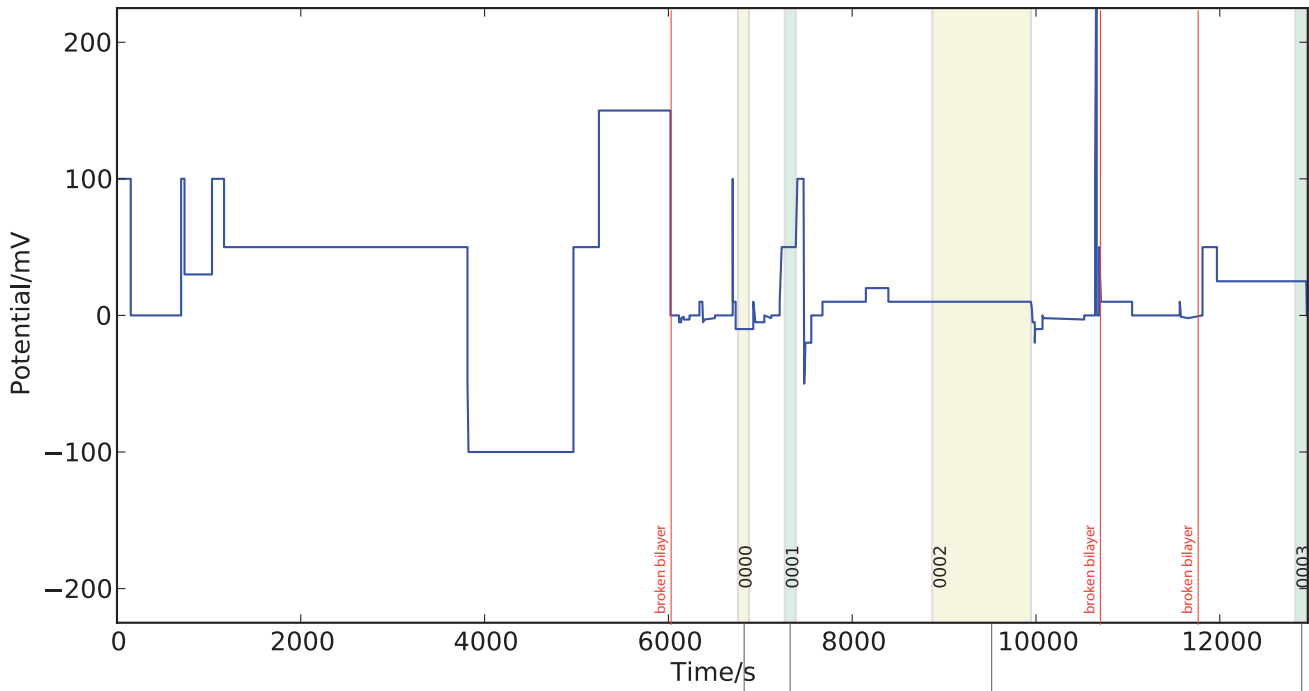
*Power Law Fitting* The list of opening durations, obtained above as a plain-text file, can then be fitted using the method of Clauset *et al*<sup>2</sup>, implemented in python<sup>3</sup>. The code performs the Maximum Likelihood Estimate fit, and provides  $\alpha$ ,  $x_{\min}$ ,  $n$ , and p-value as outputs.

#### *Summary of bilayer activity*

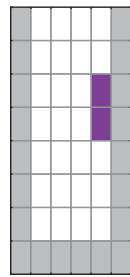
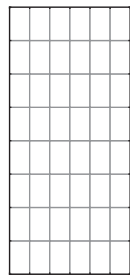
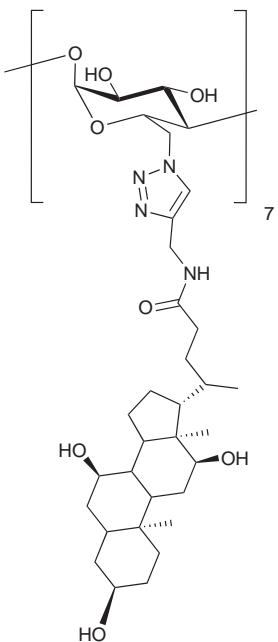
Annotated activity grids, as well as full conductance records (and expansions where appropriate), are provided below for every compound studied. The activity grids were prepared as previously described<sup>4</sup>. The summaries are arranged first by compound, then individual experiments. Within each 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.

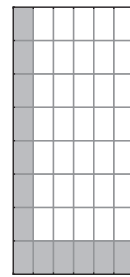
# JC-154 bCD-CholateAmide 1M CsCl pH 7



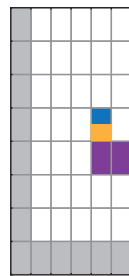
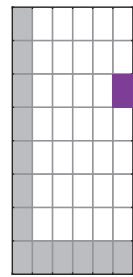
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brush transfer



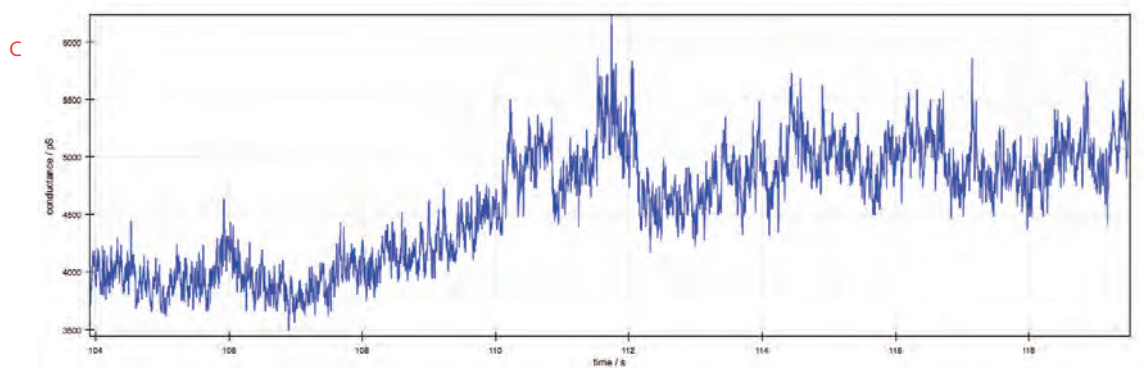
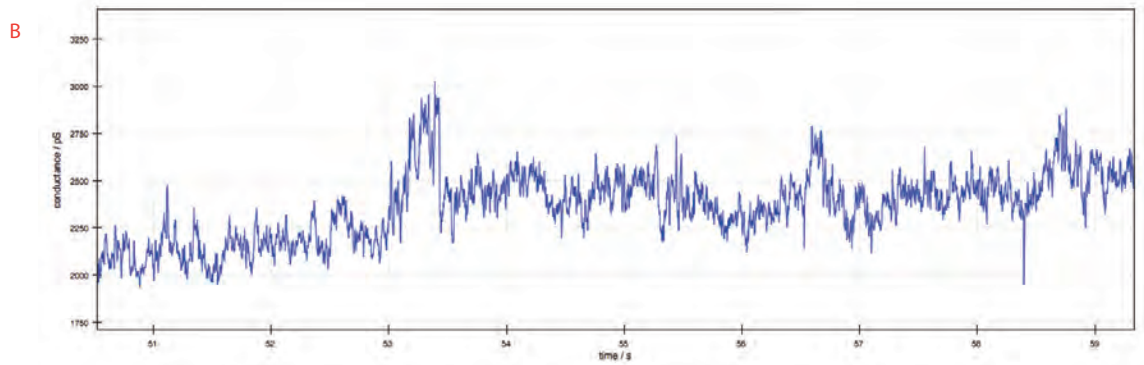
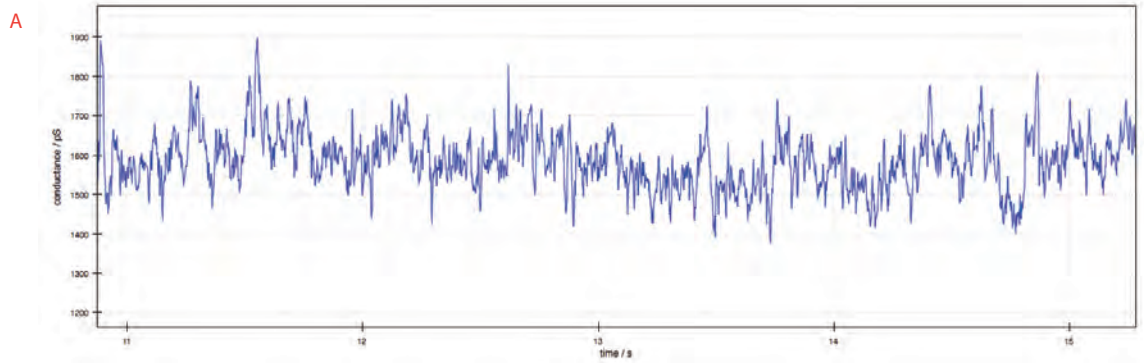
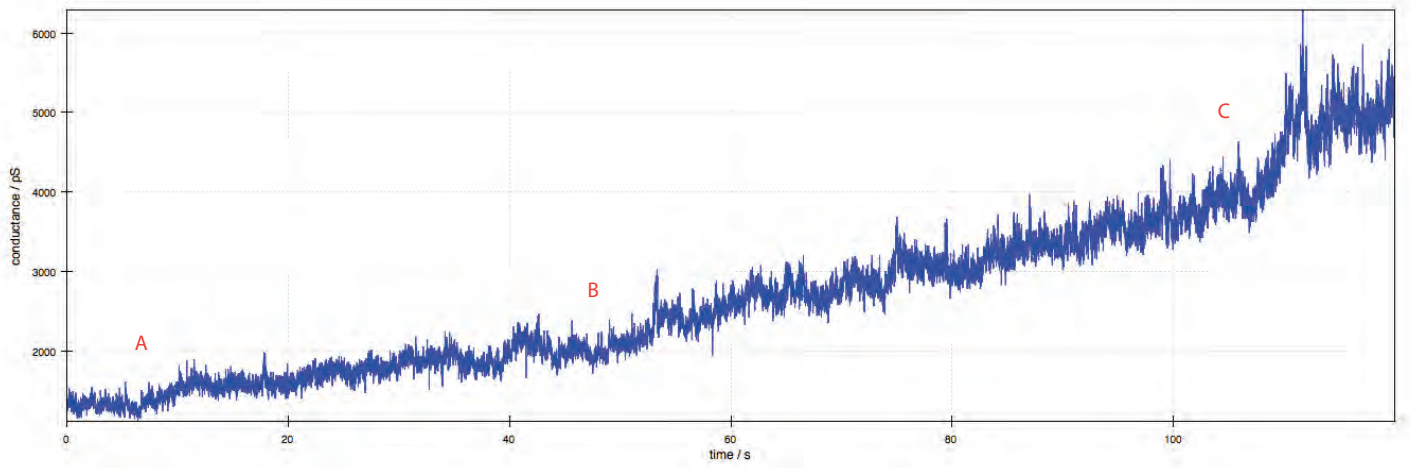
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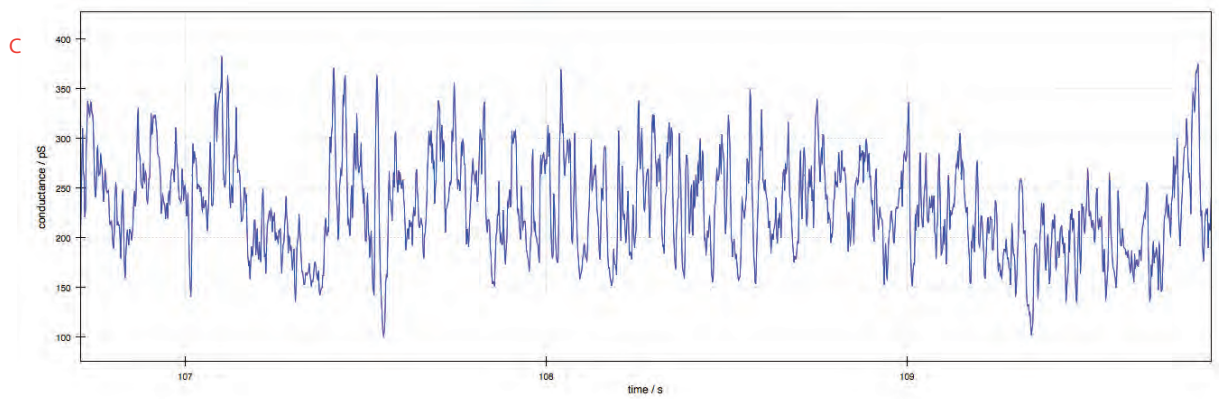
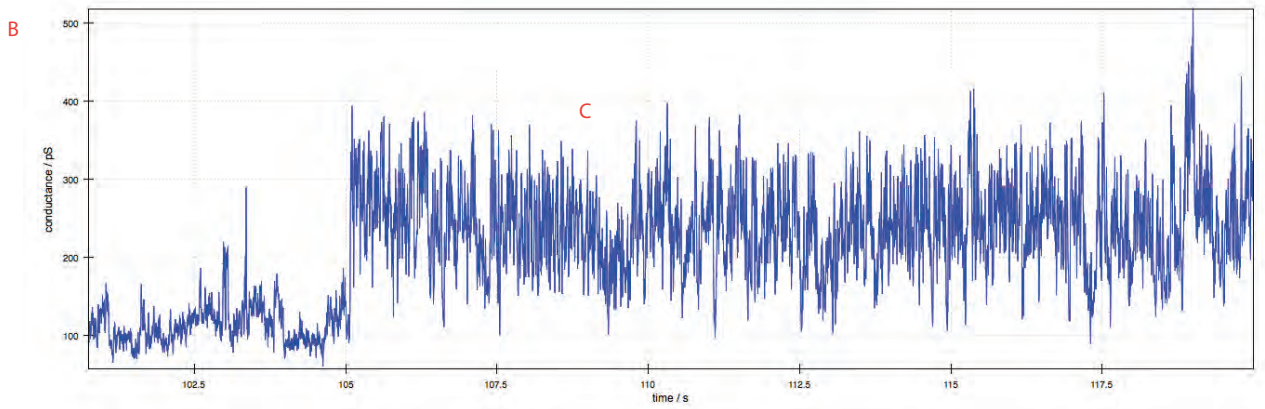
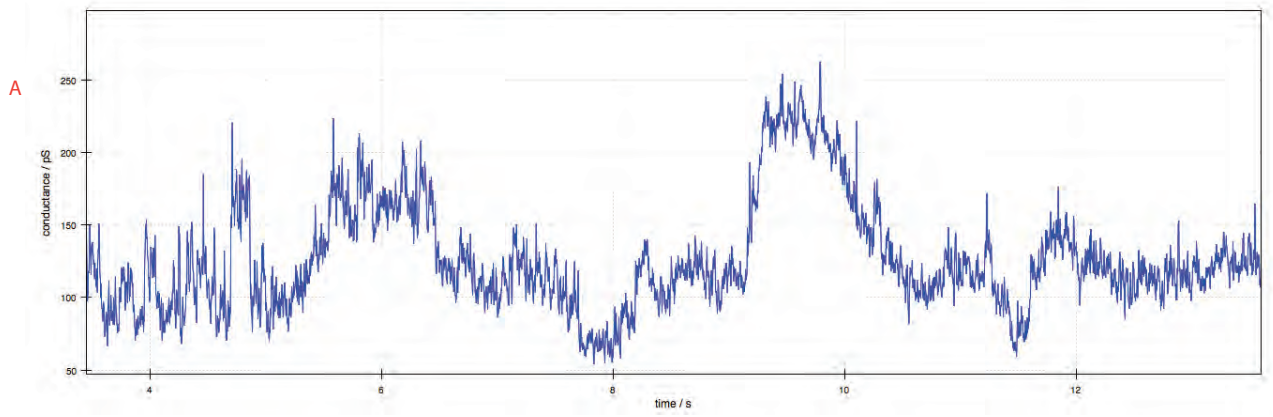
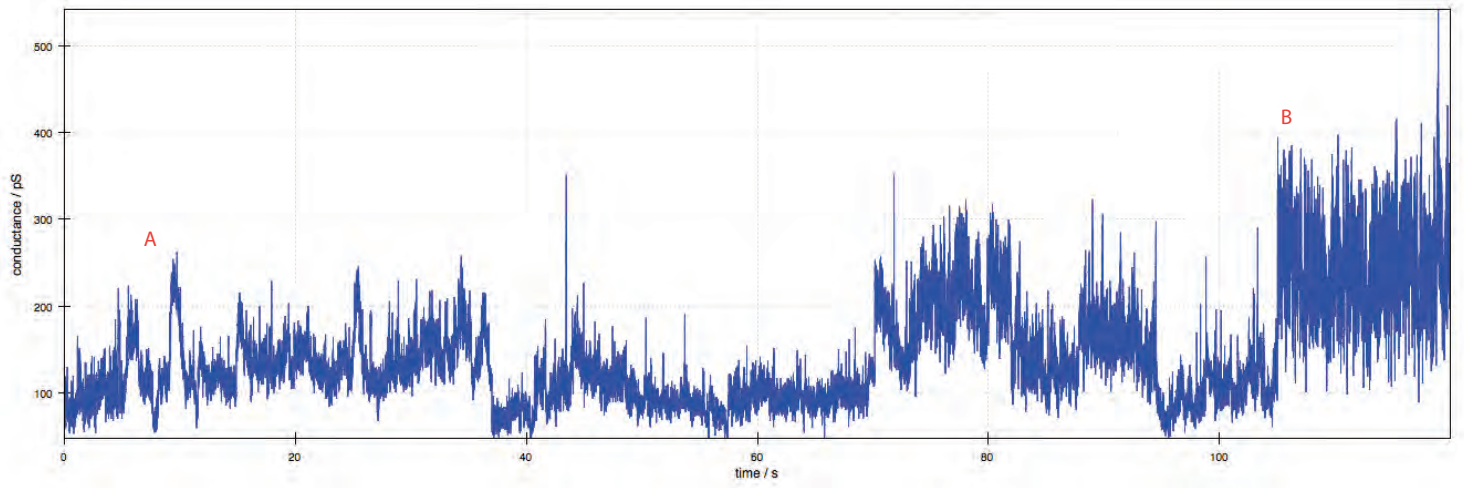
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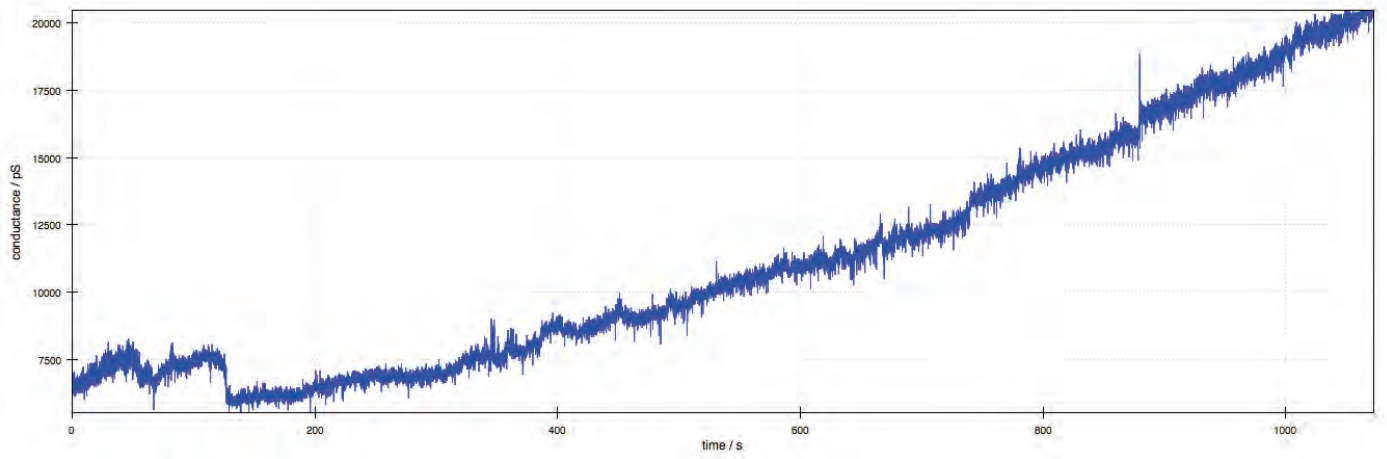
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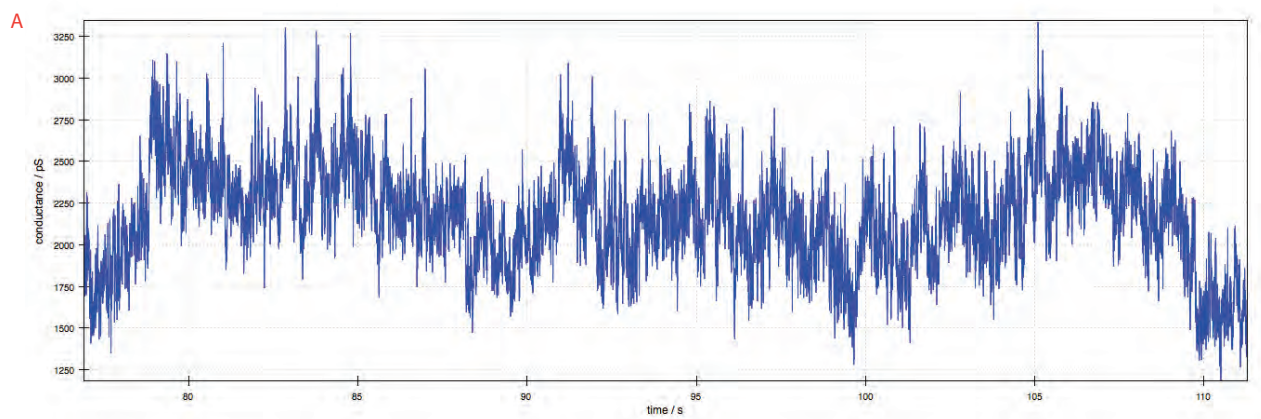
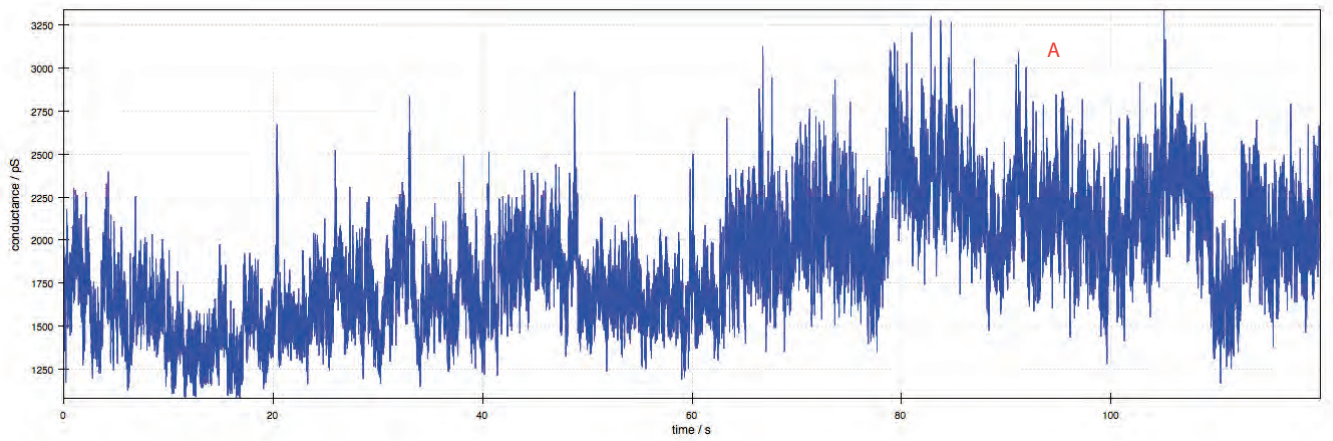
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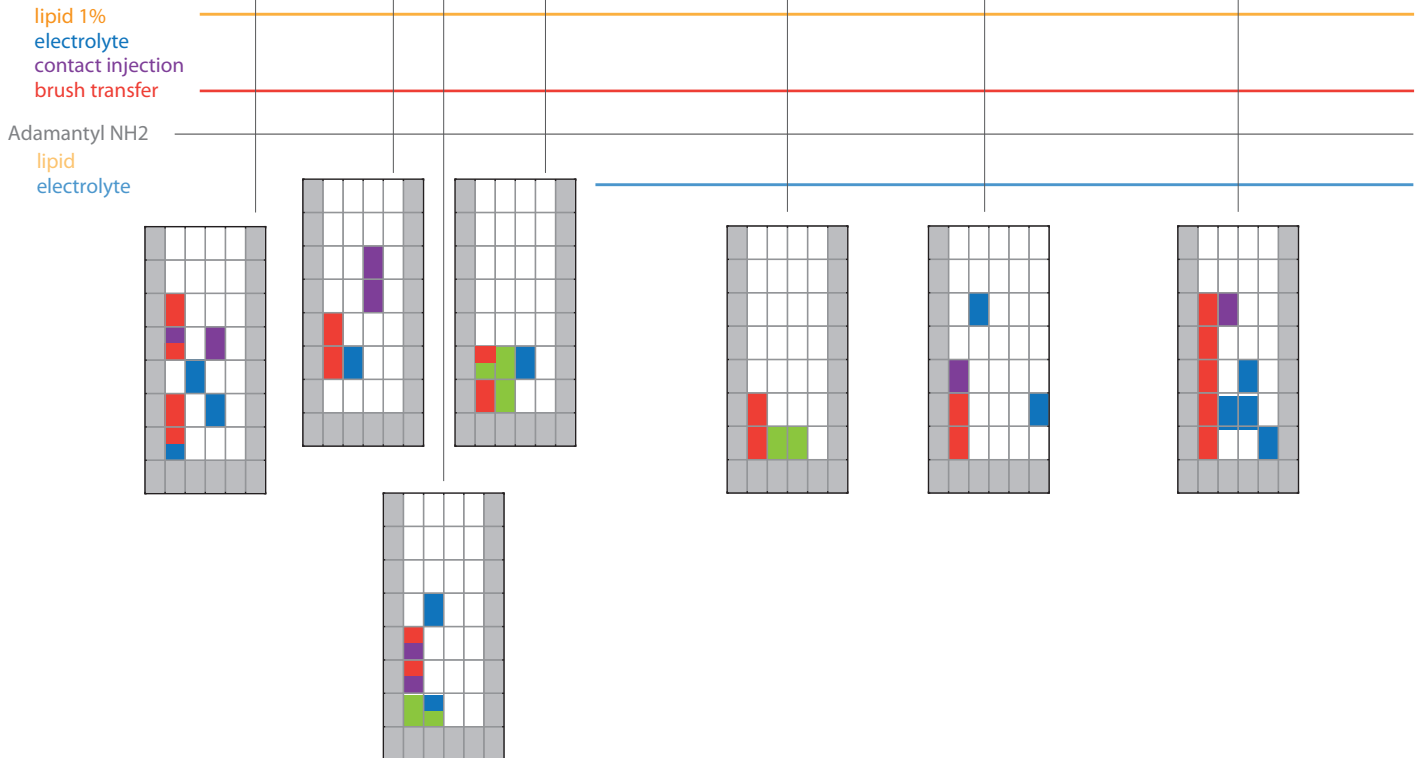
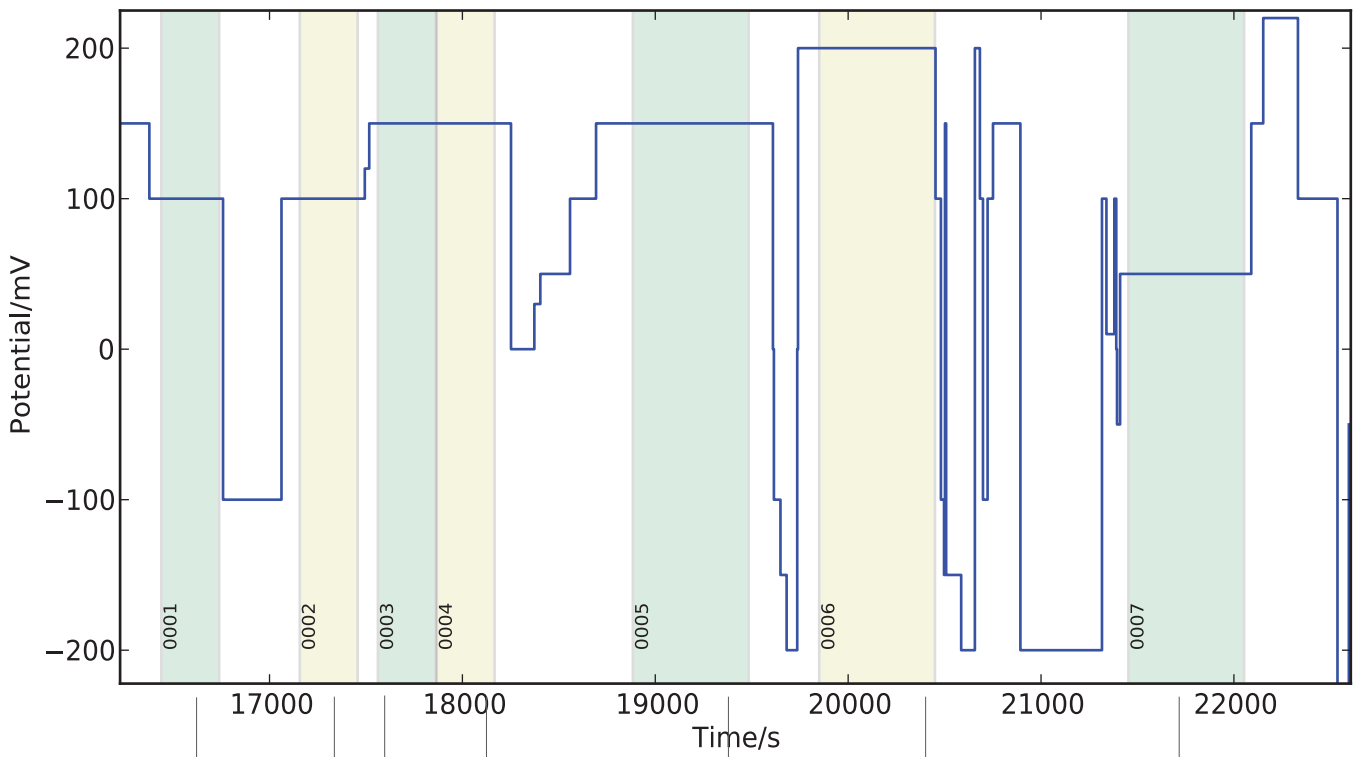
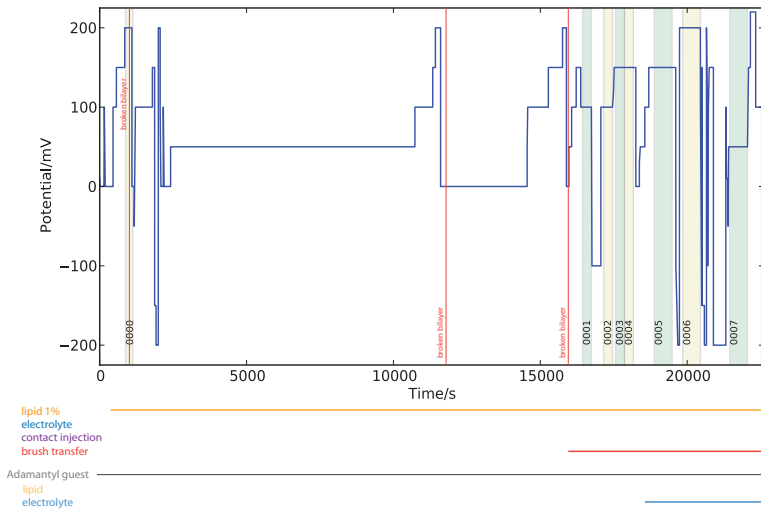
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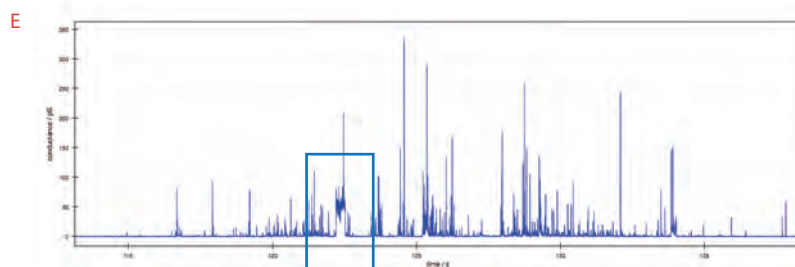
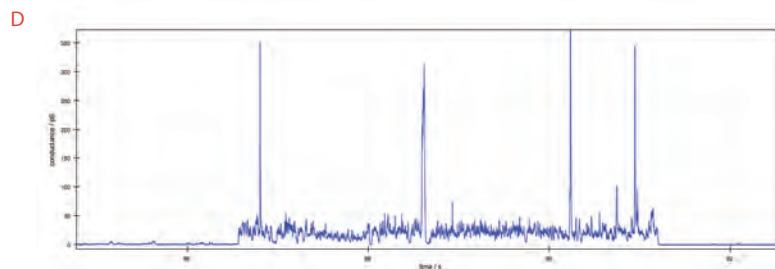
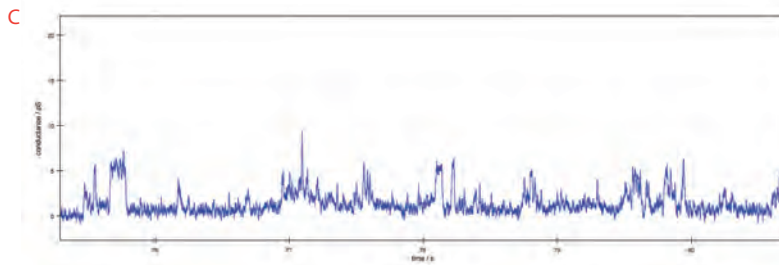
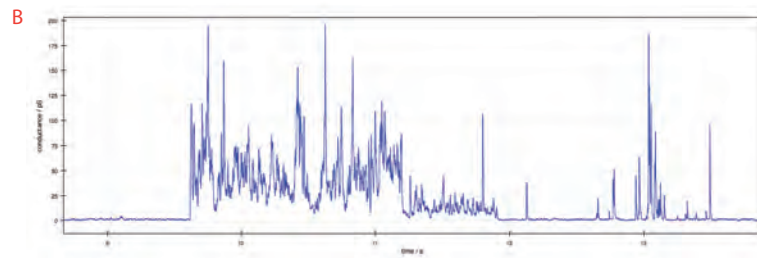
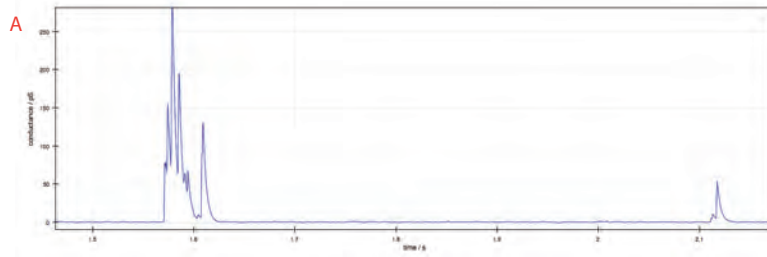
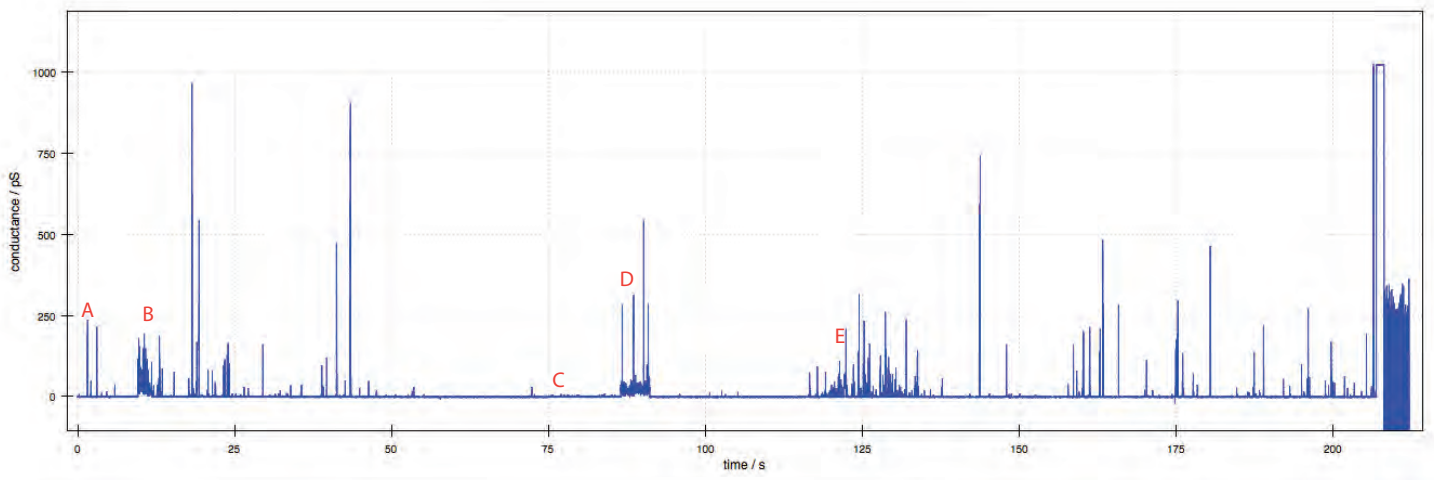


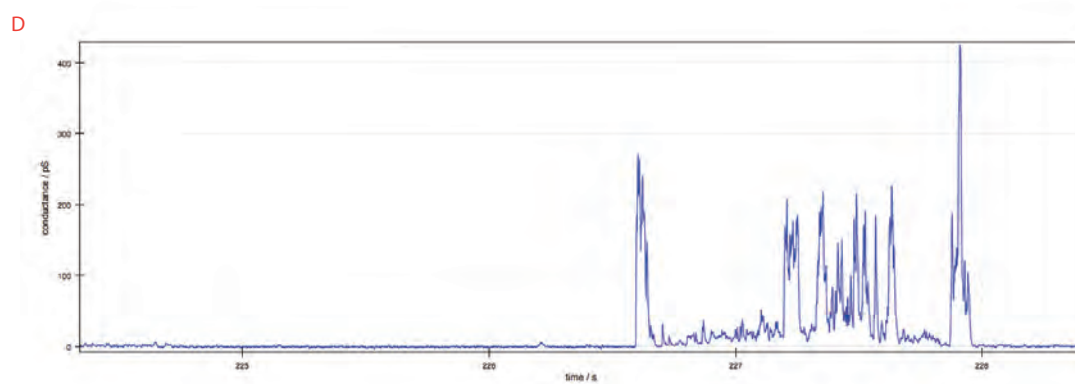
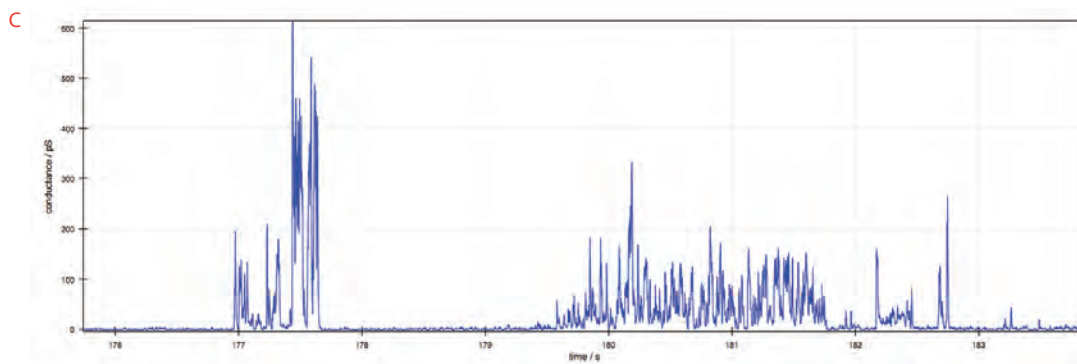
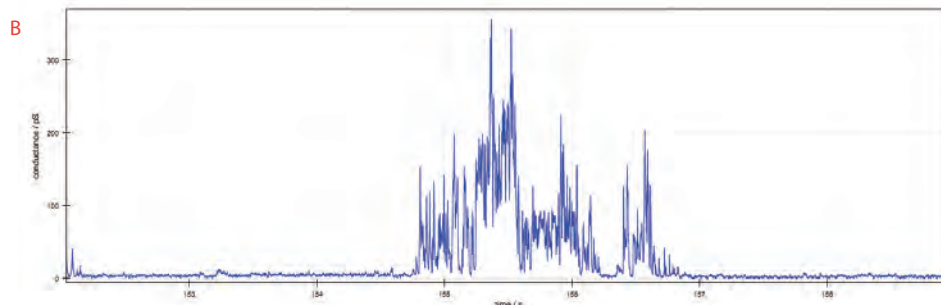
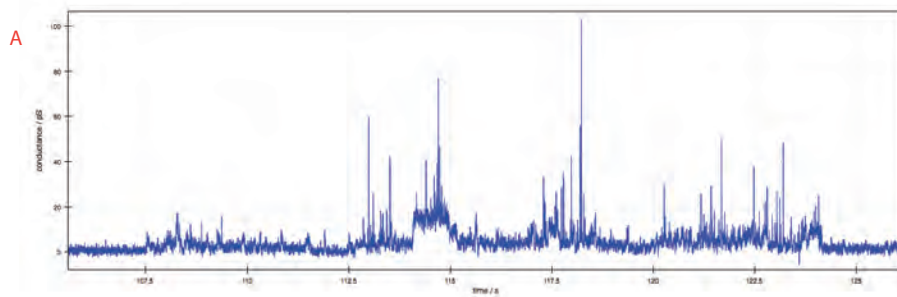
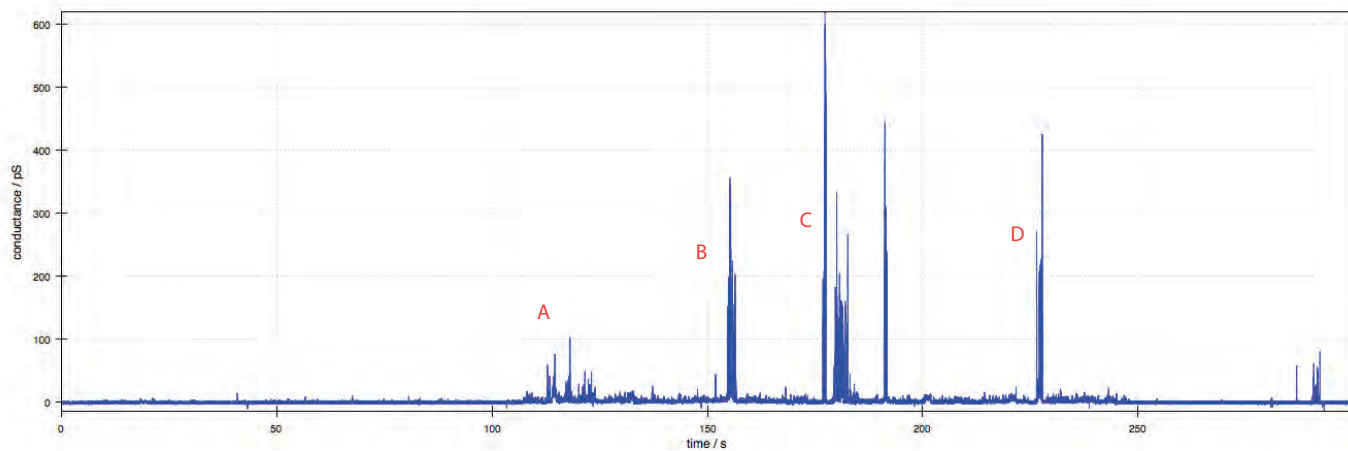
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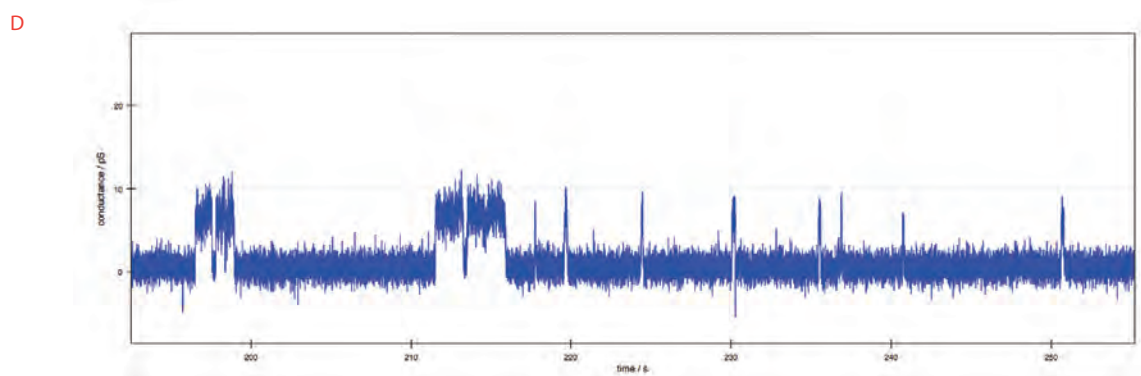
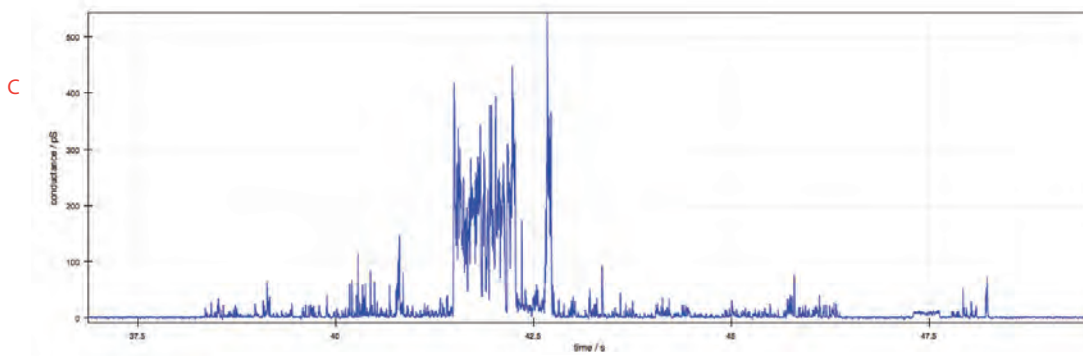
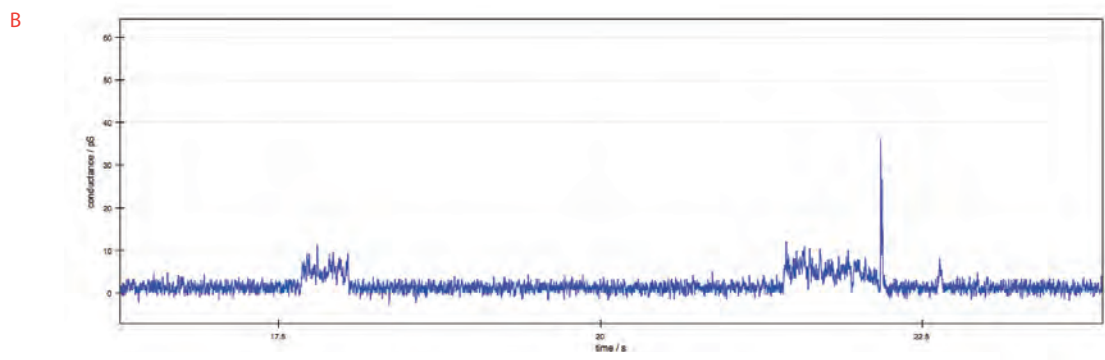
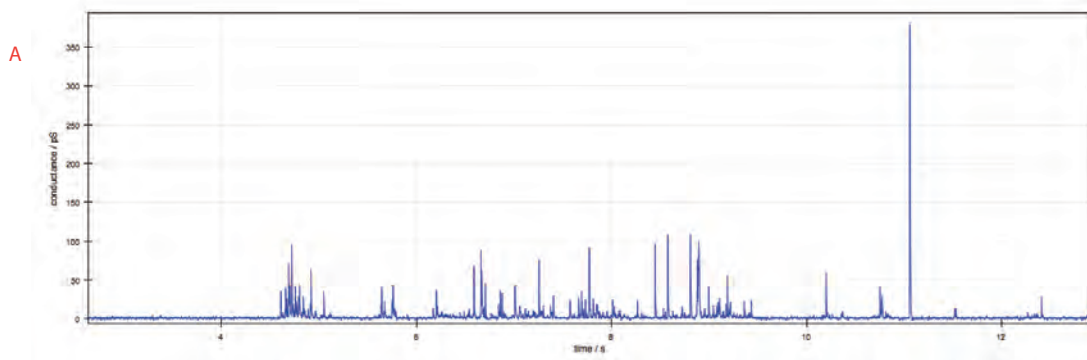
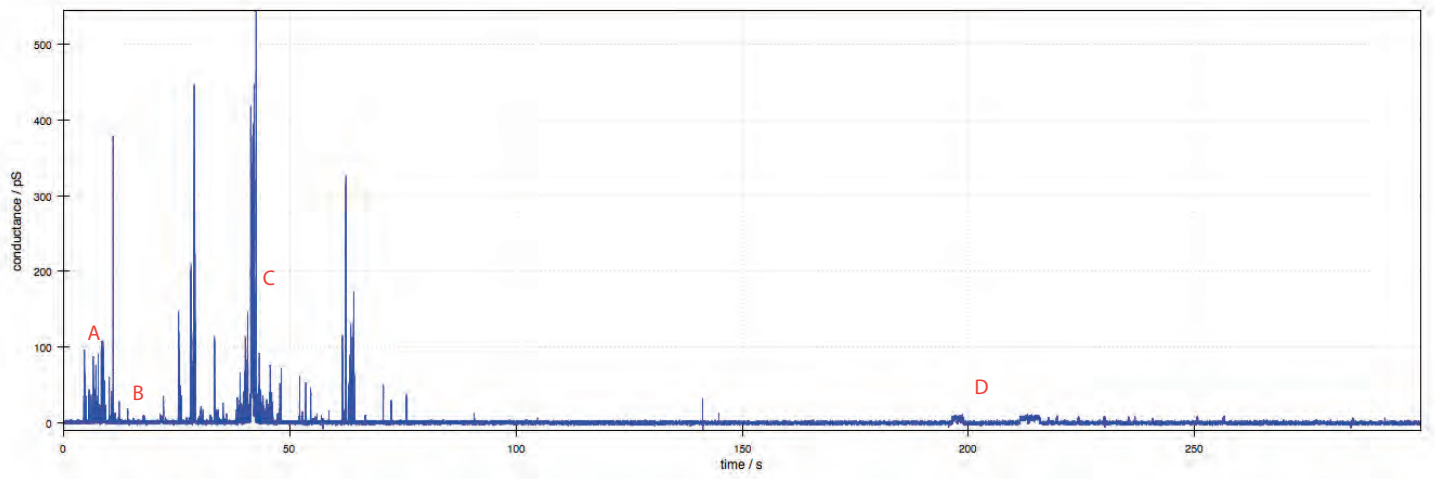


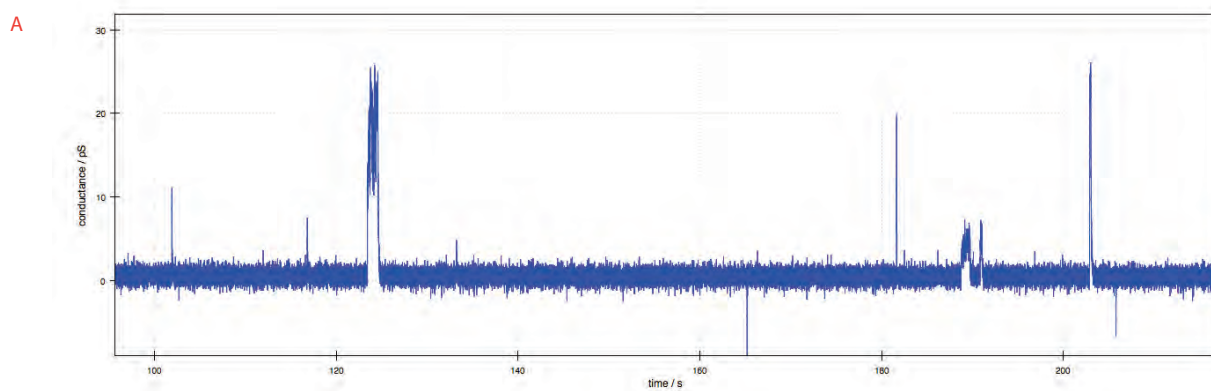
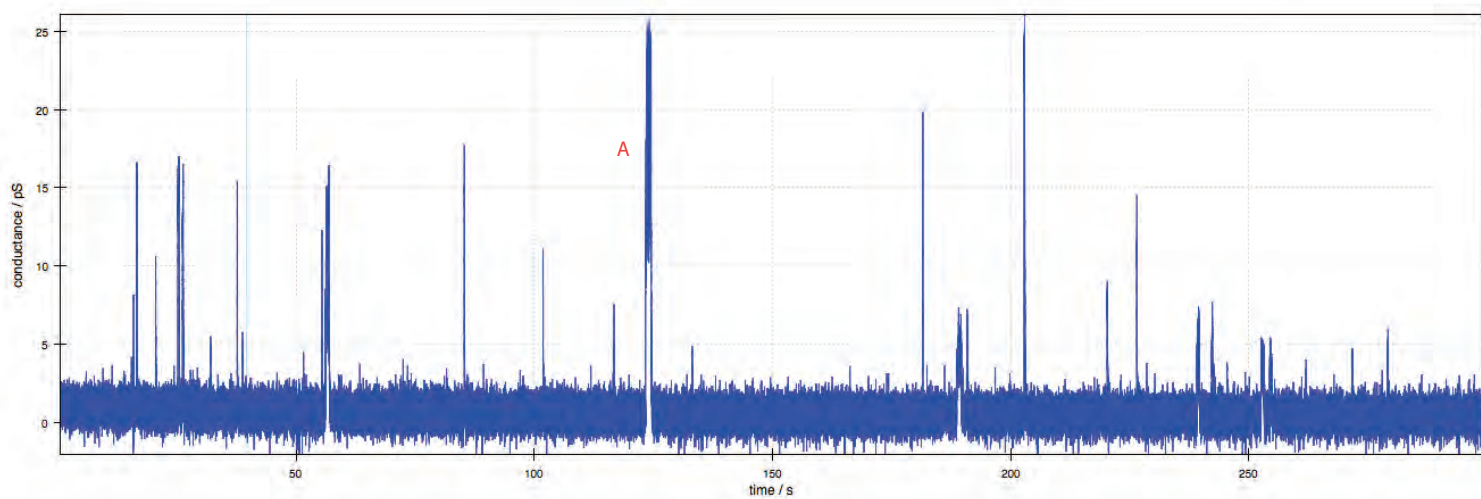
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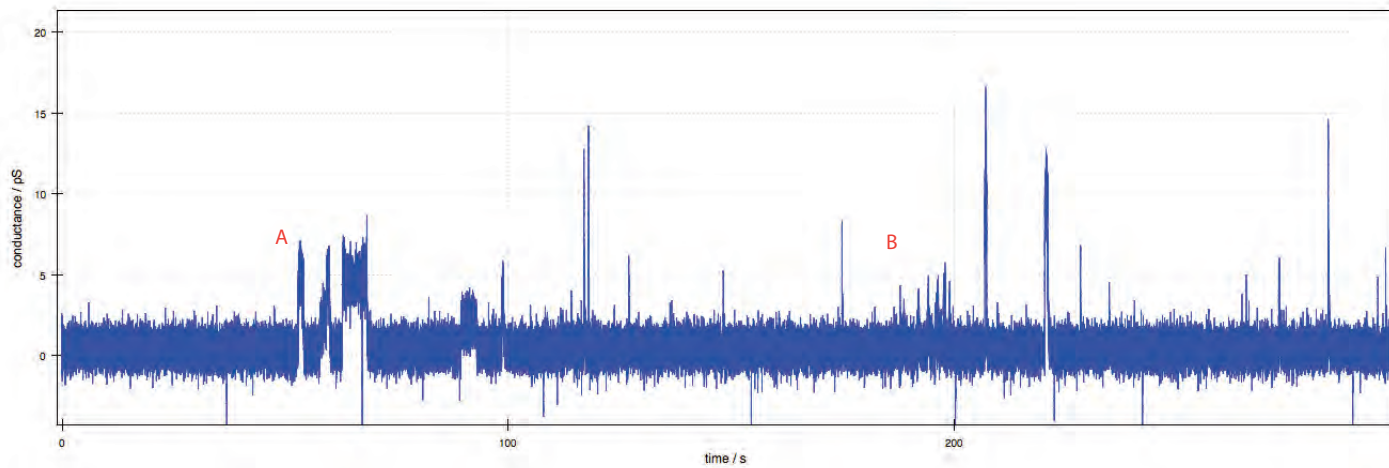




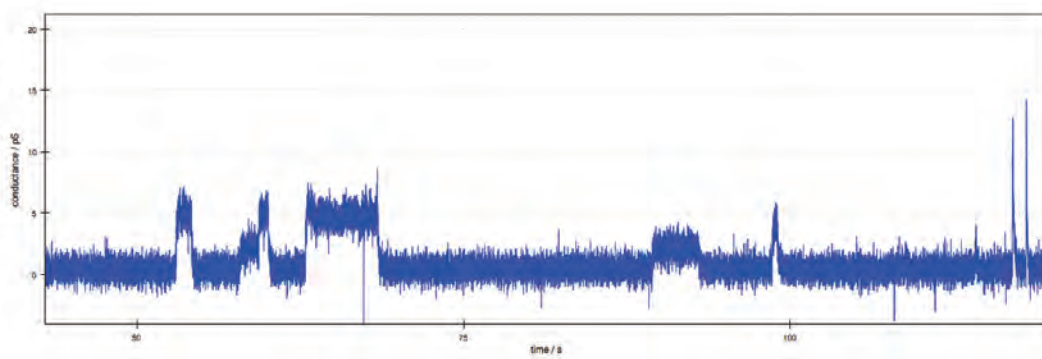




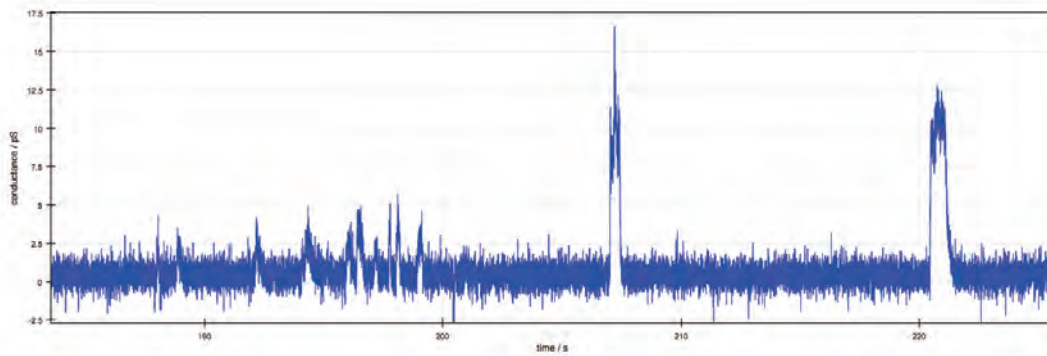


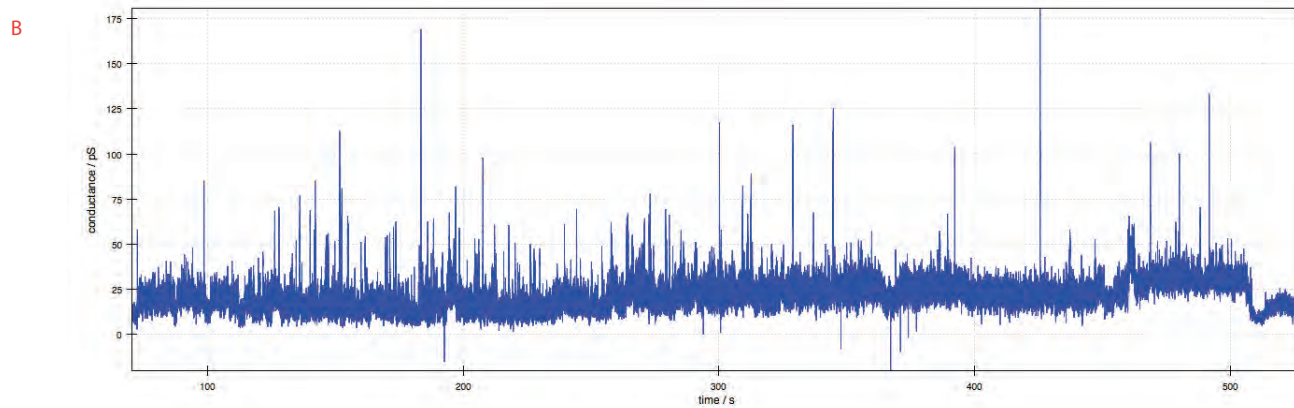
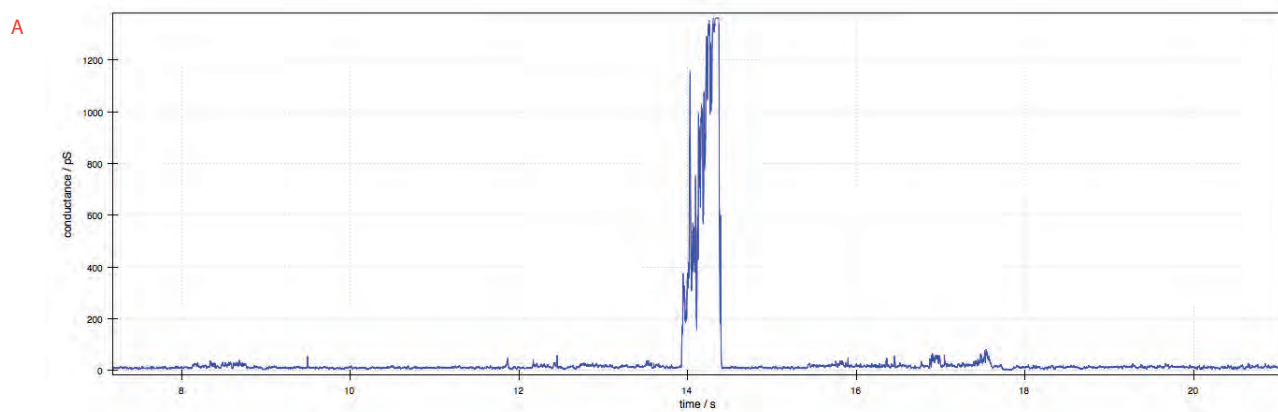
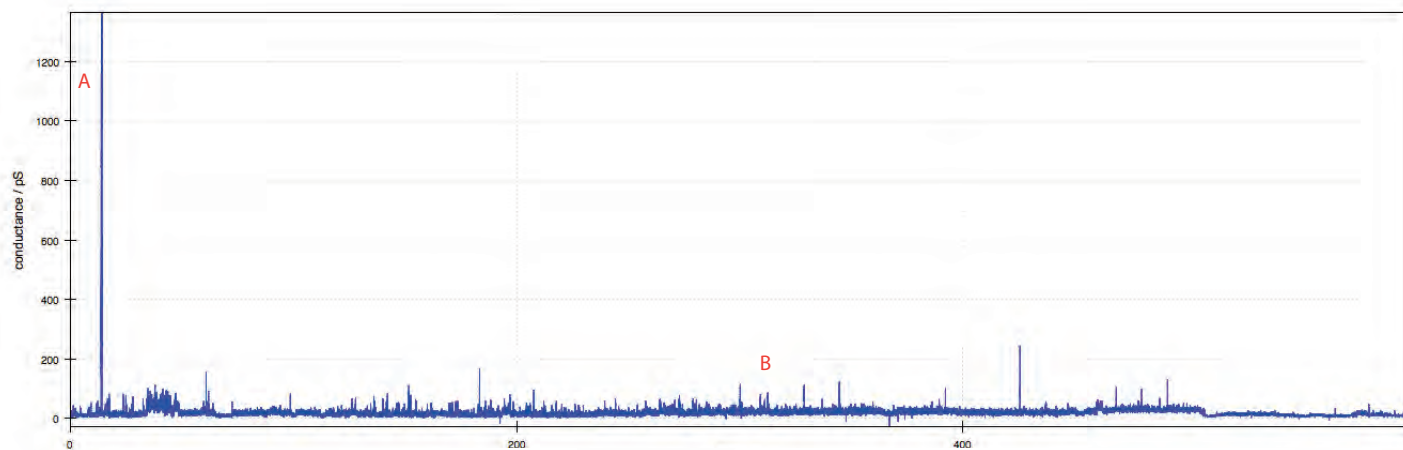


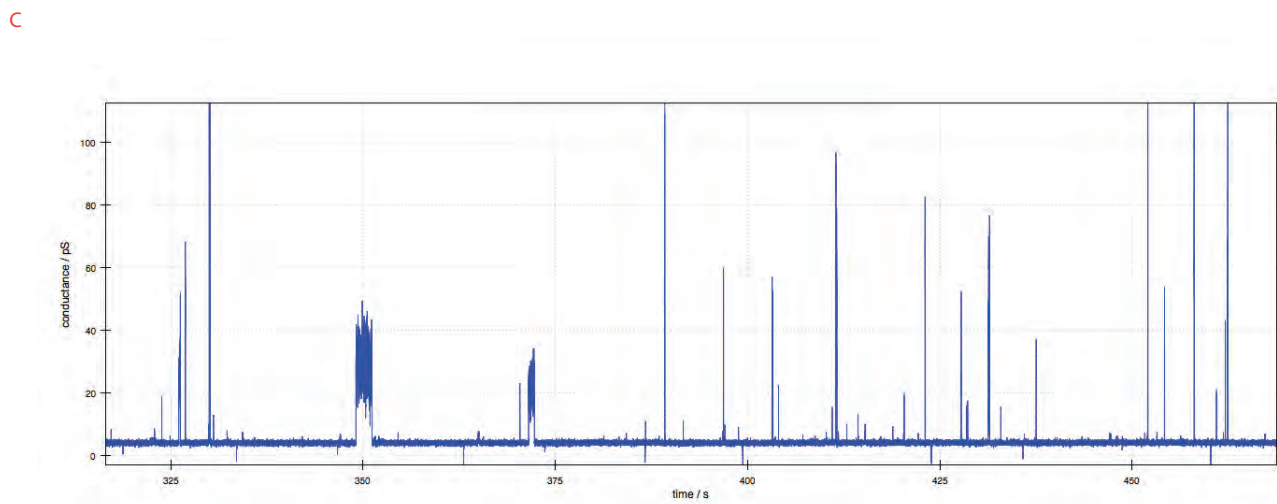
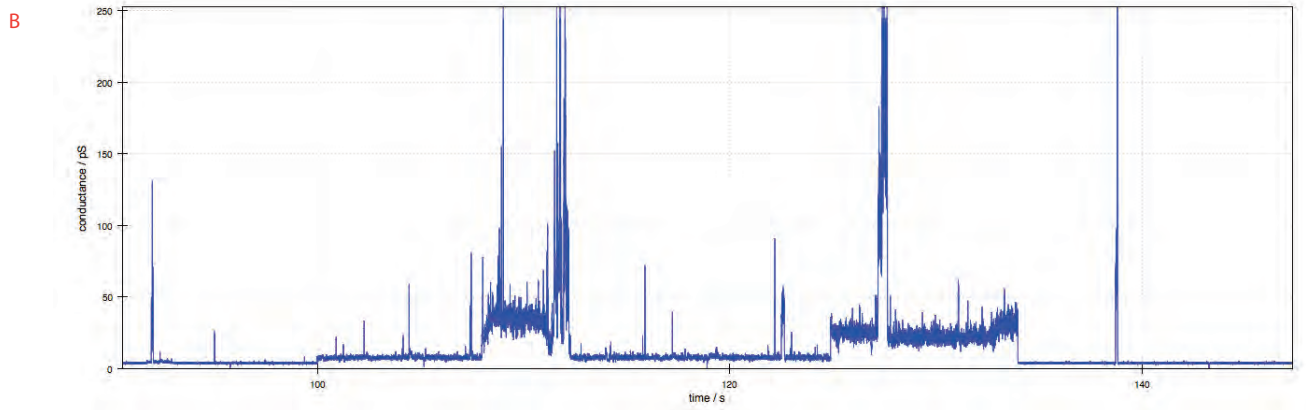
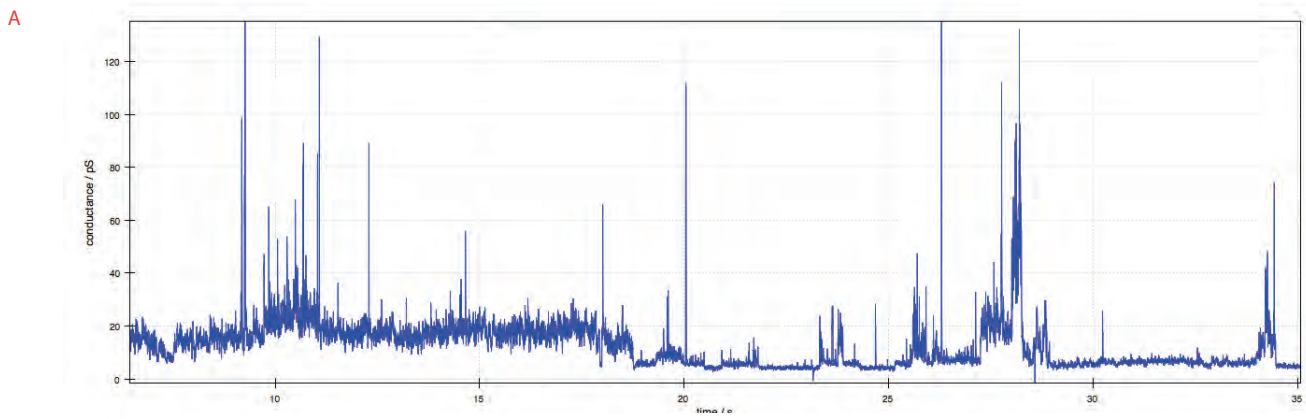
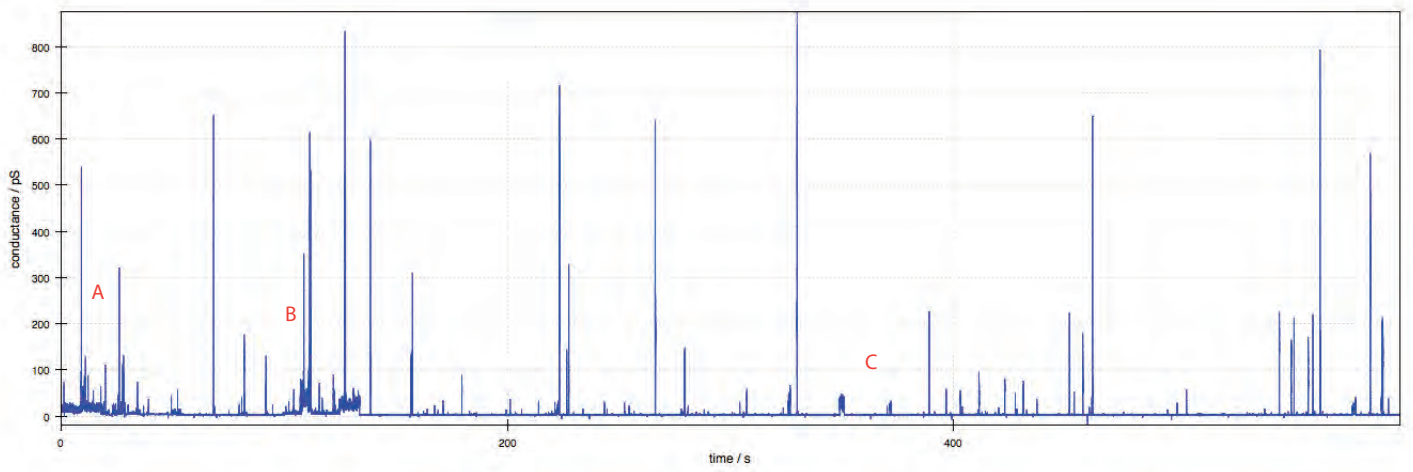
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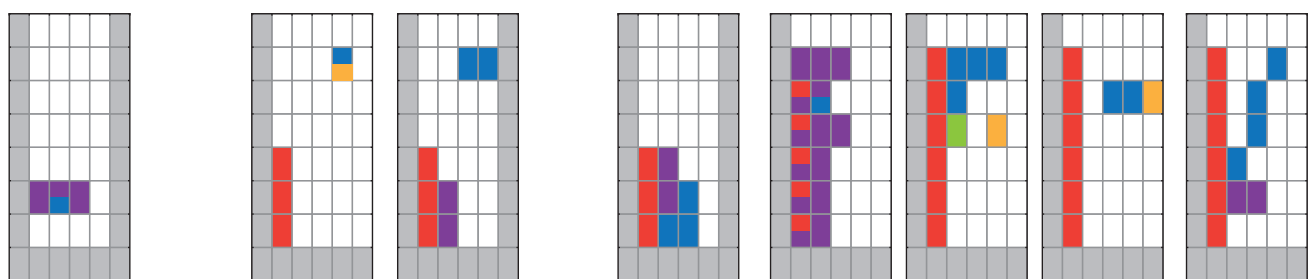
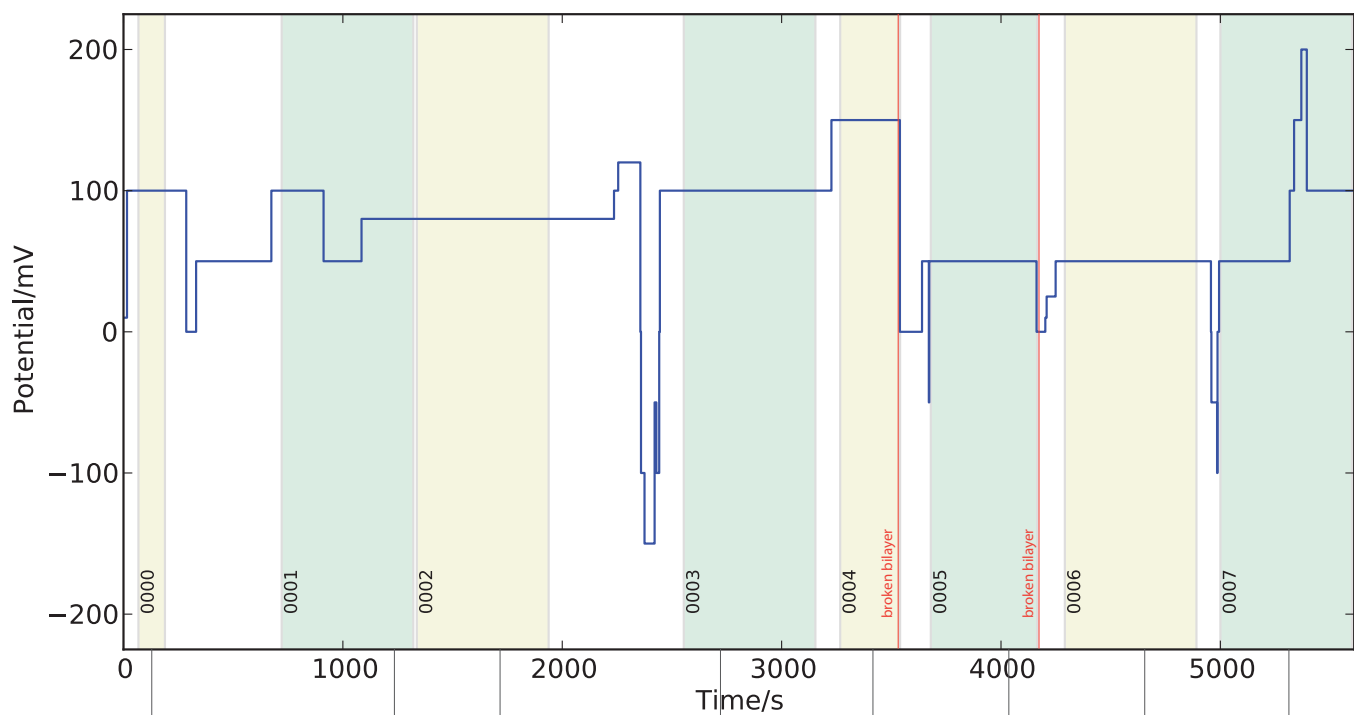
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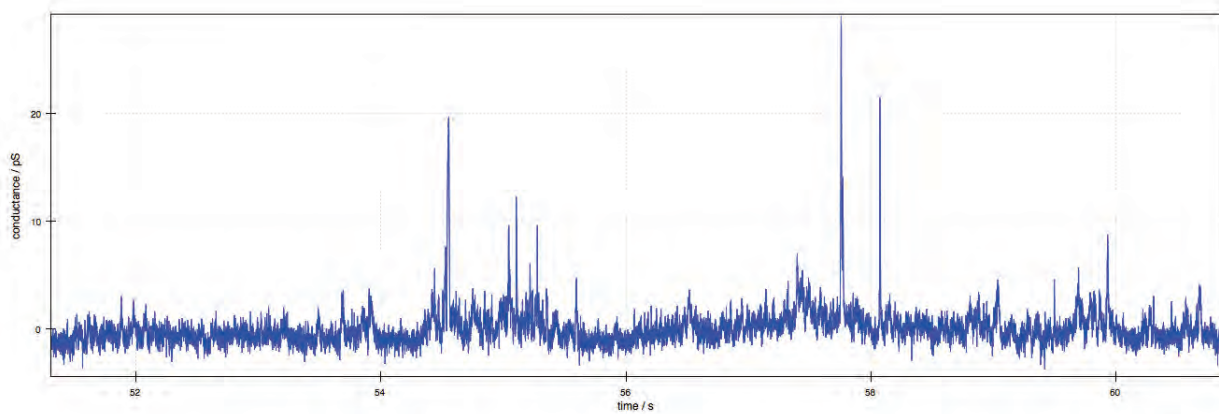
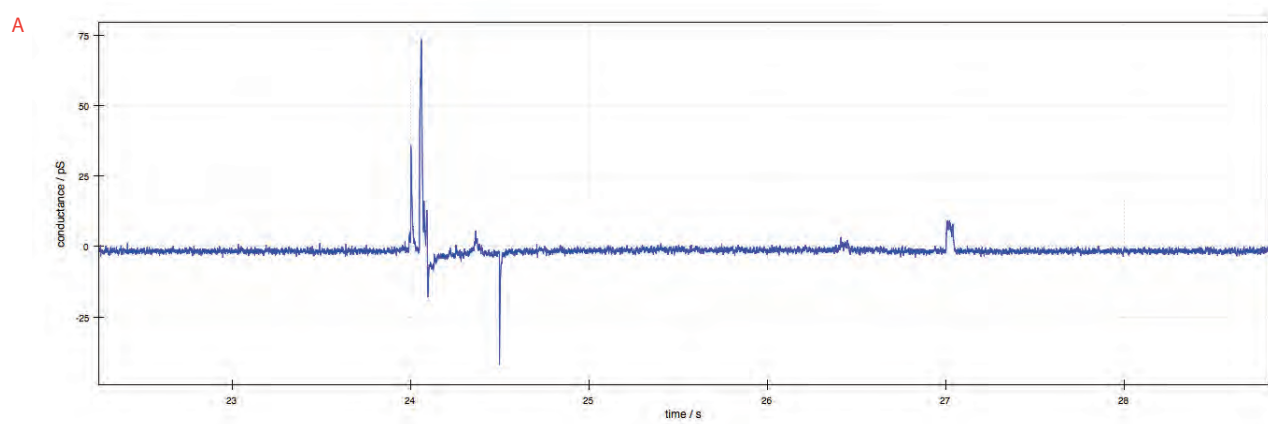
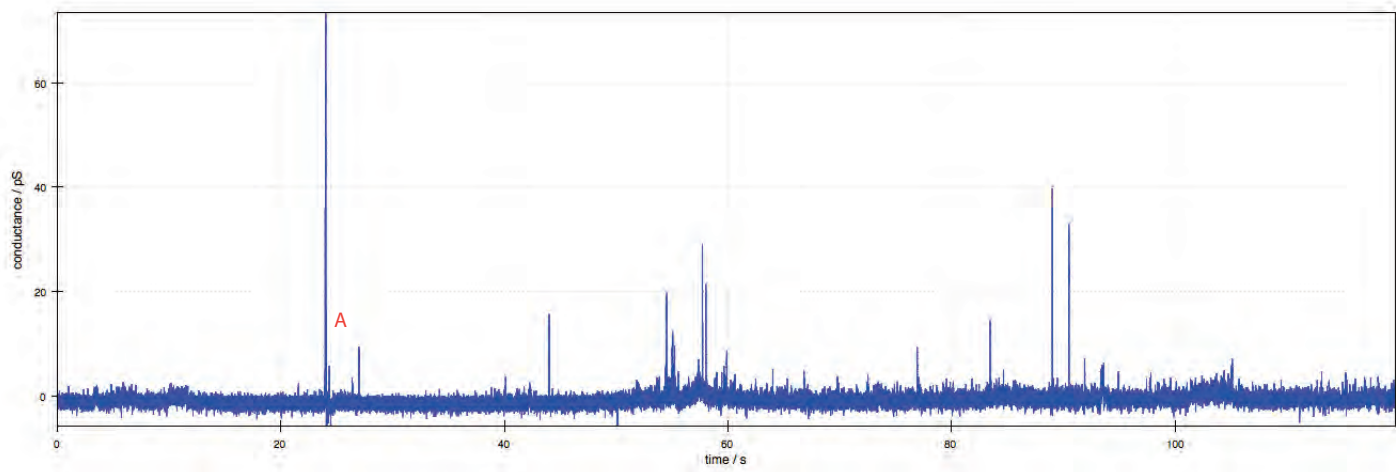


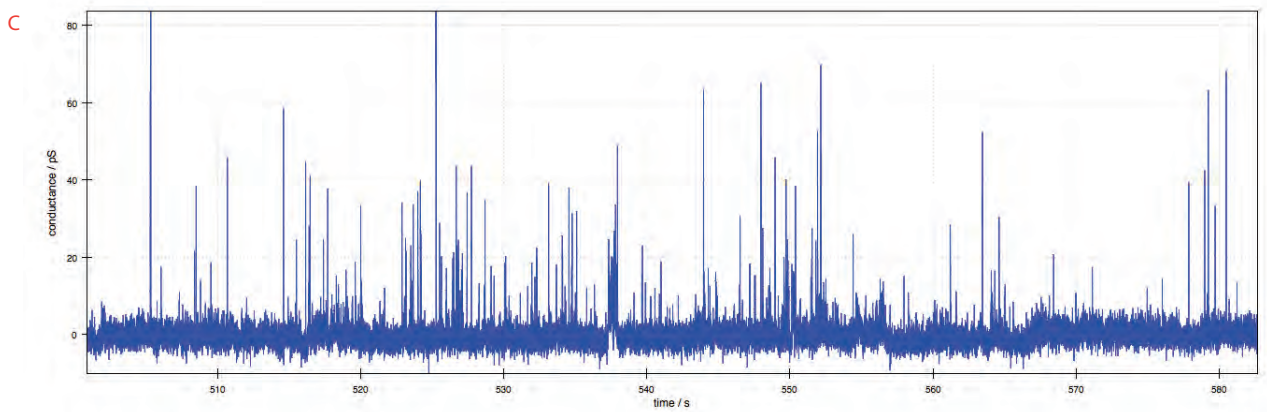
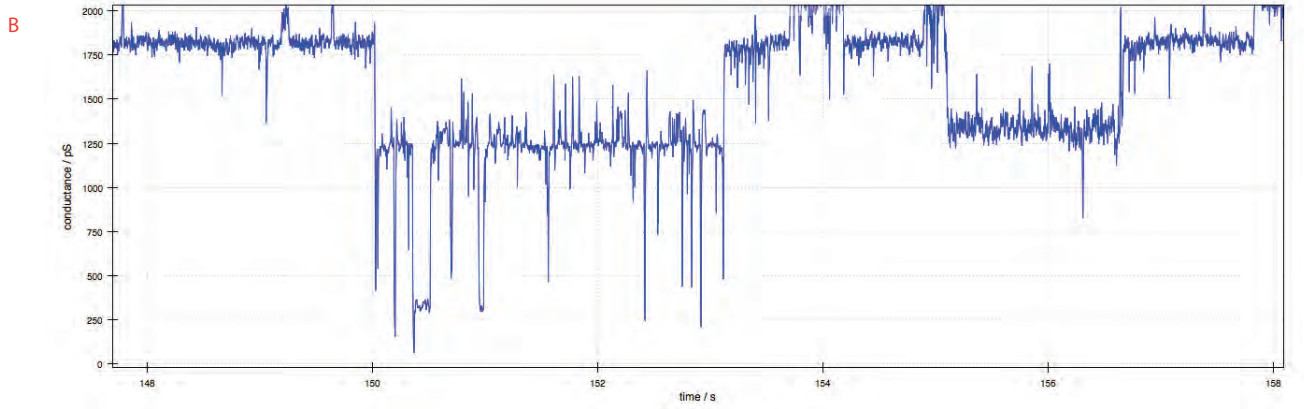
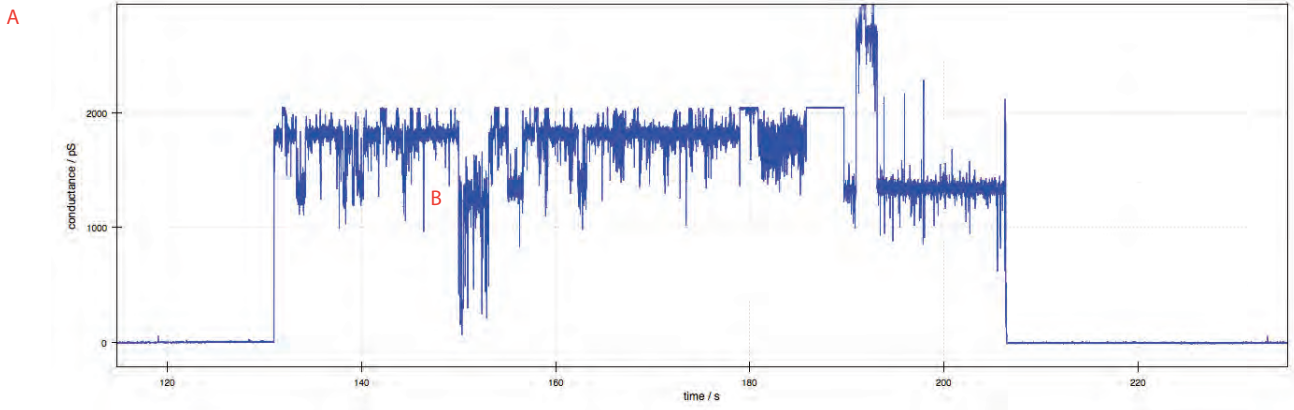
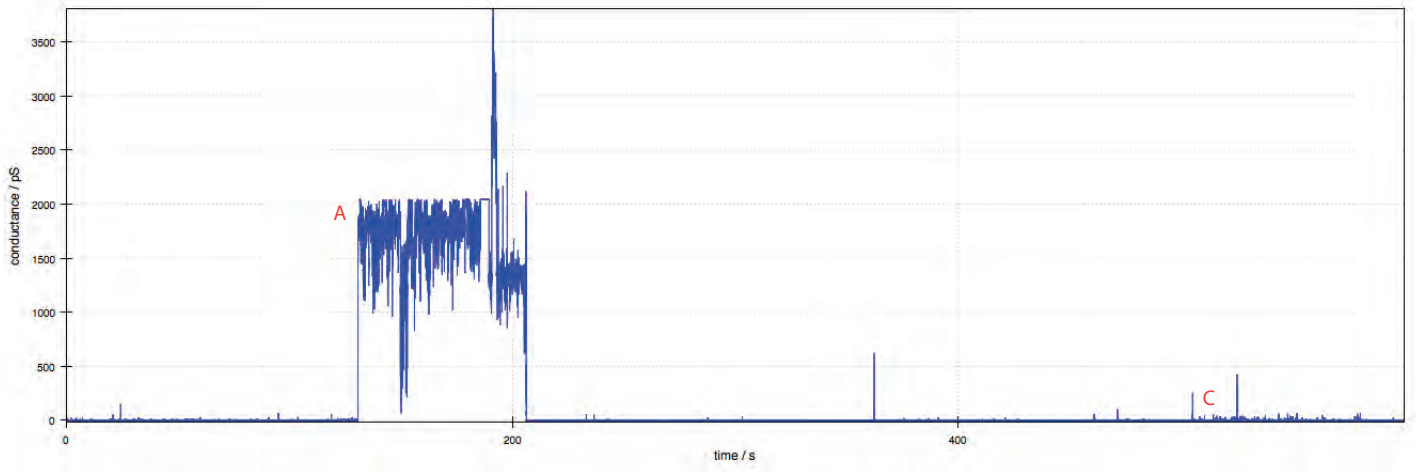


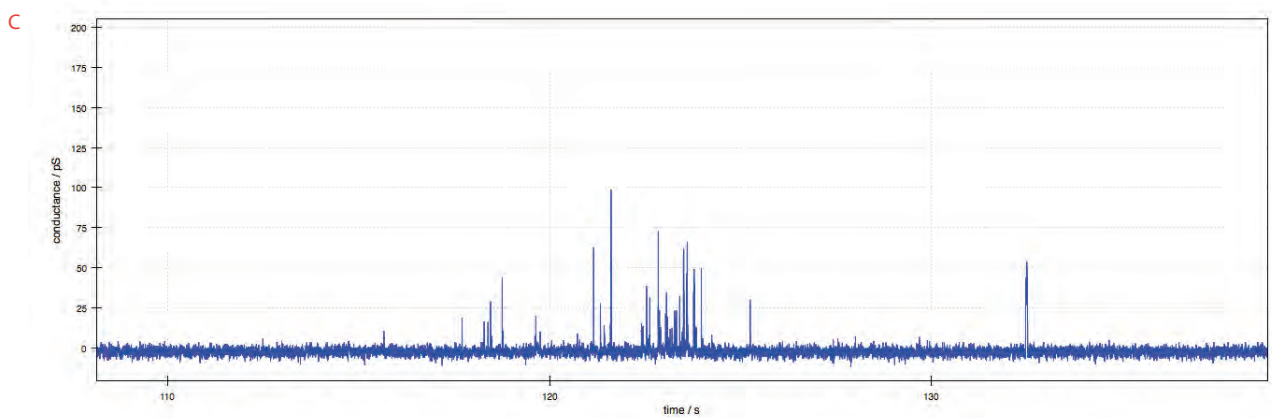
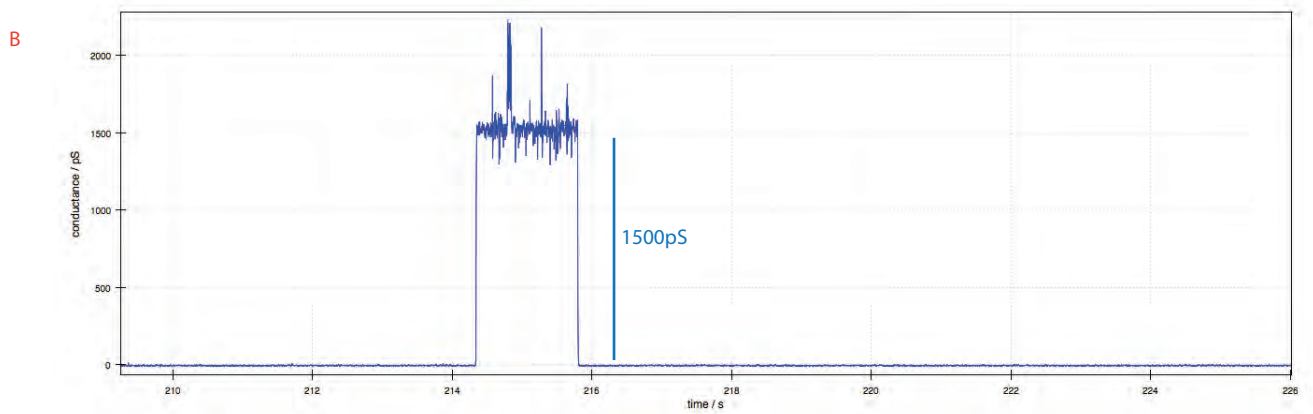
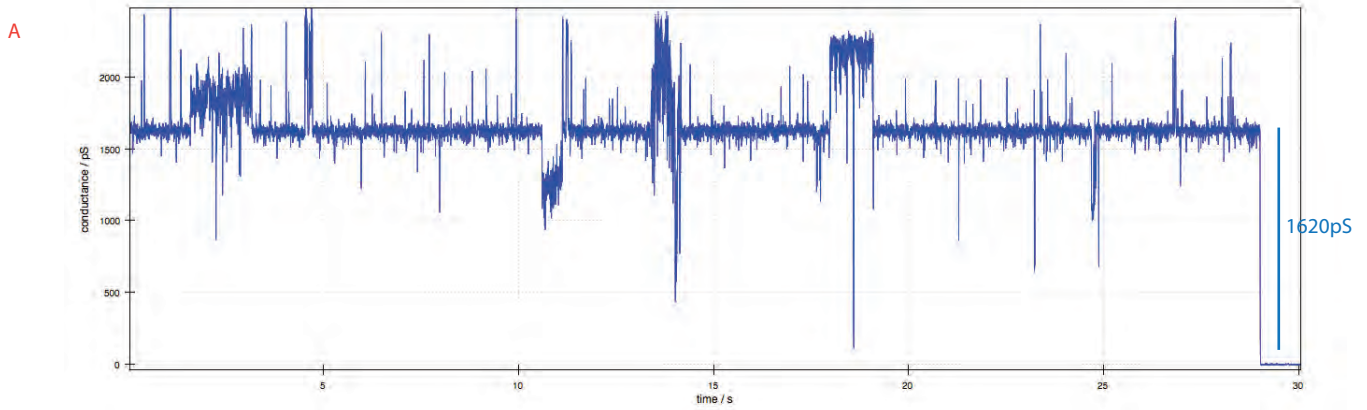
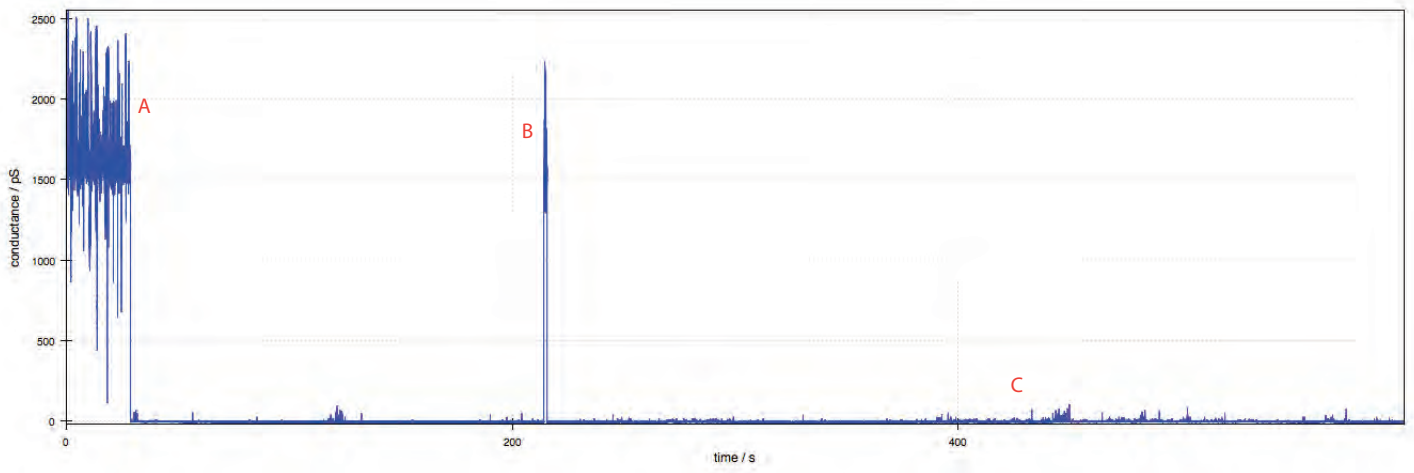


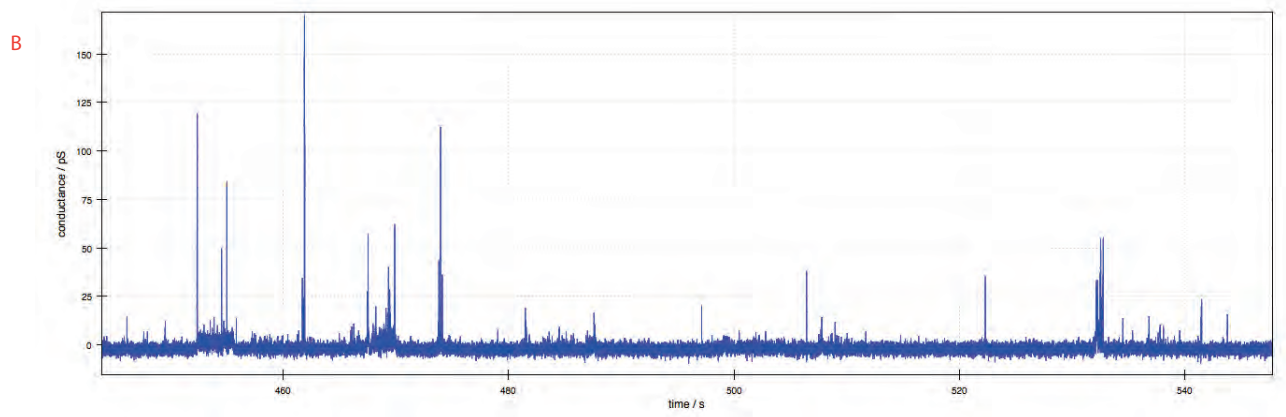
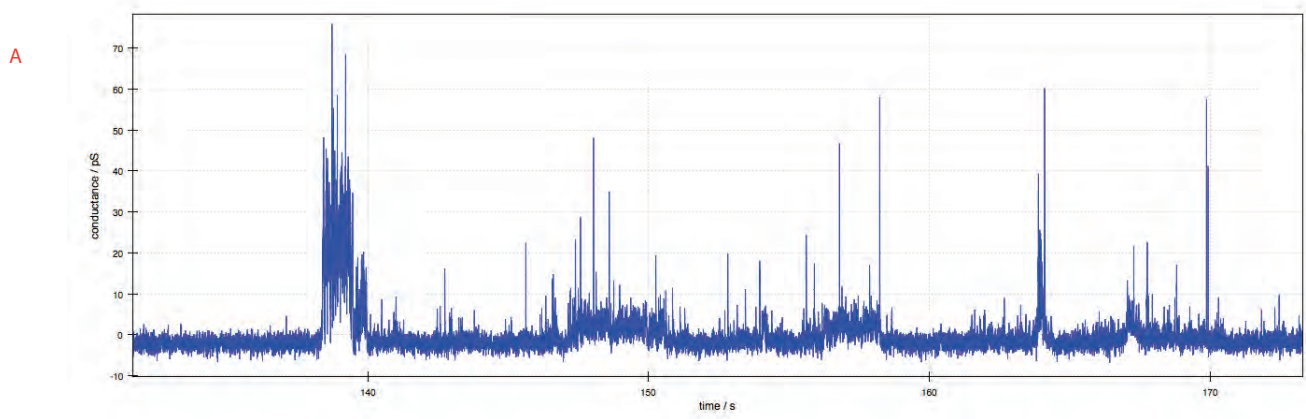
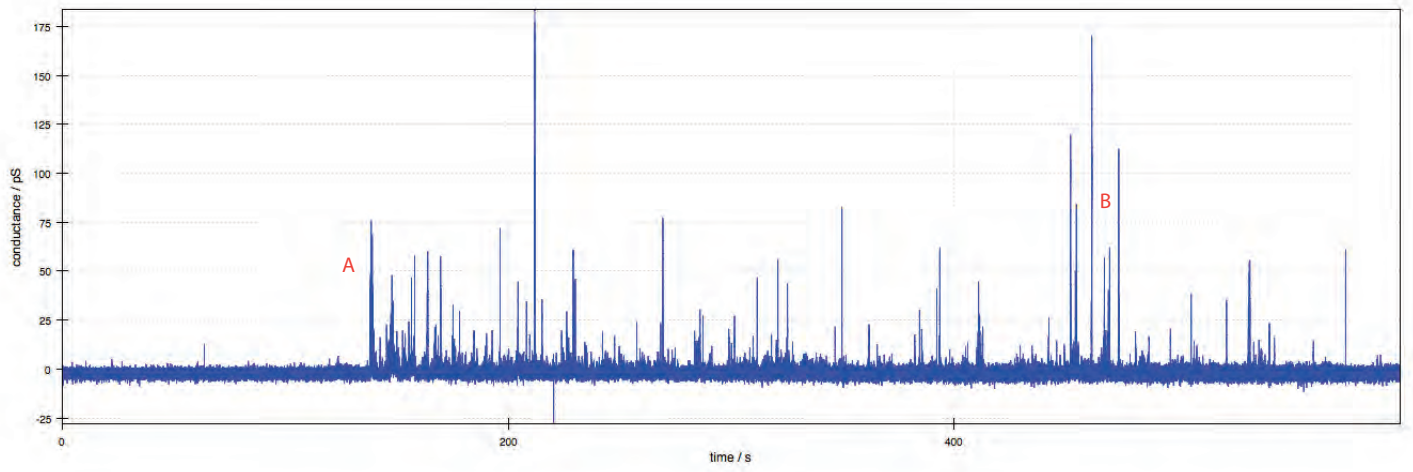
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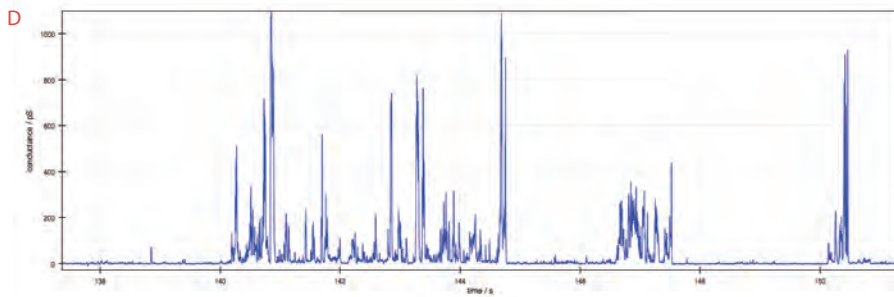
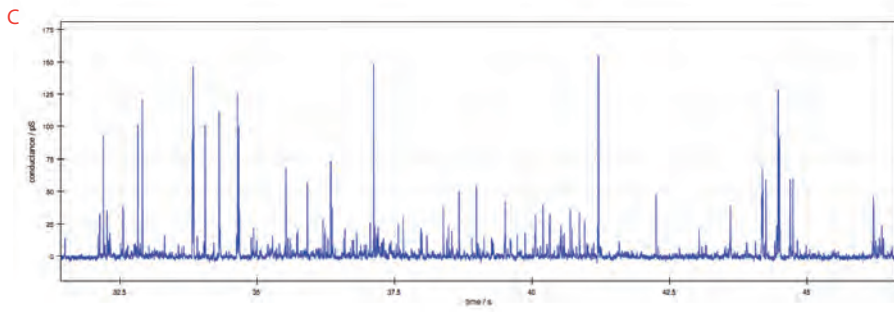
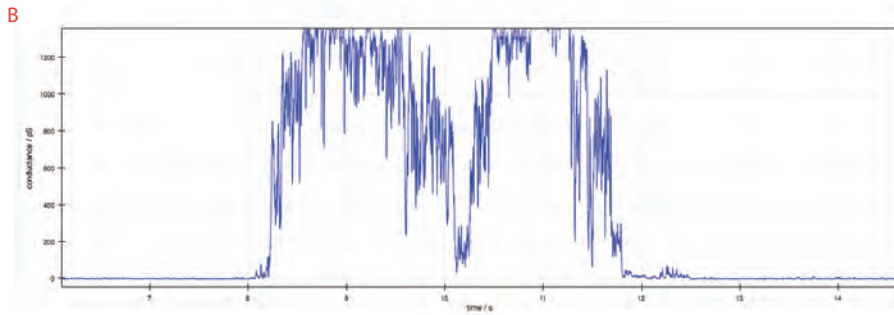
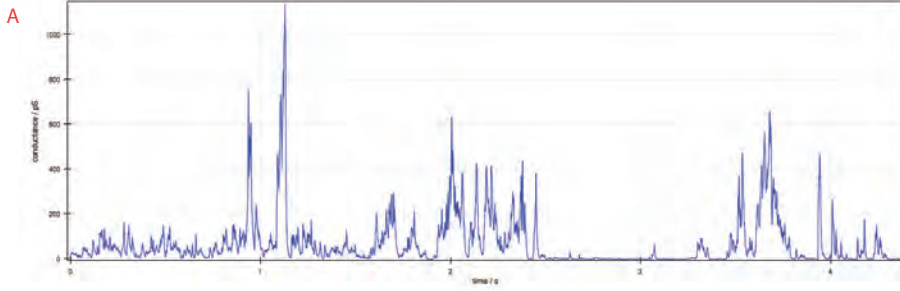
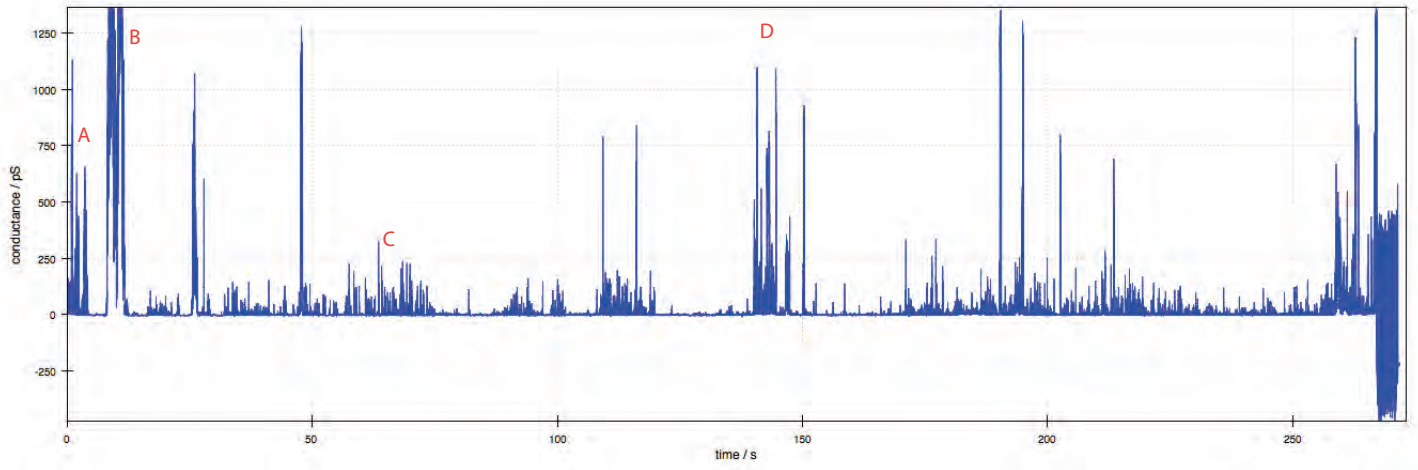




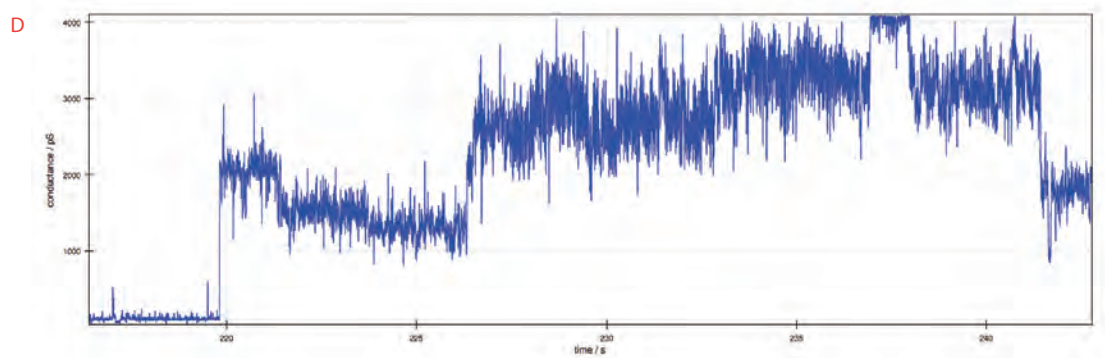
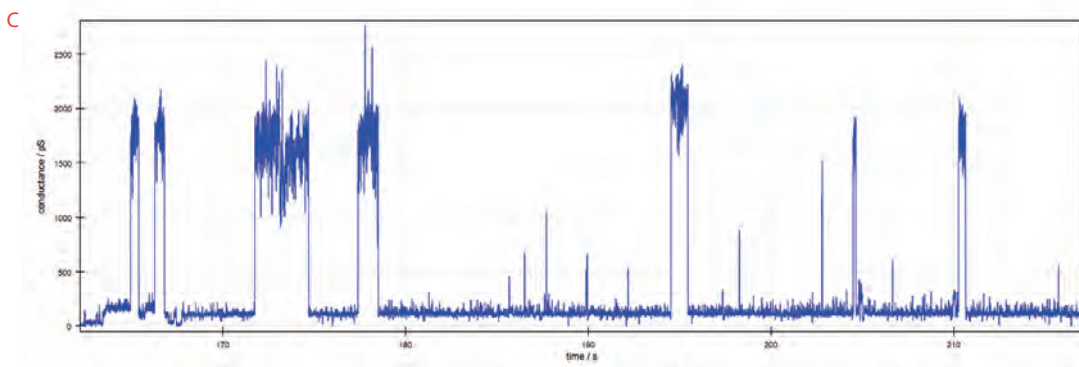
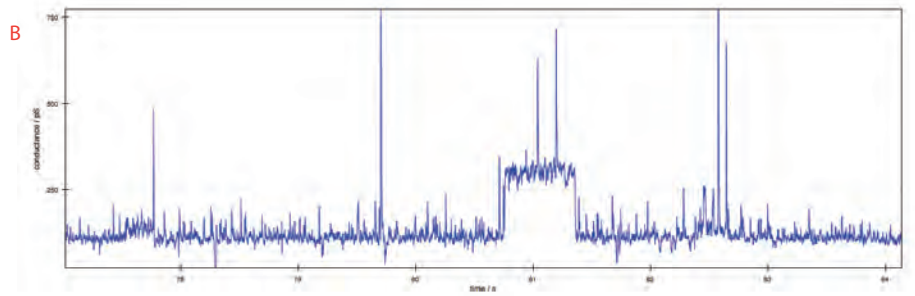
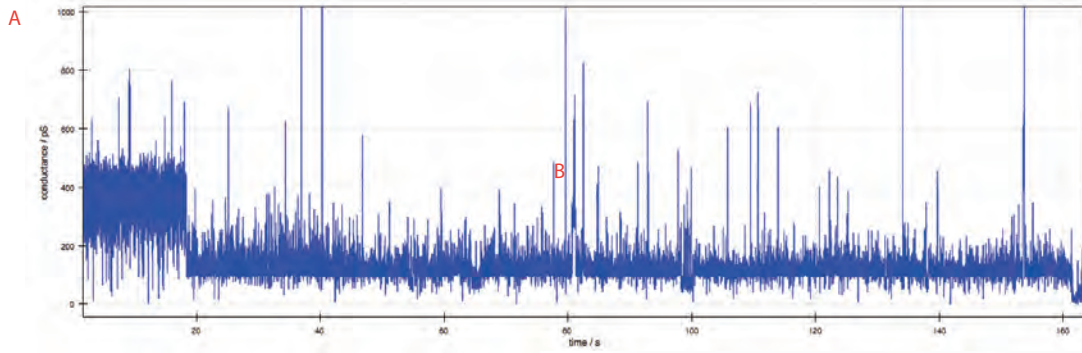
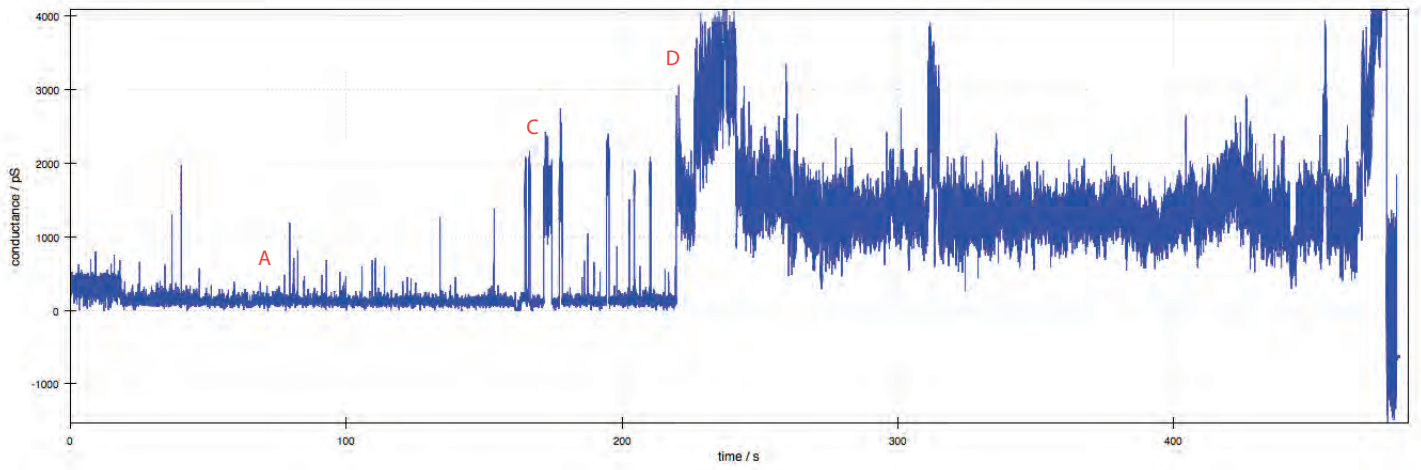


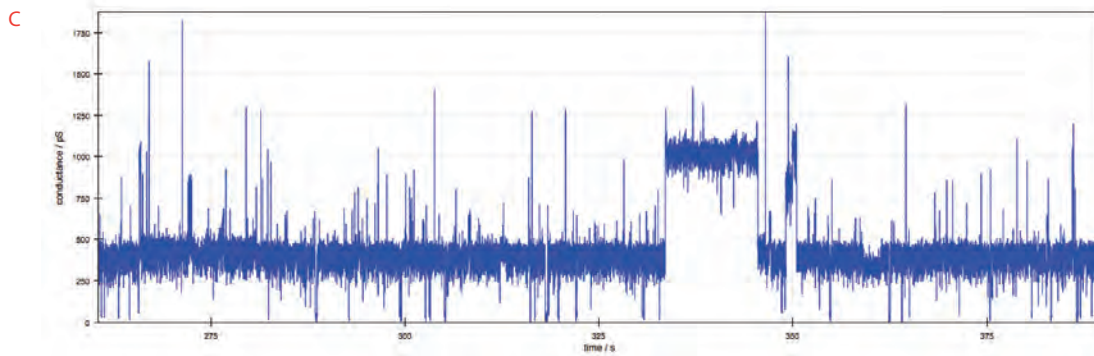
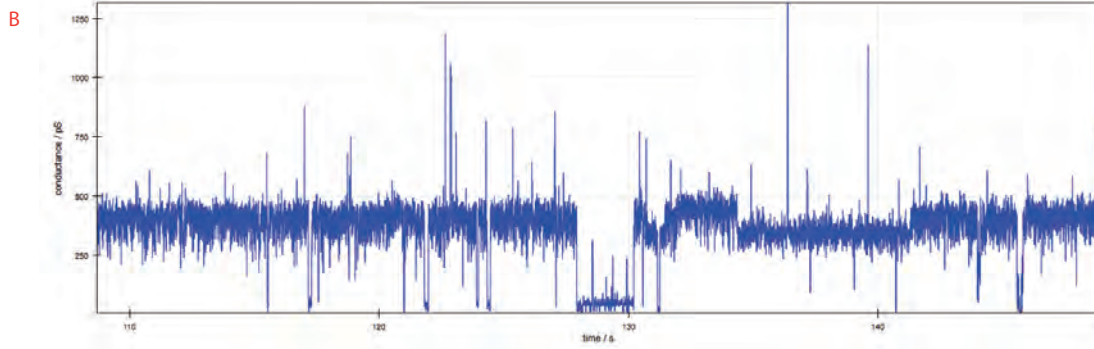
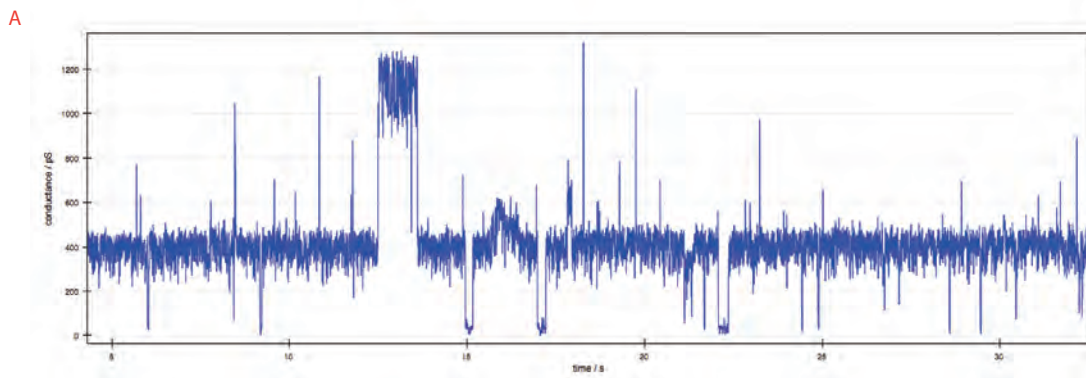
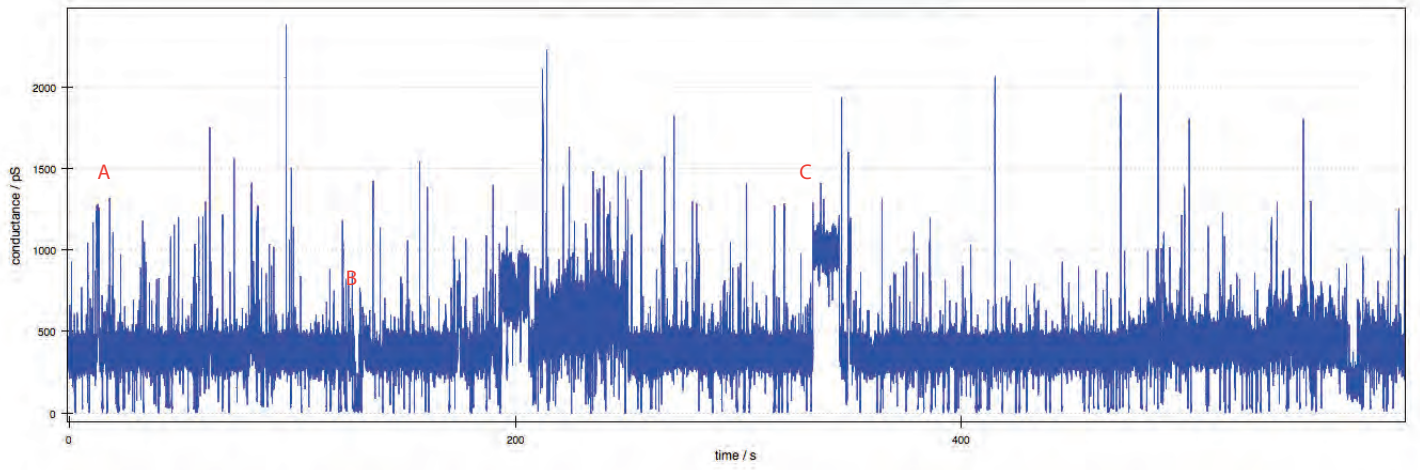


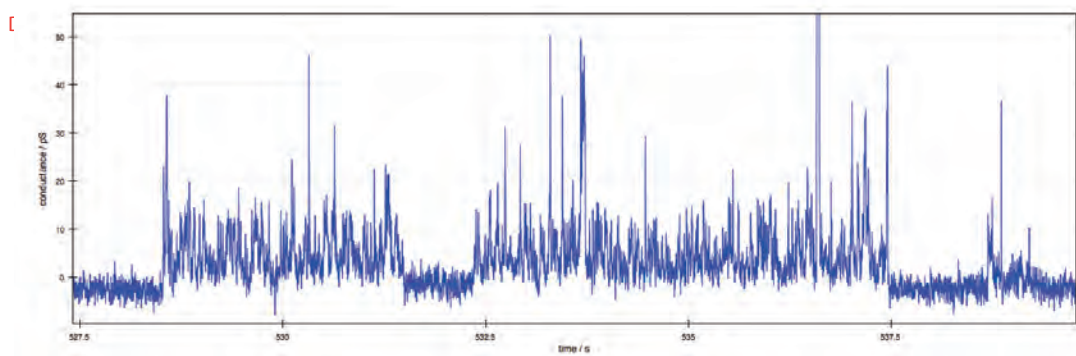
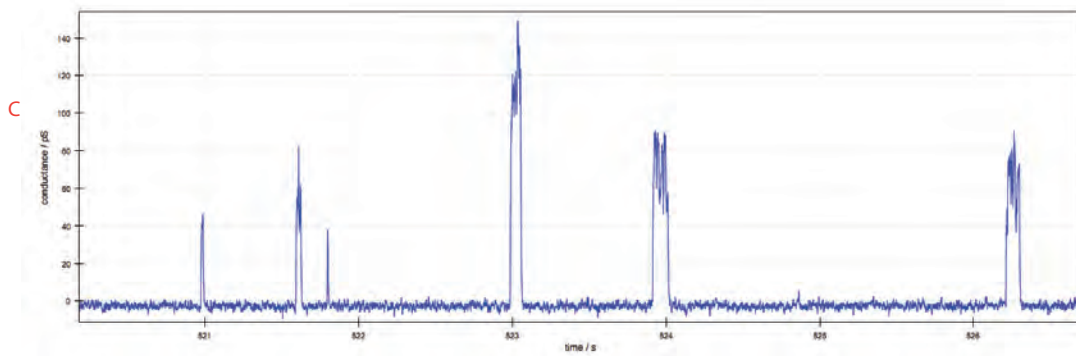
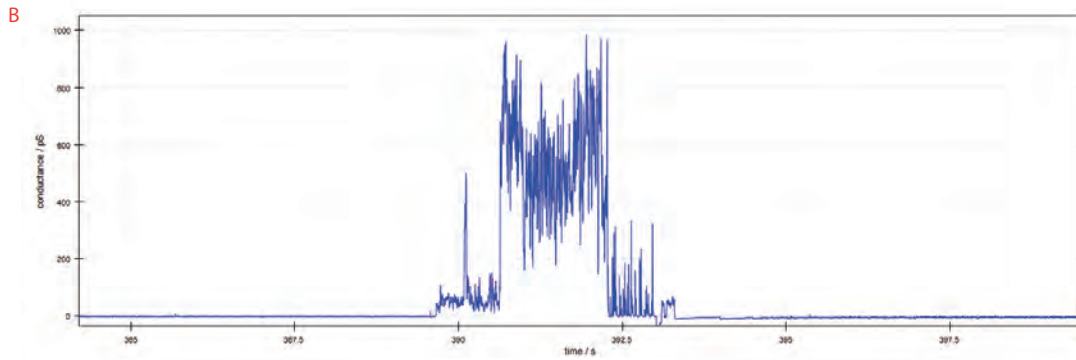
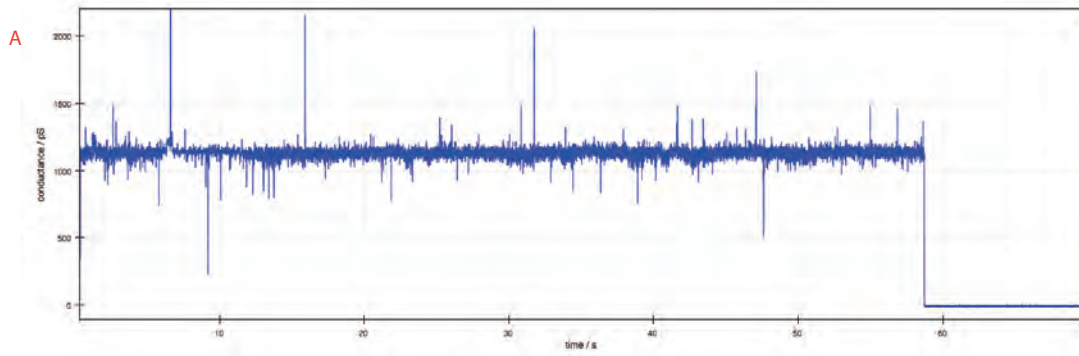
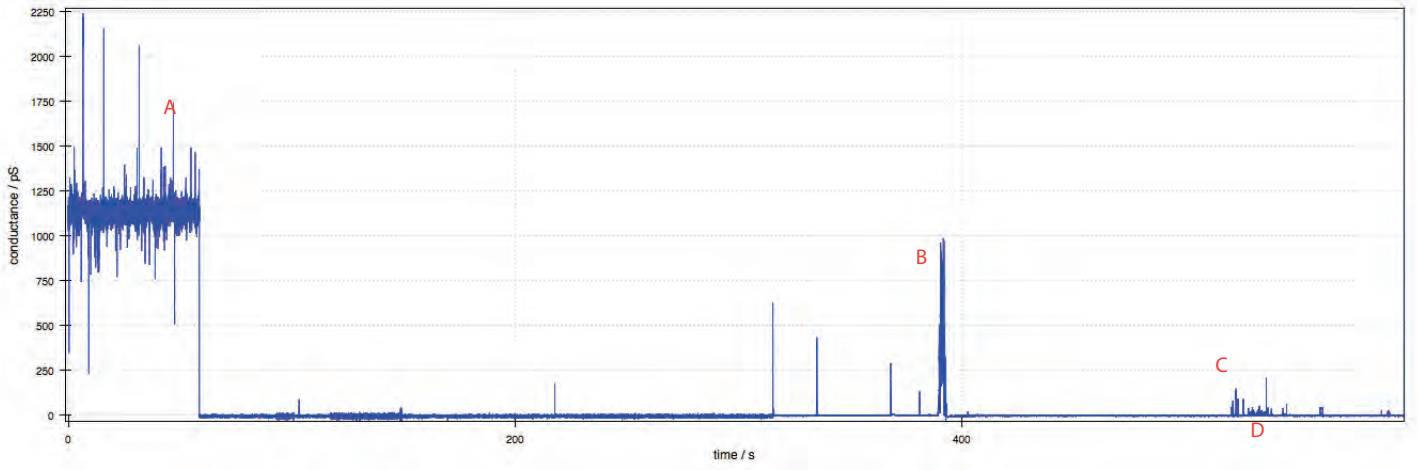
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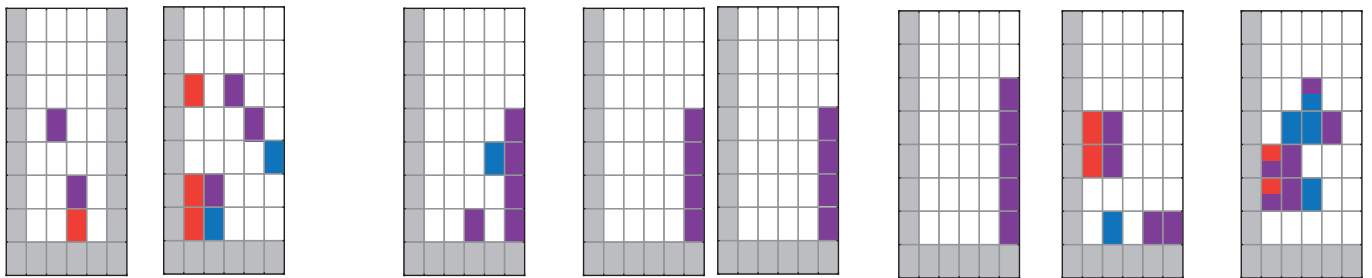
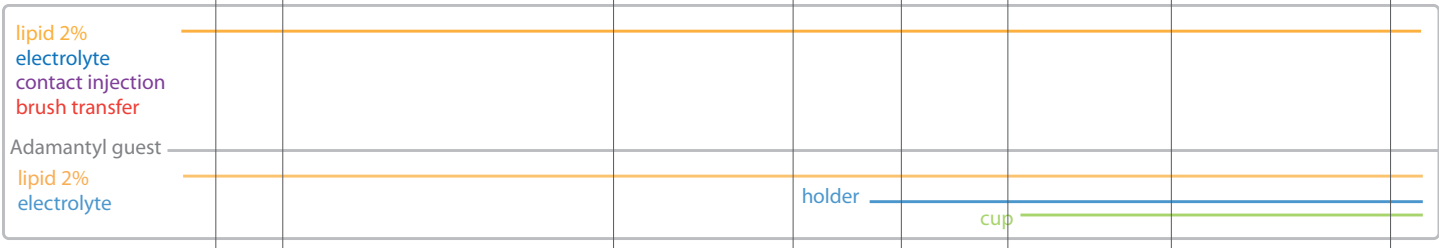
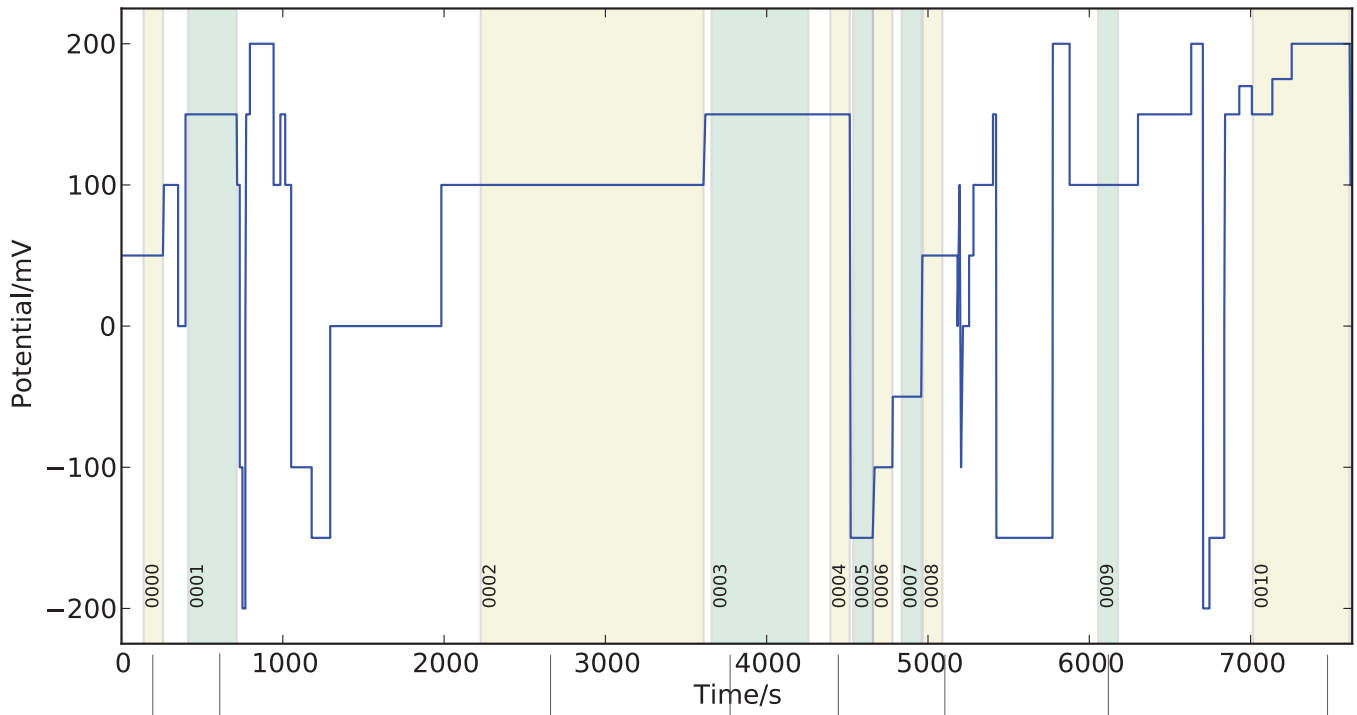
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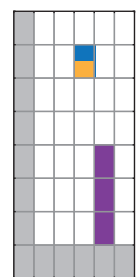
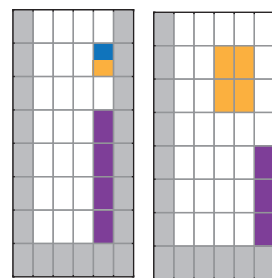




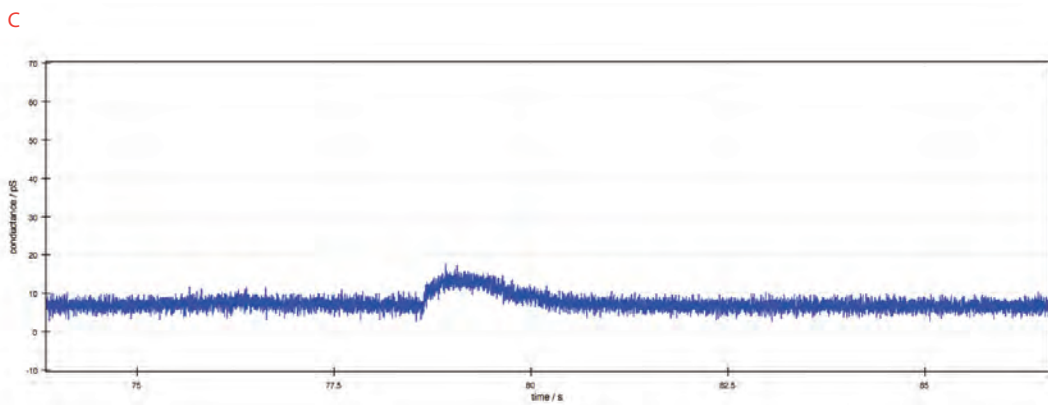
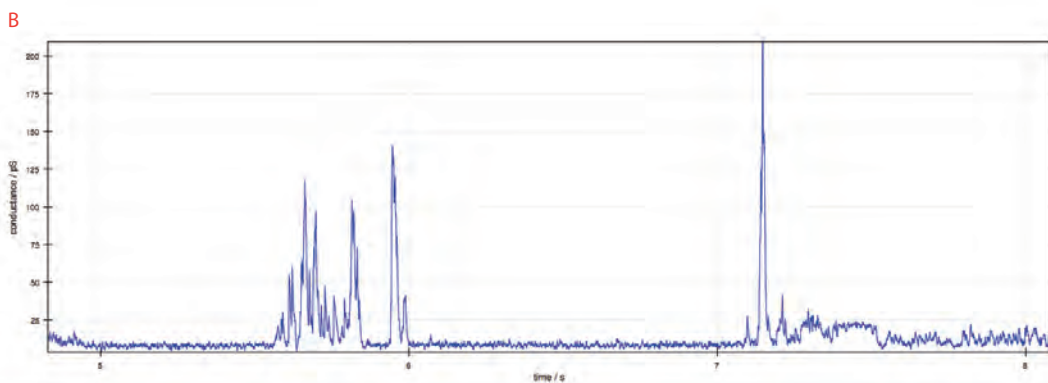
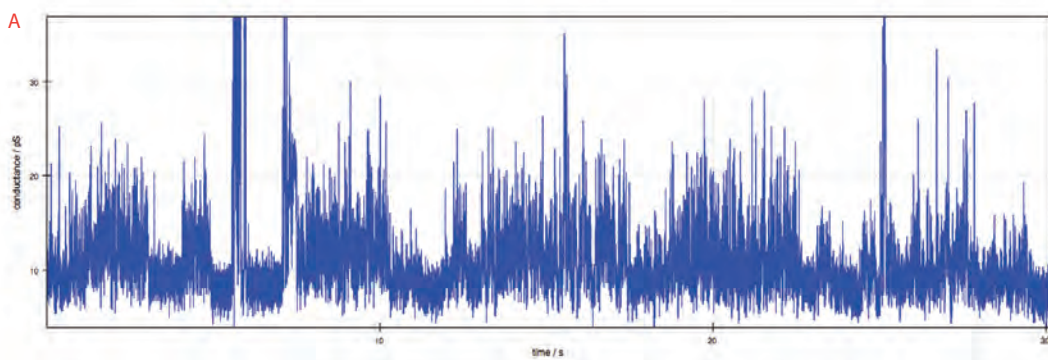
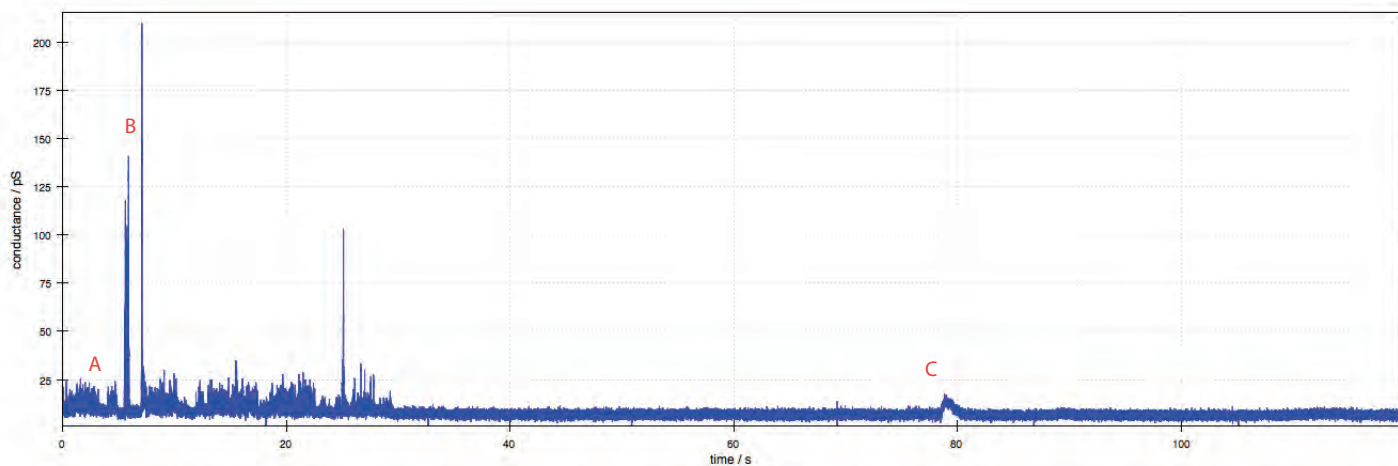
# JC-157 bCD-CholateAmide 2percent 1M CsCl AdCOOH pH 7

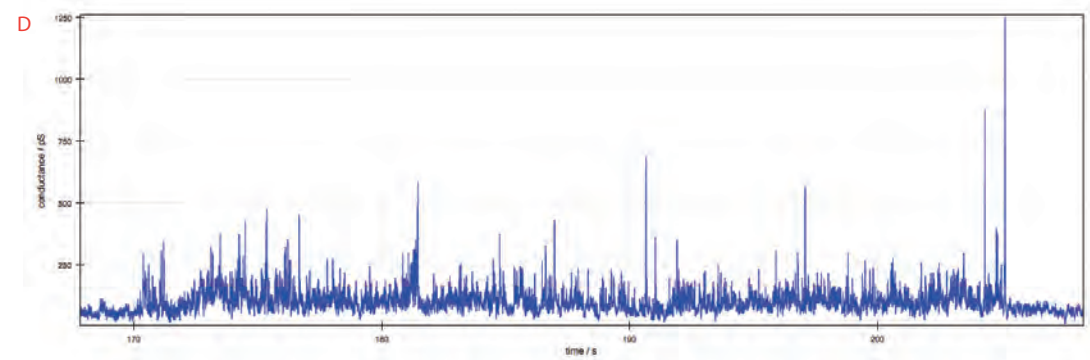
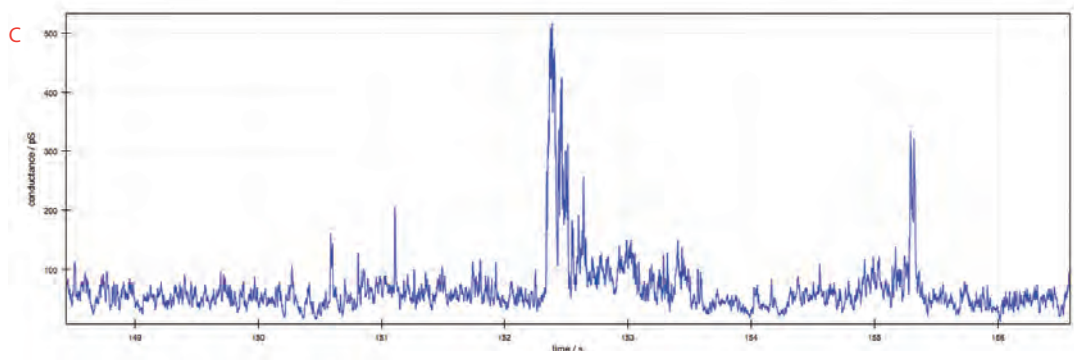
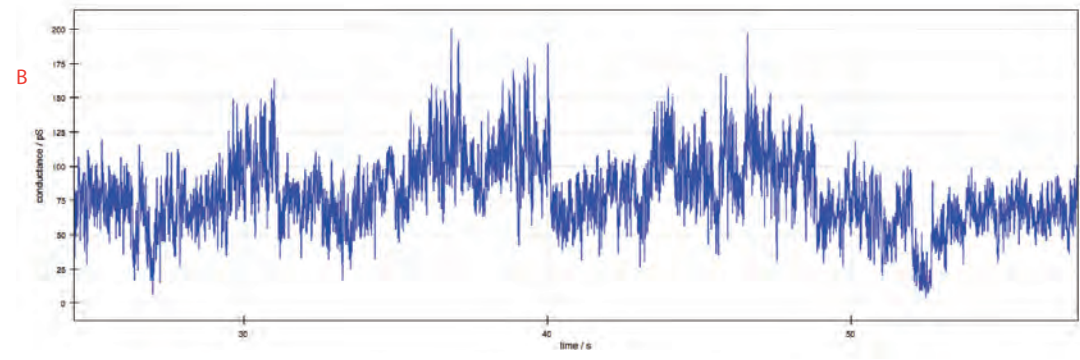
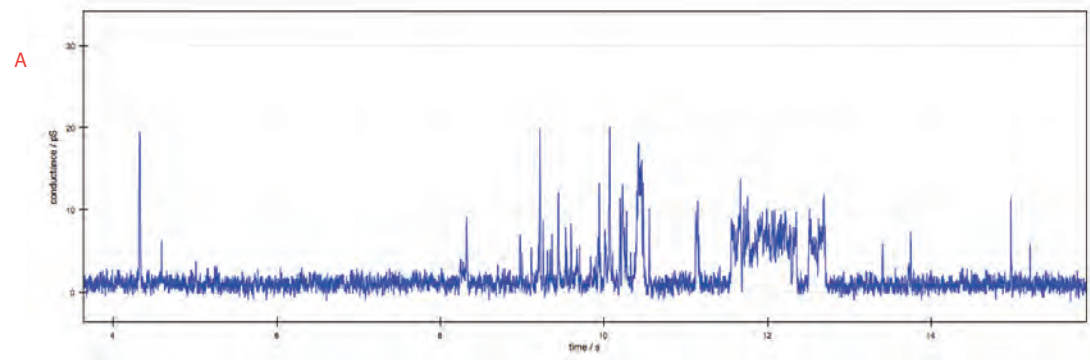
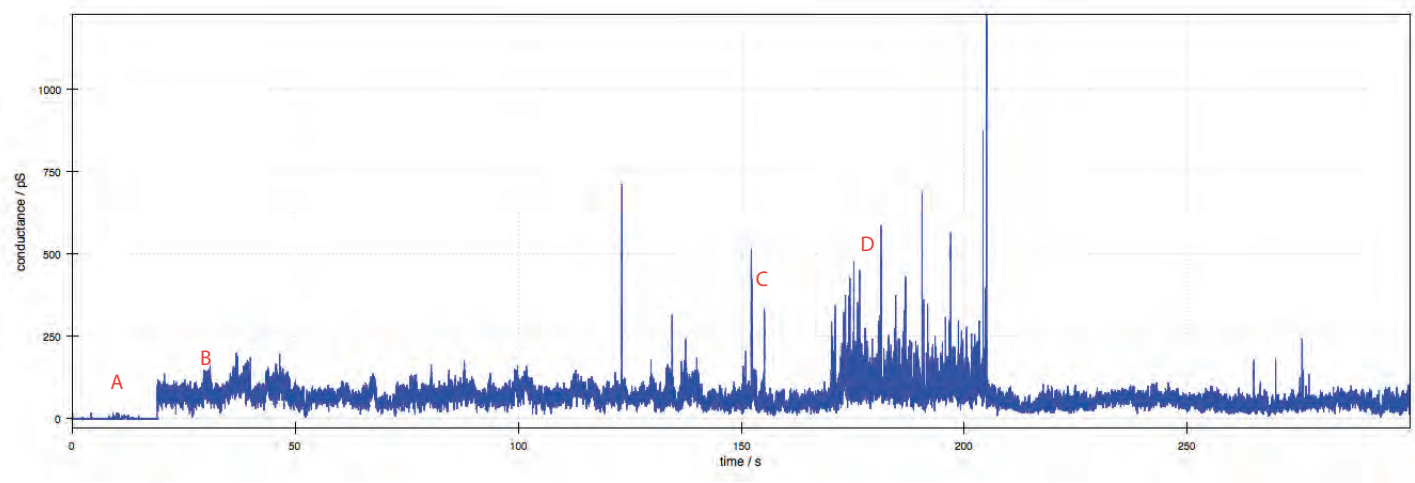


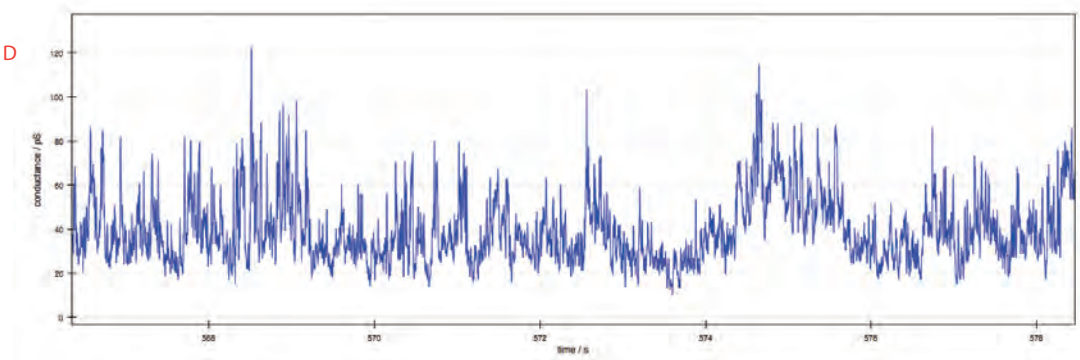
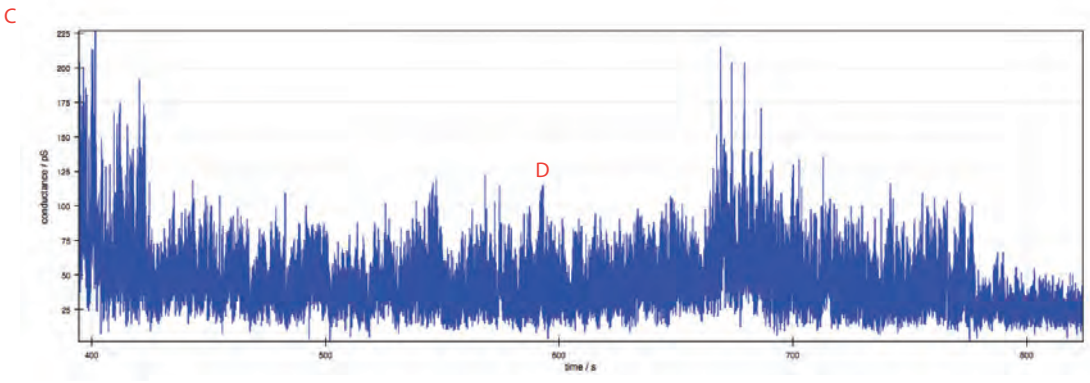
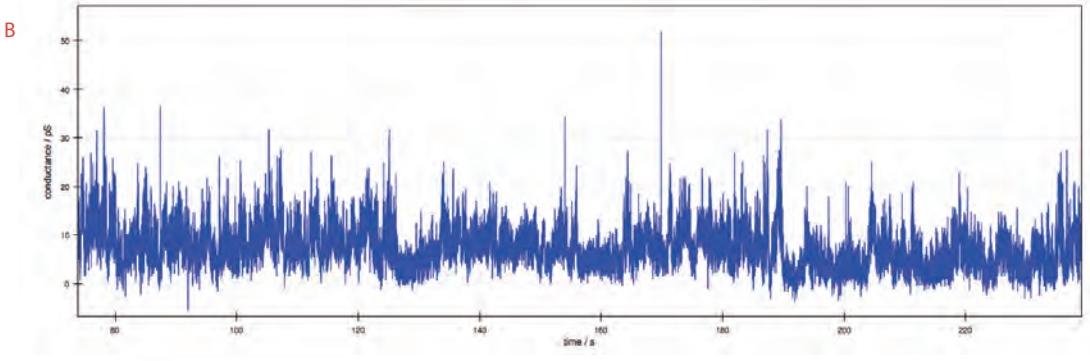
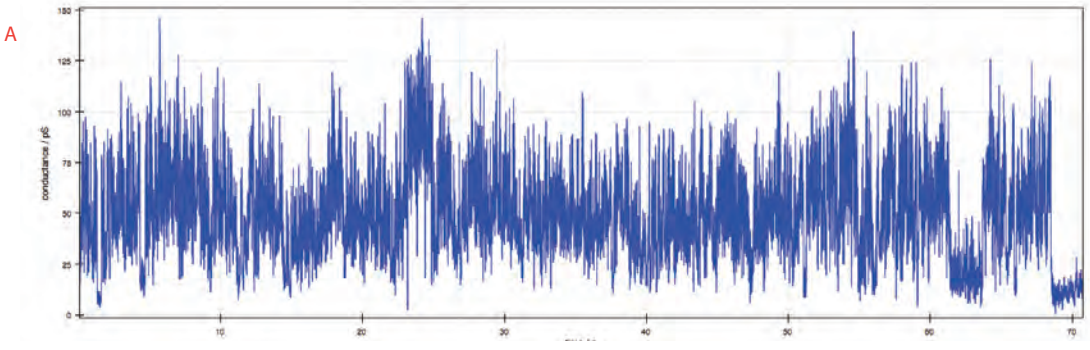
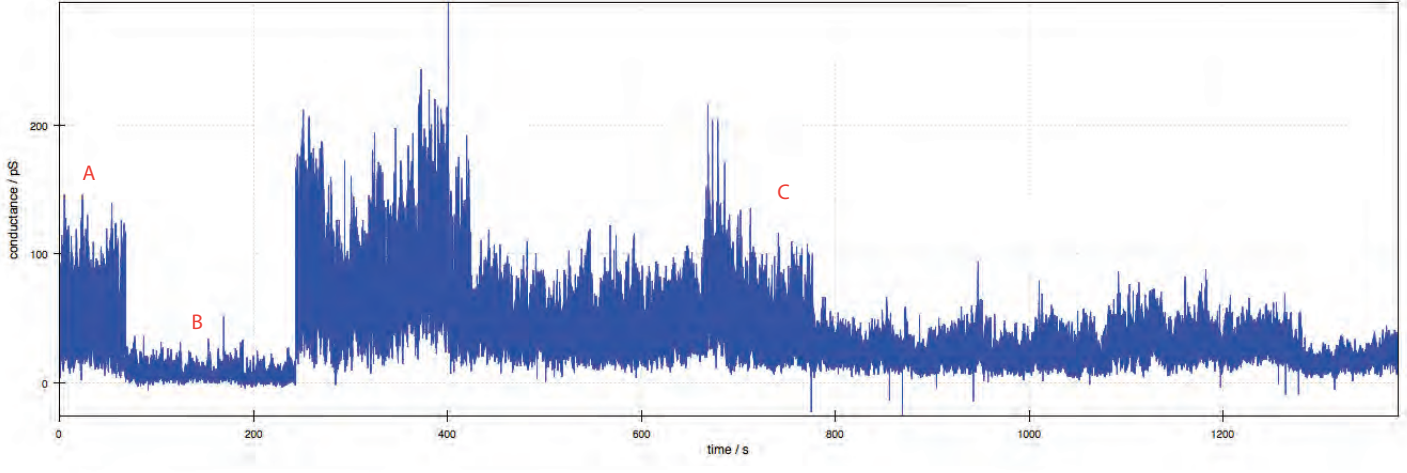
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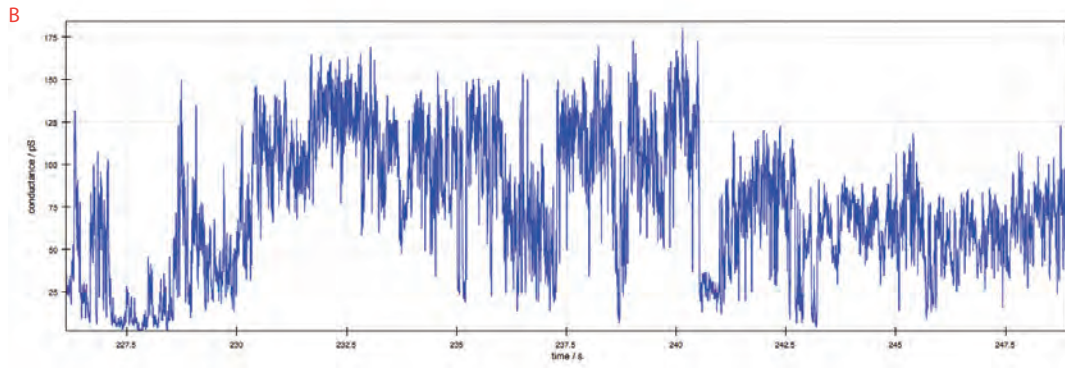
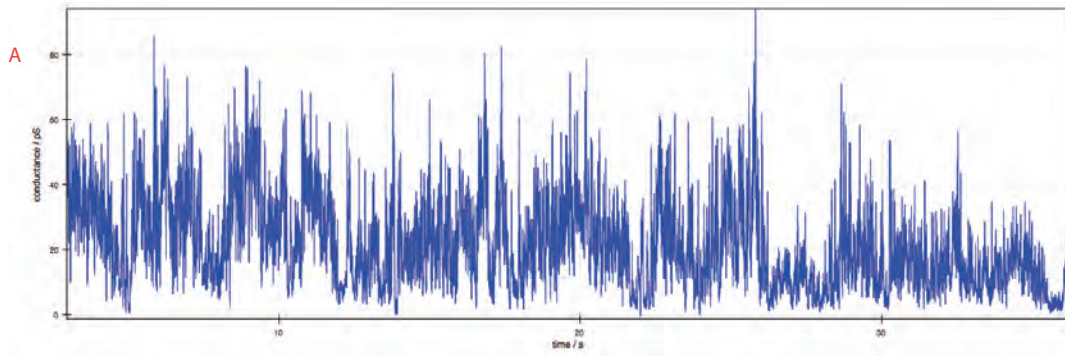
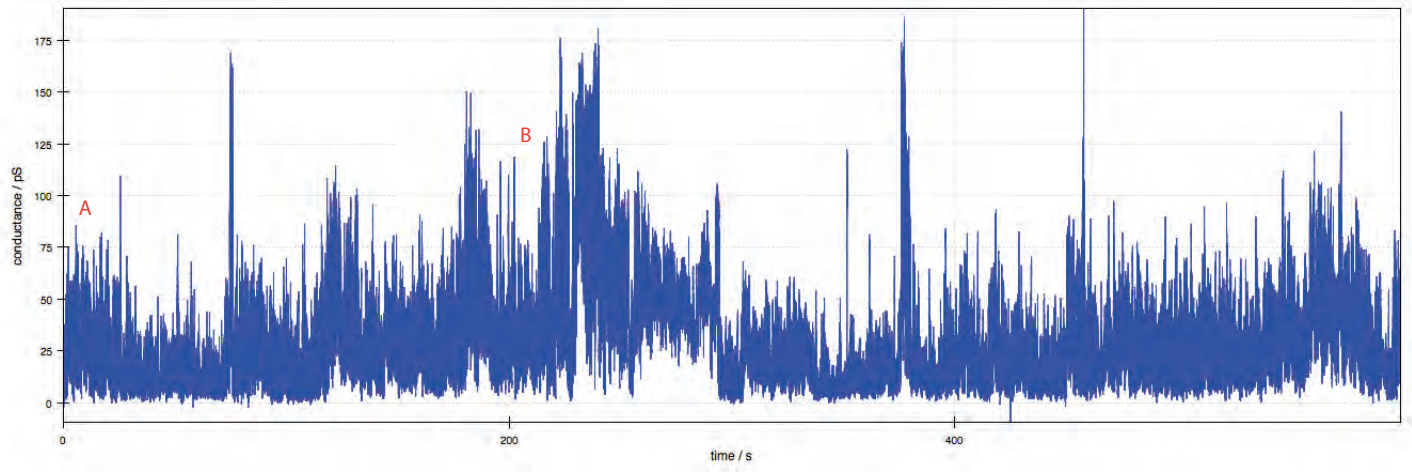


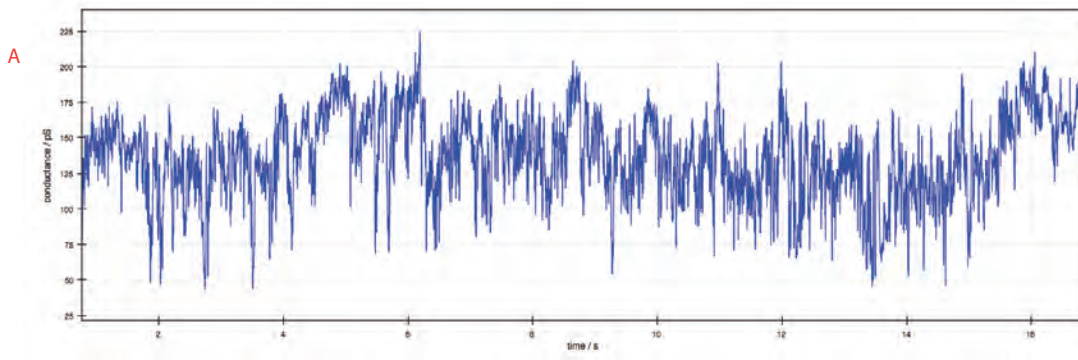
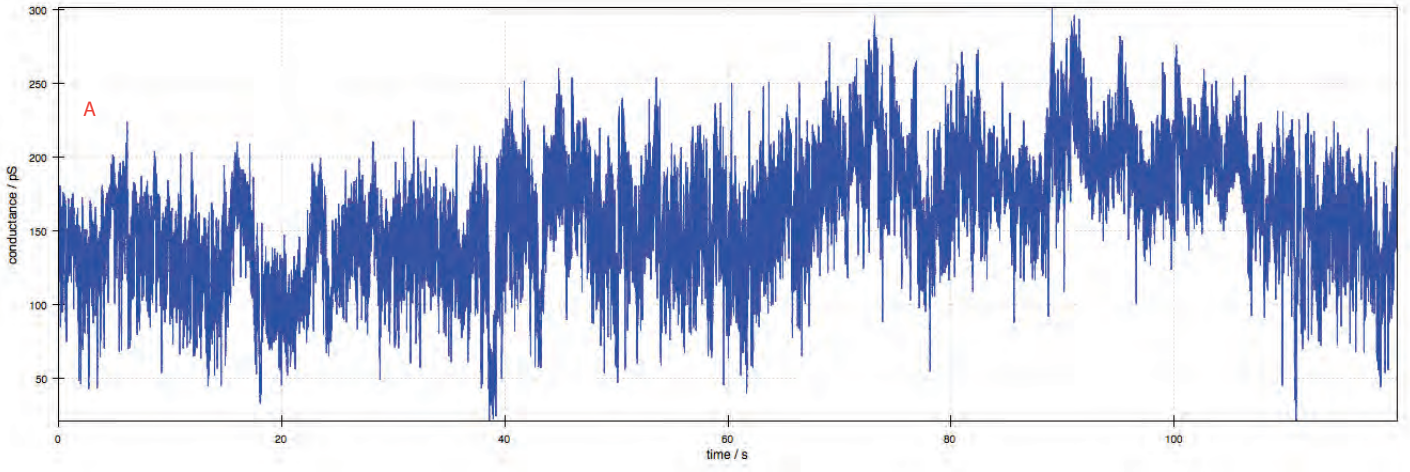
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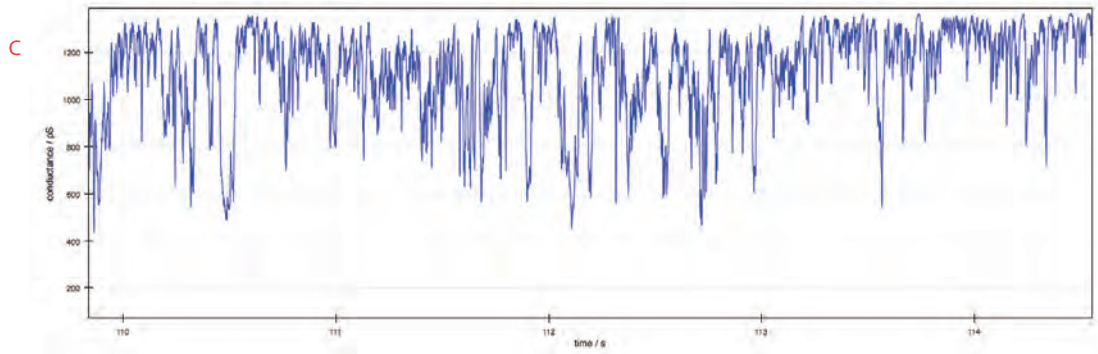
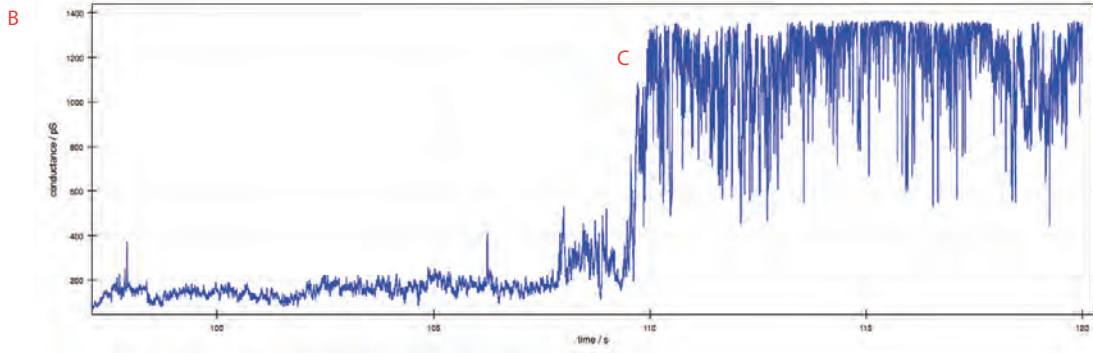
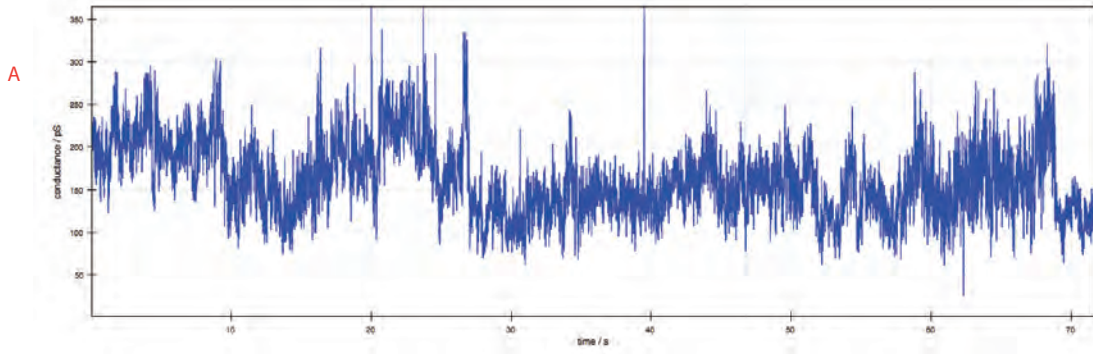
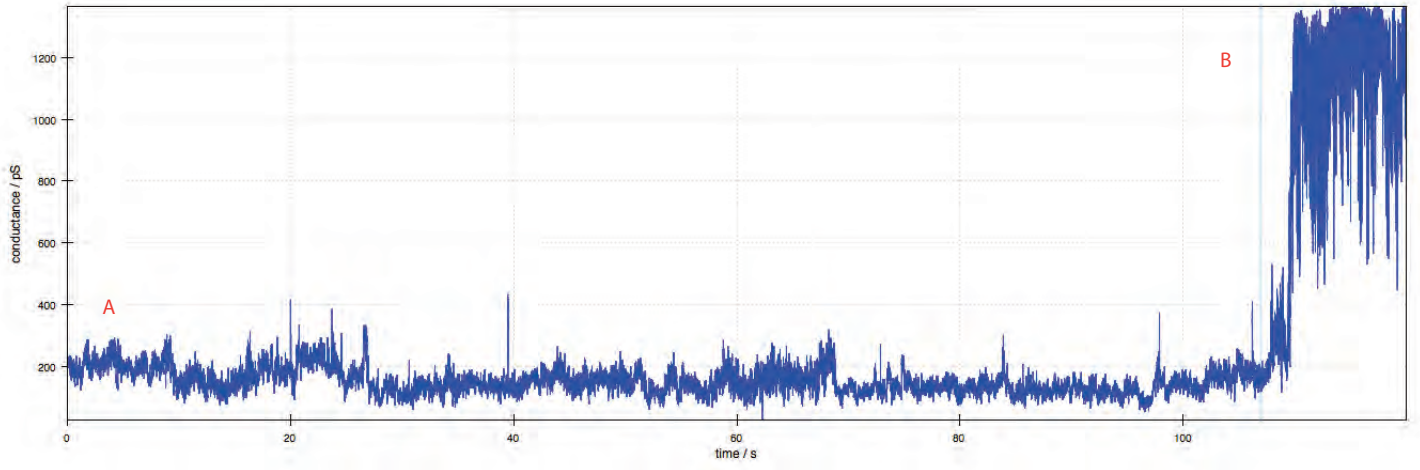


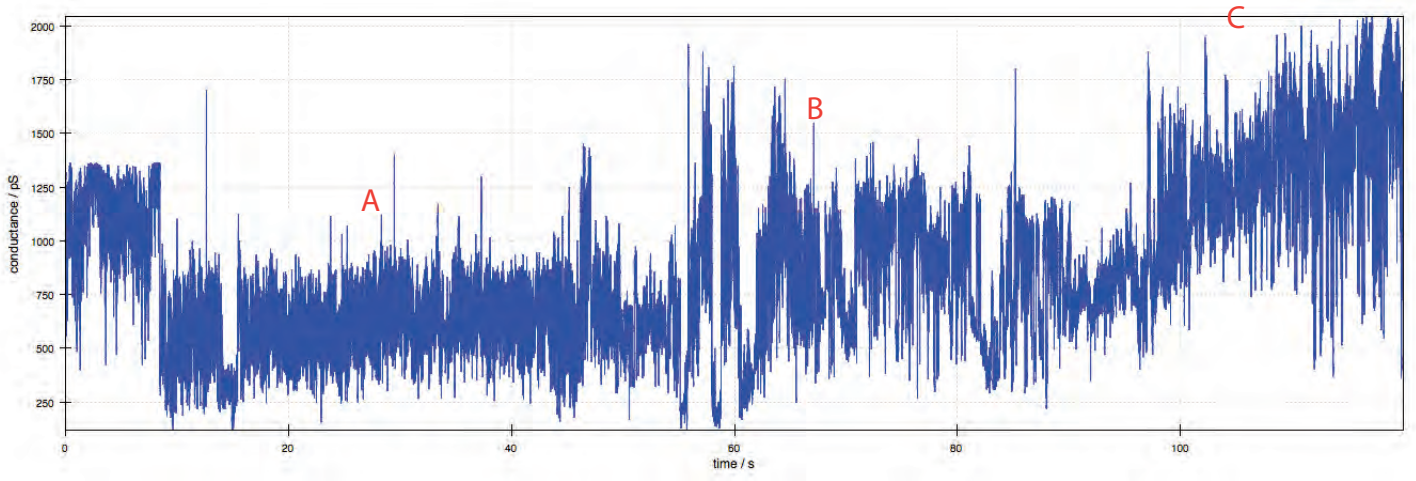




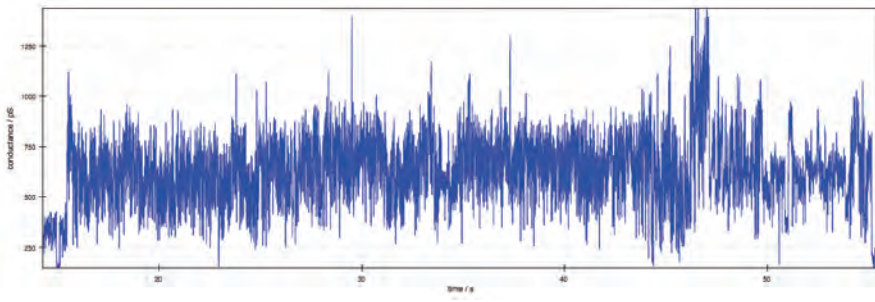




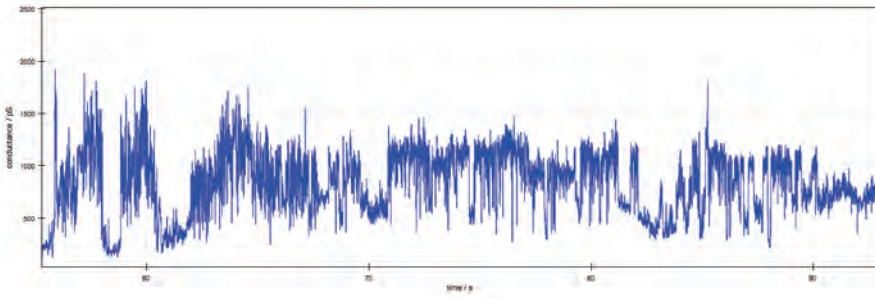




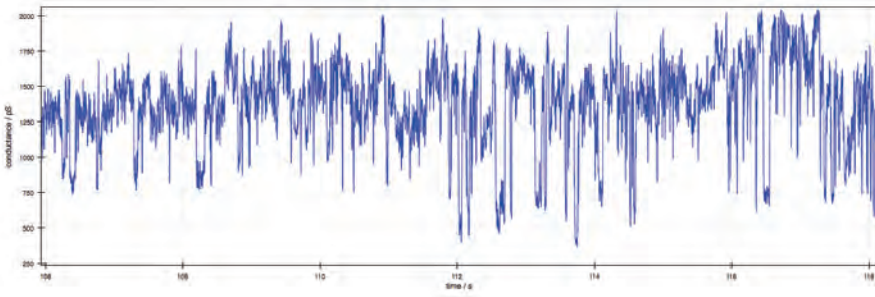
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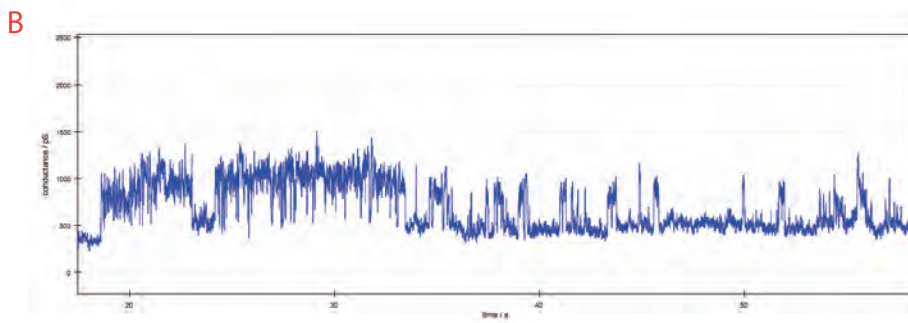
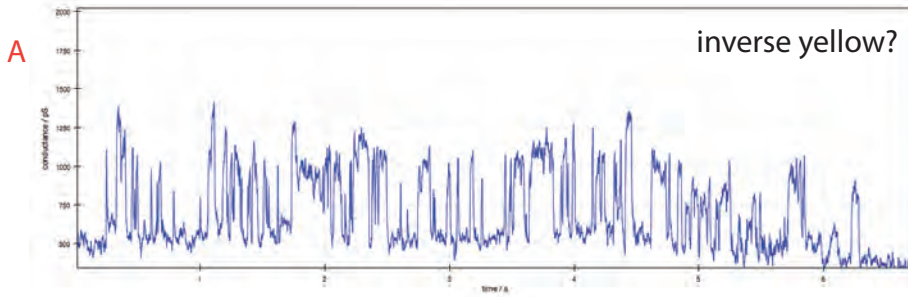
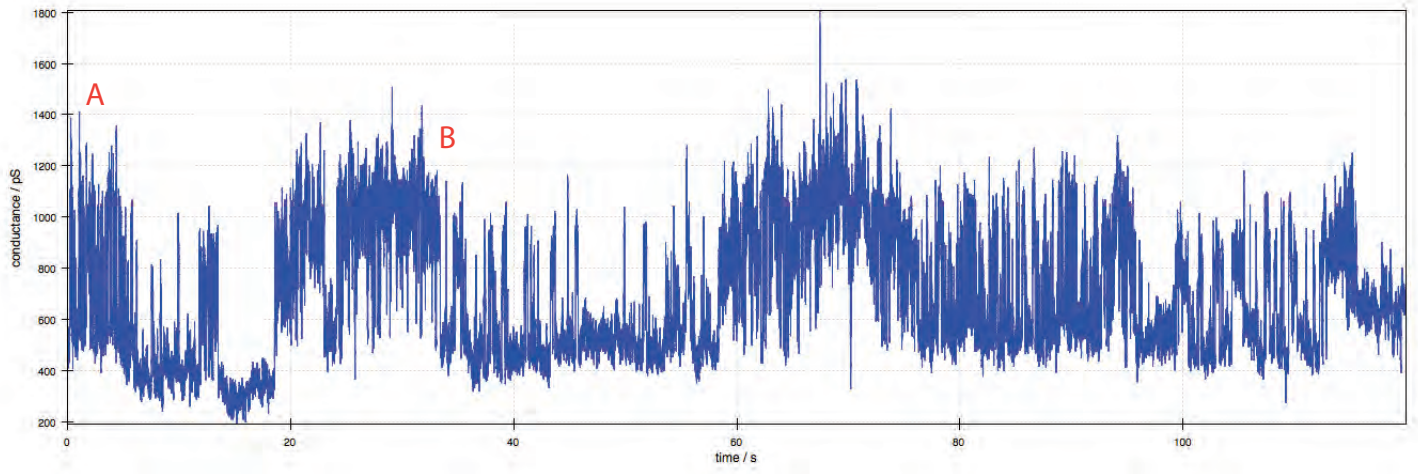


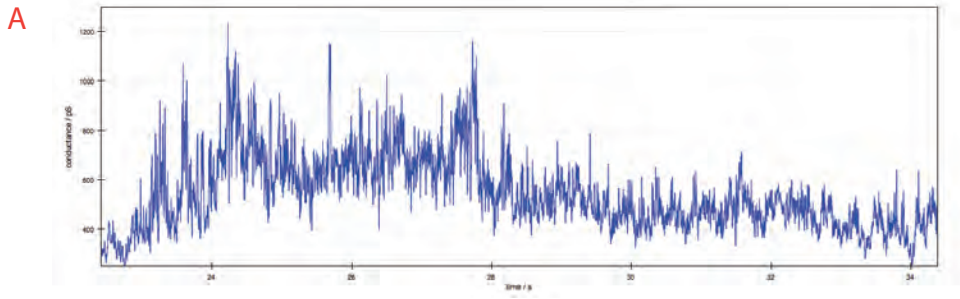
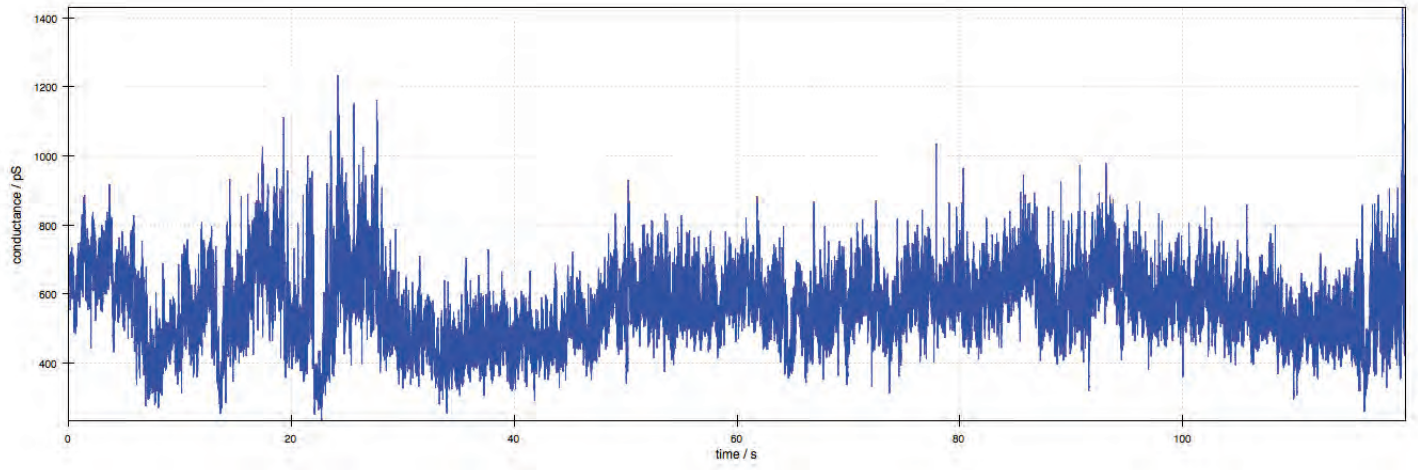
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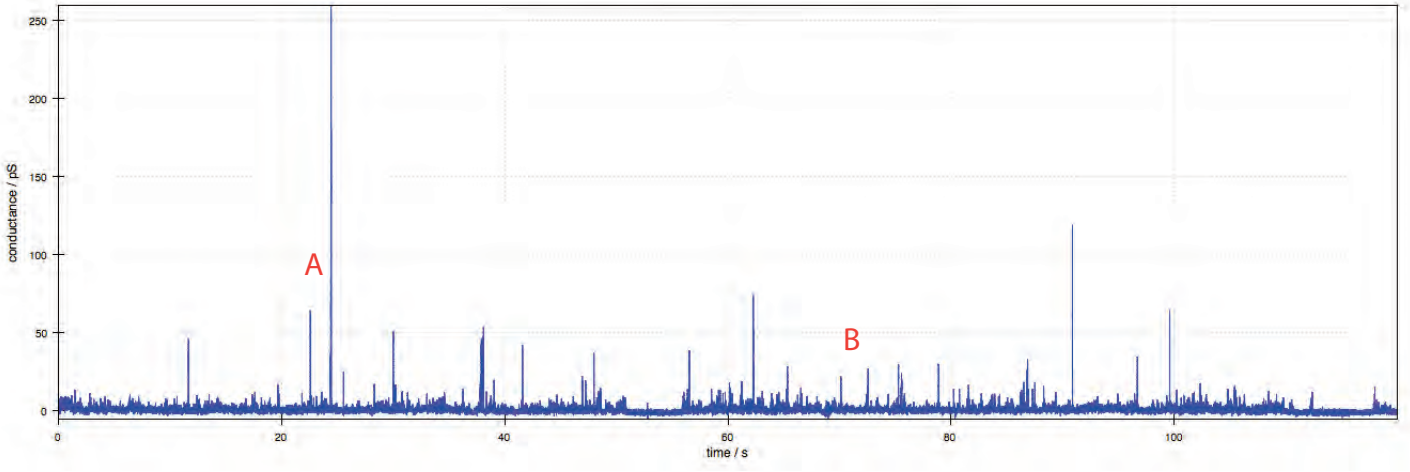


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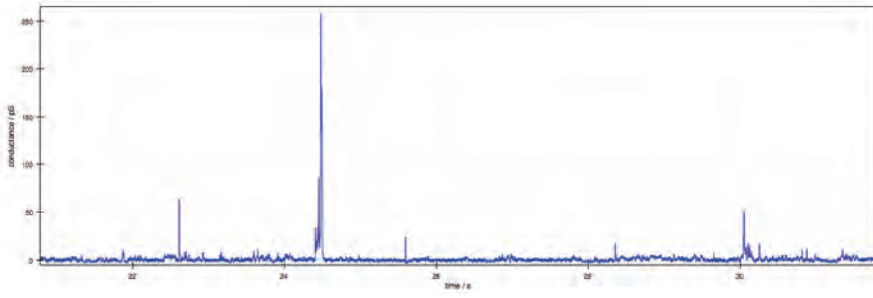




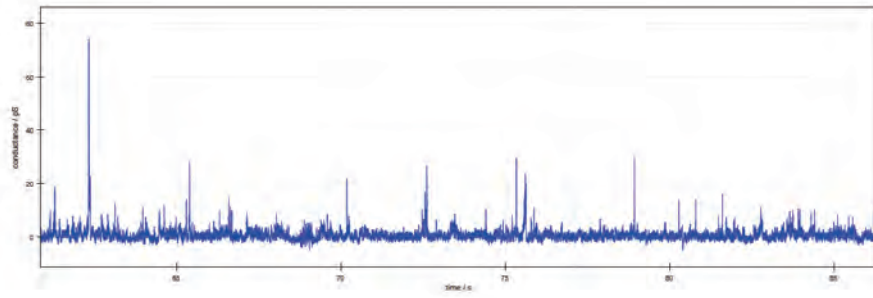


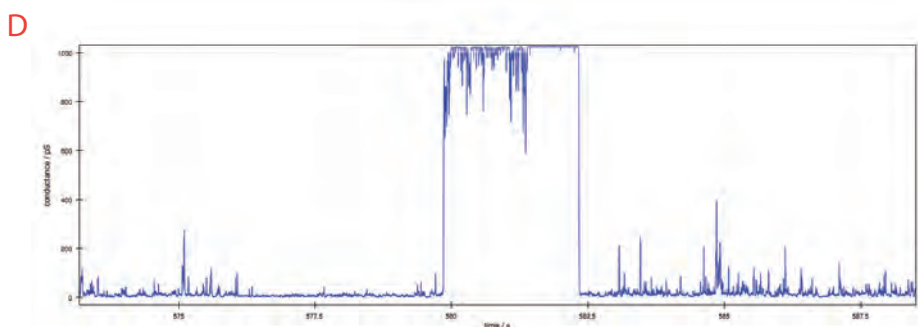
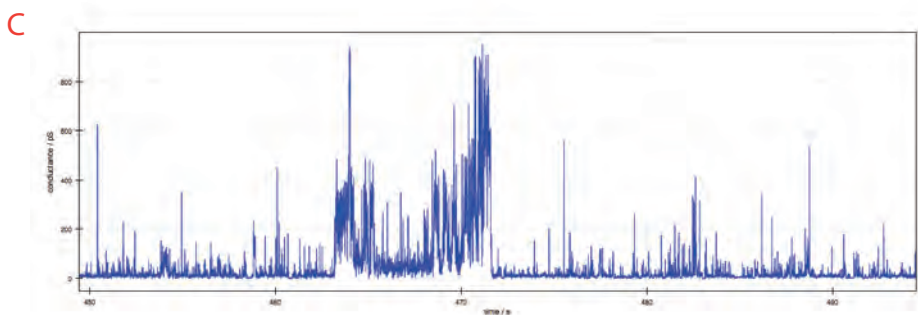
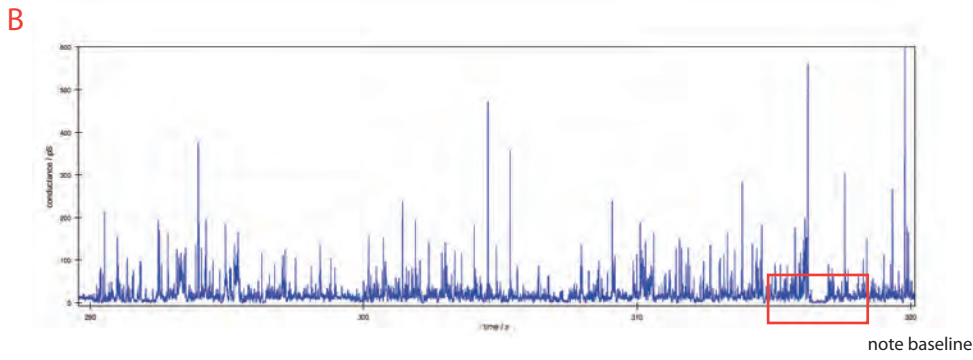
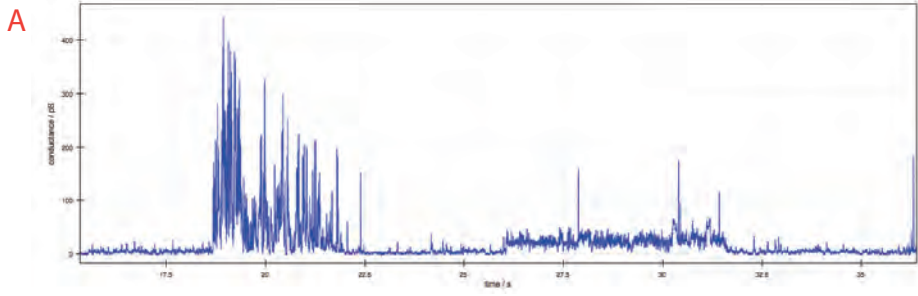
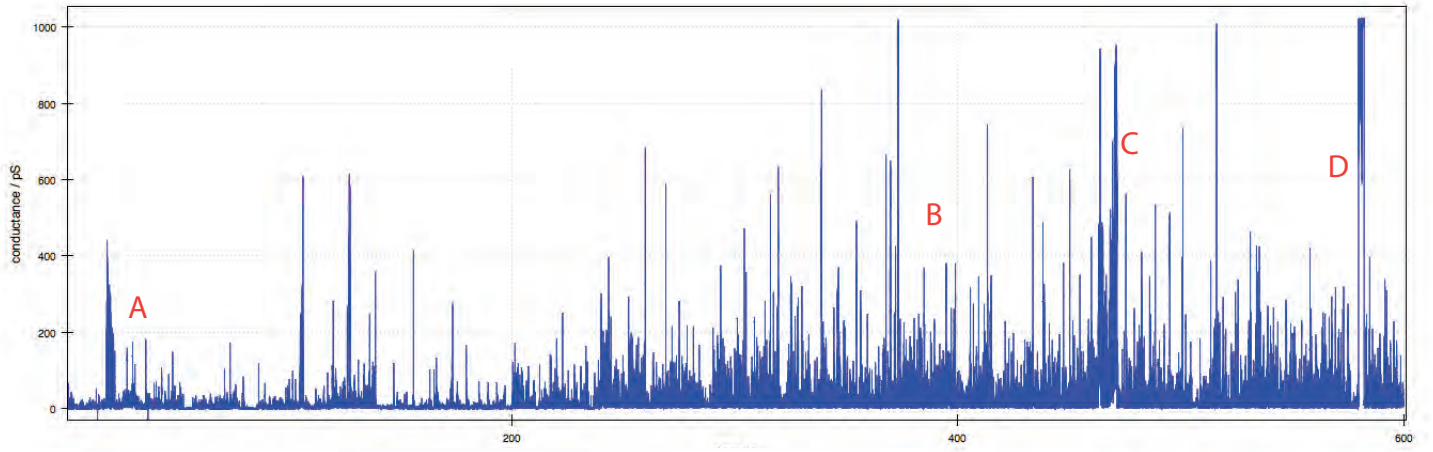


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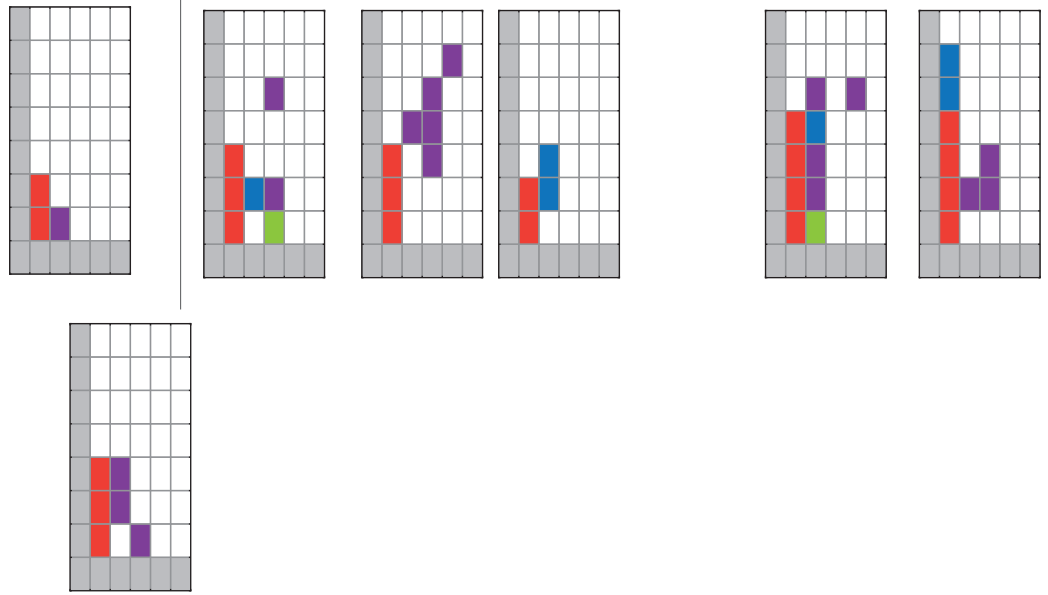
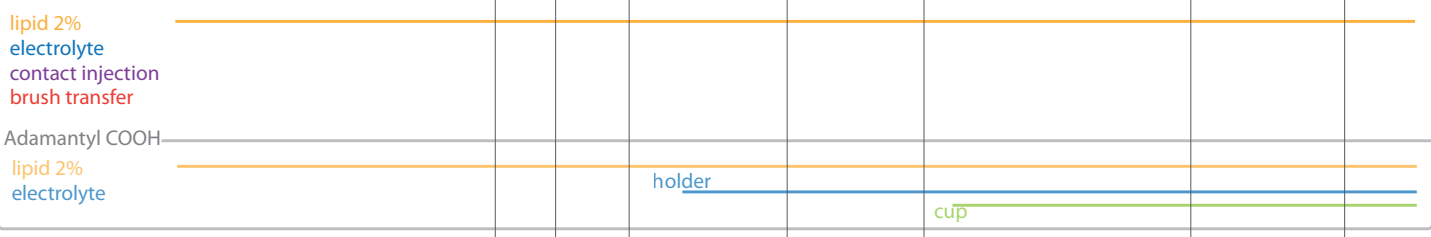
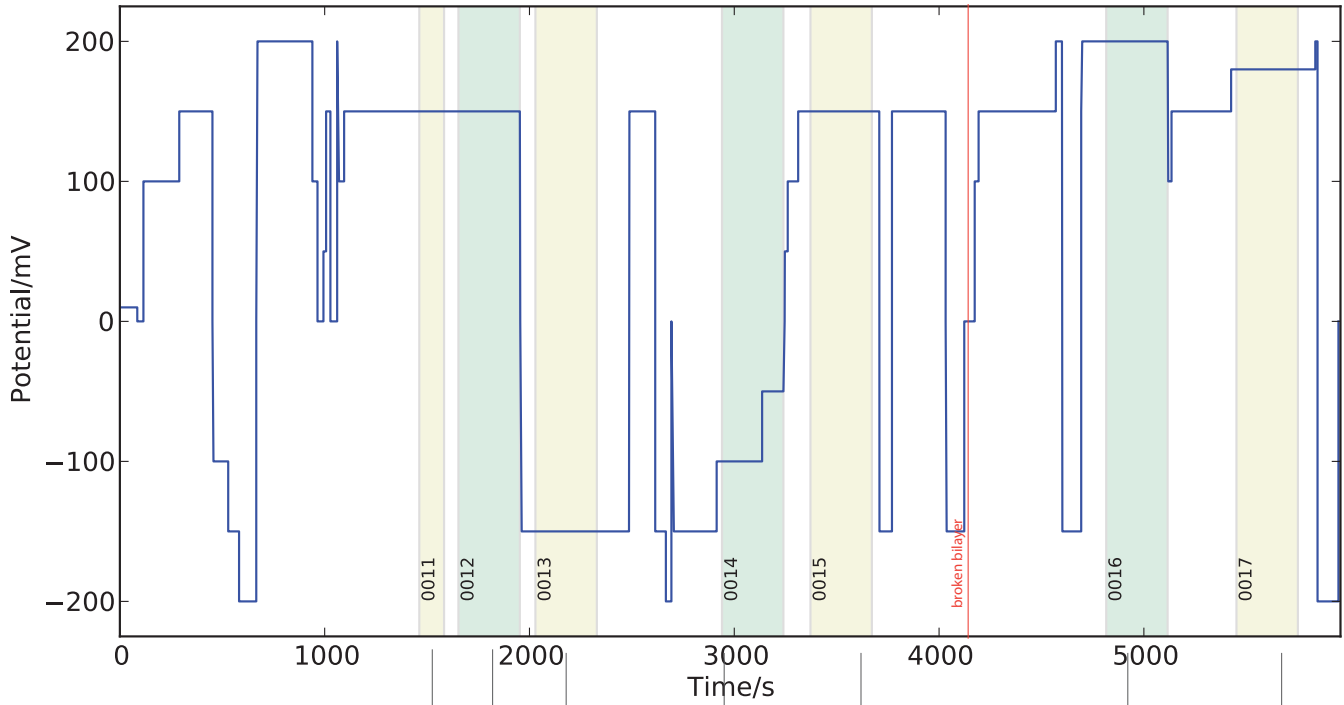


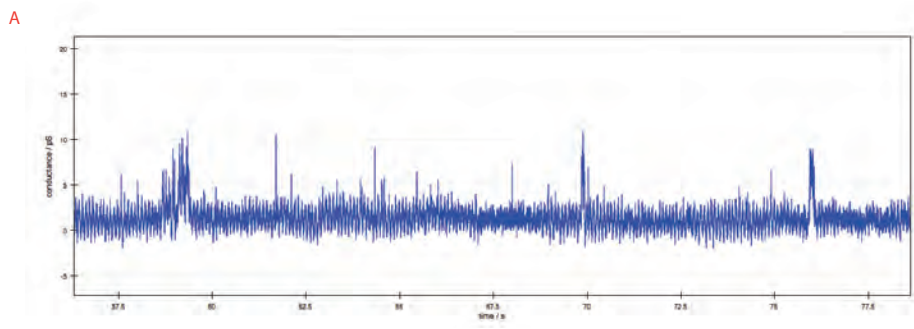
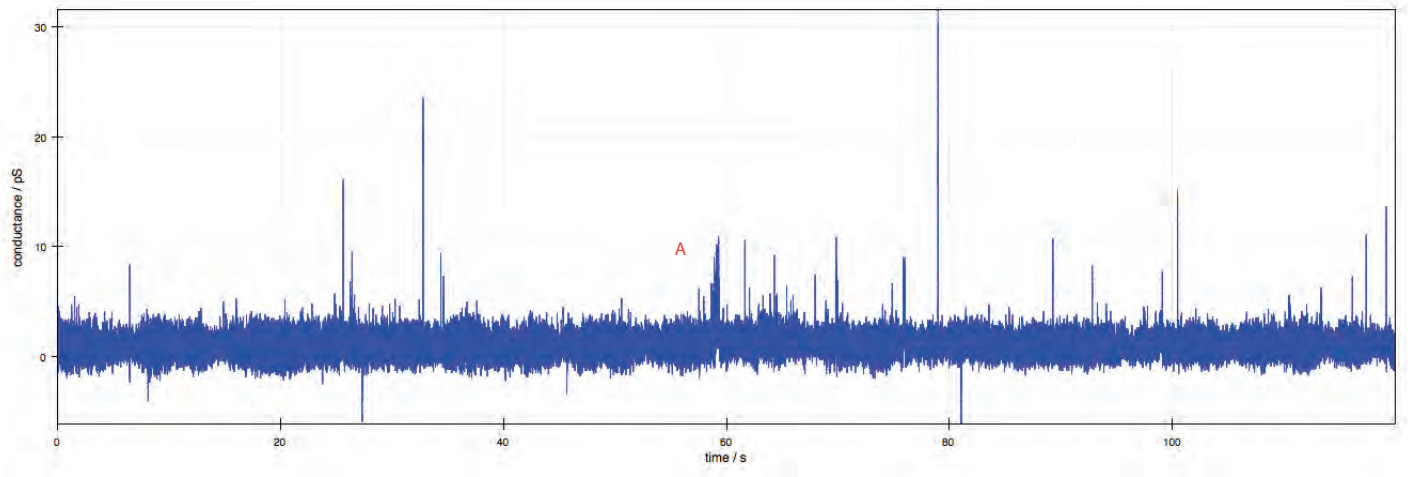
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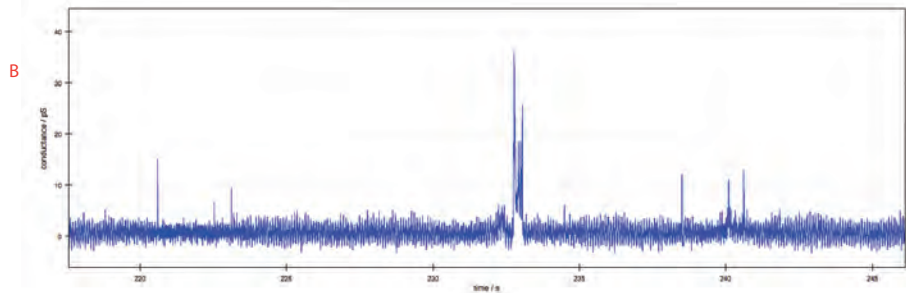
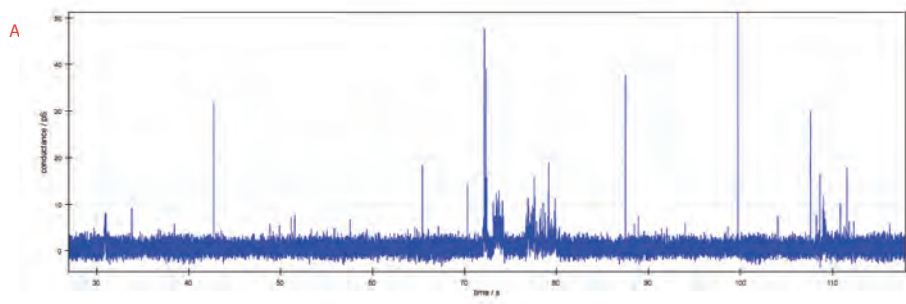
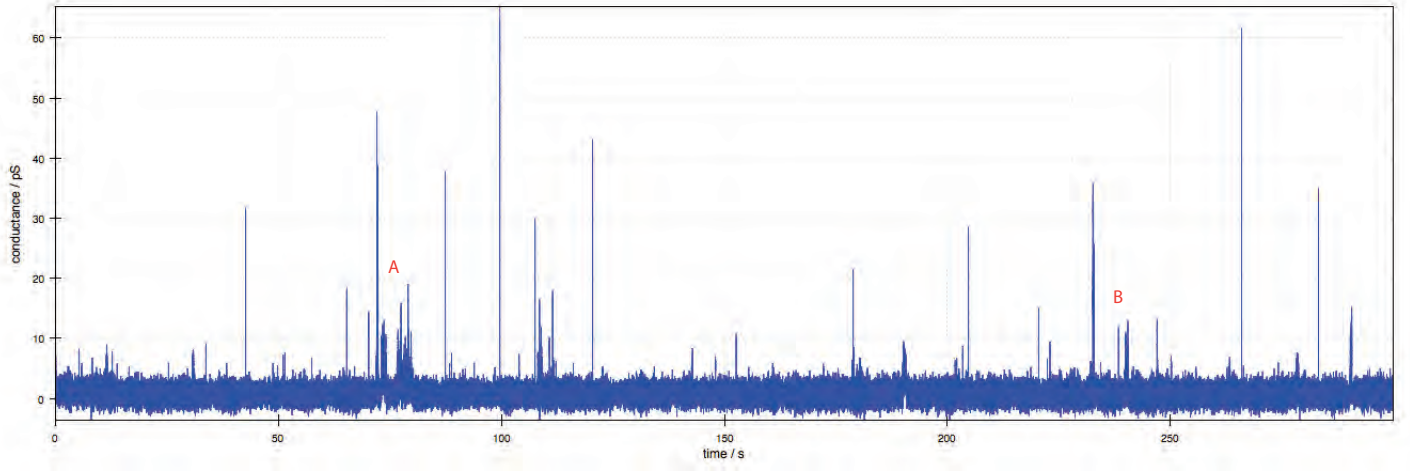


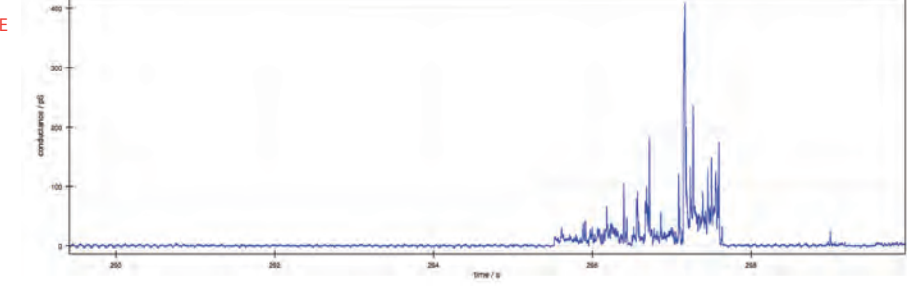
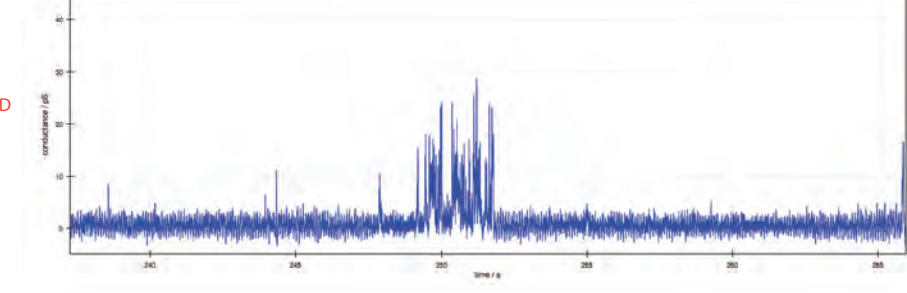
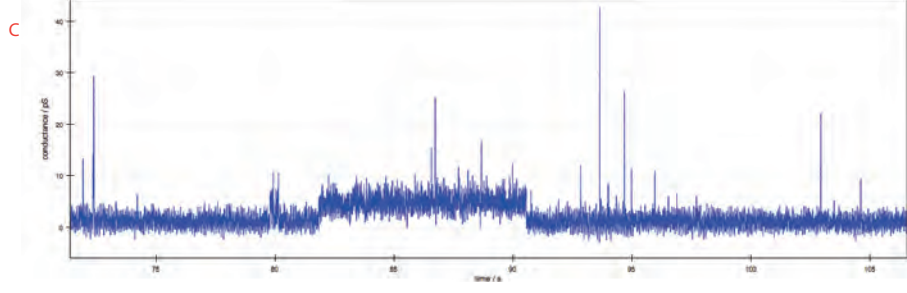
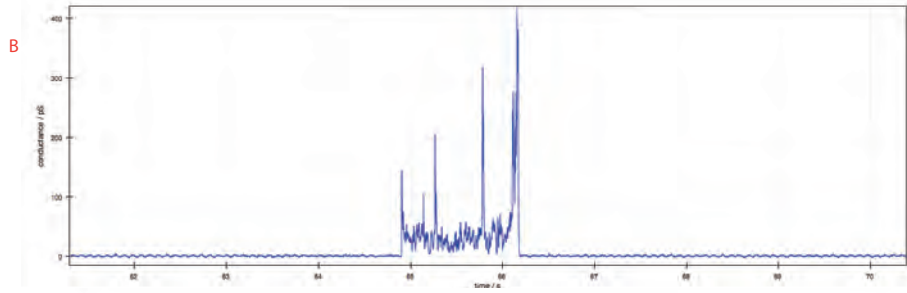
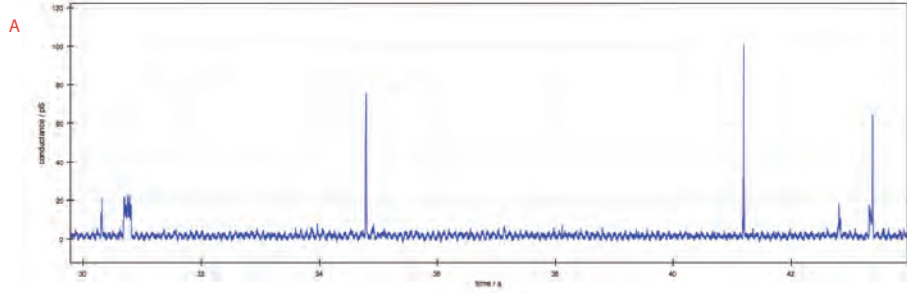
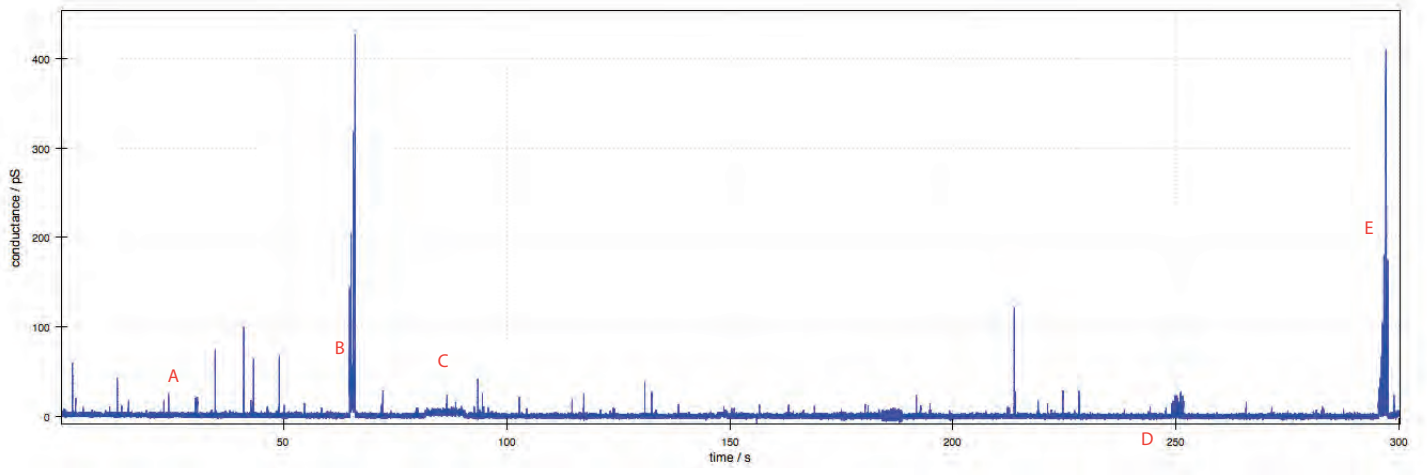


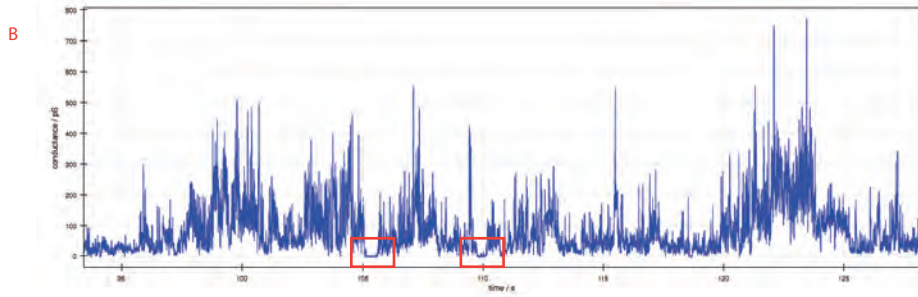
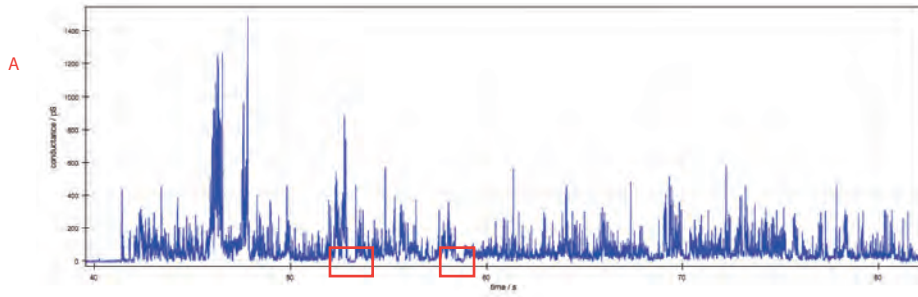
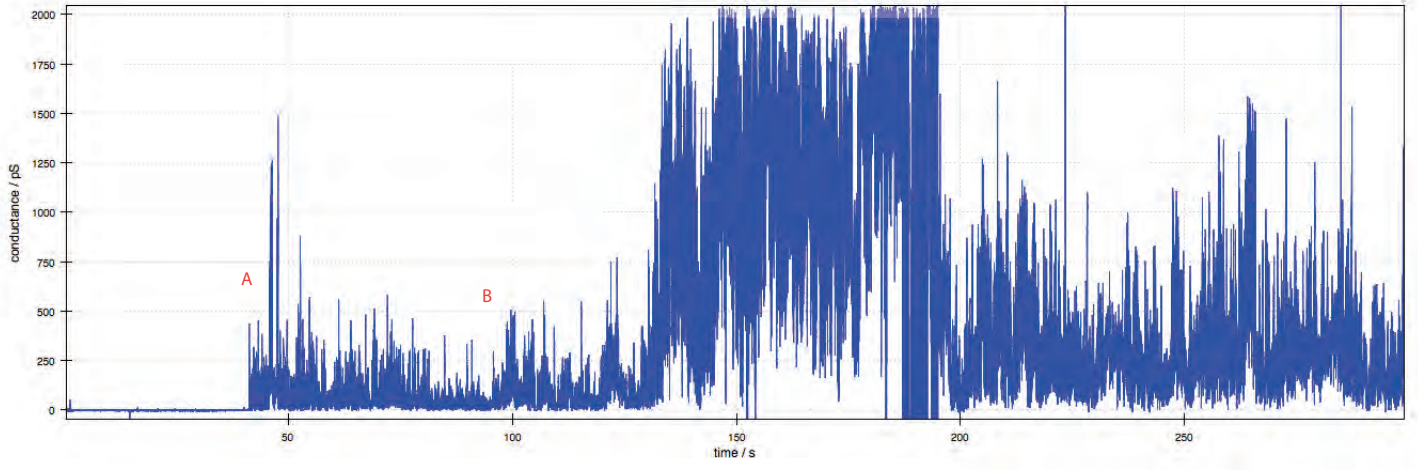
# JC-158 bCD-CholateAmide 2percent 1M KCl AdCOOH pH 5

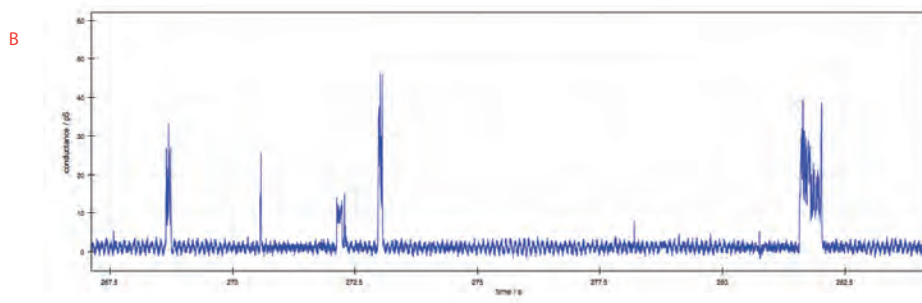
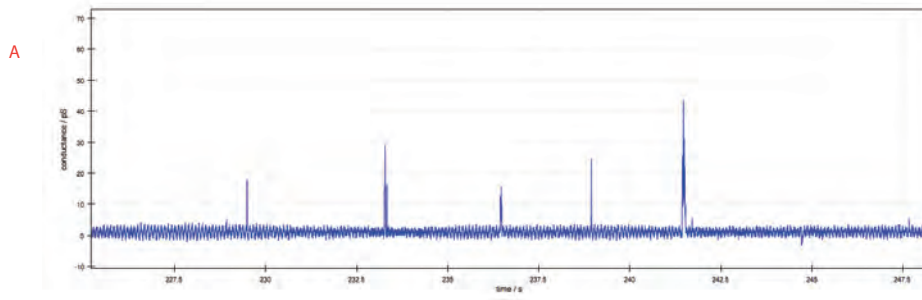
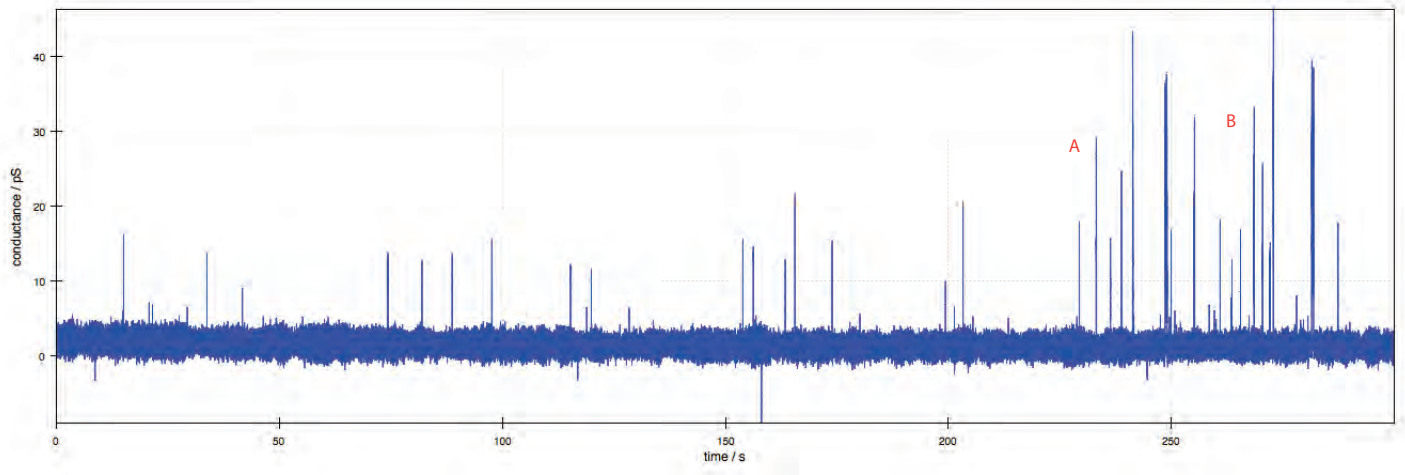


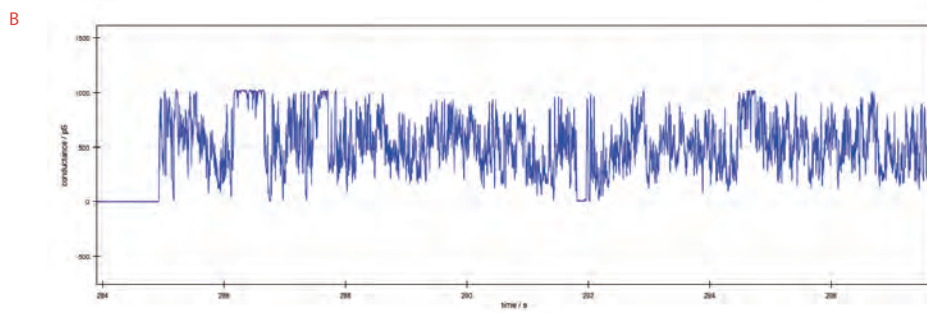
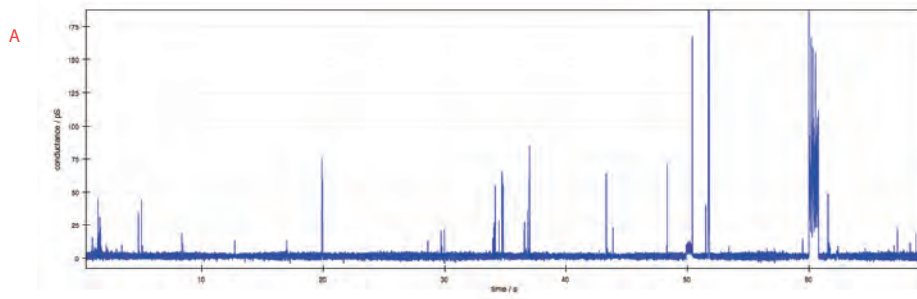
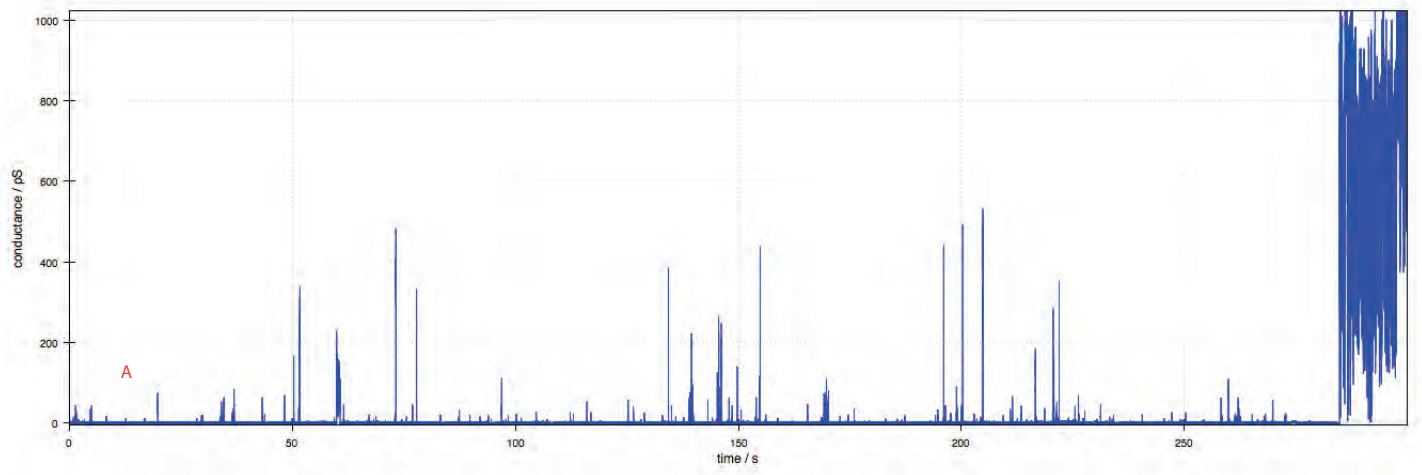


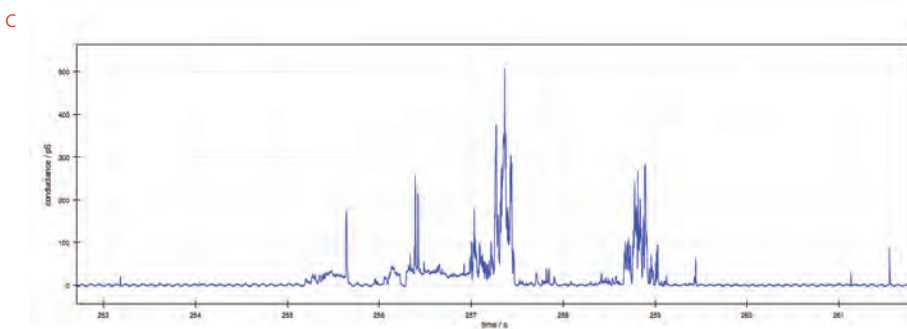
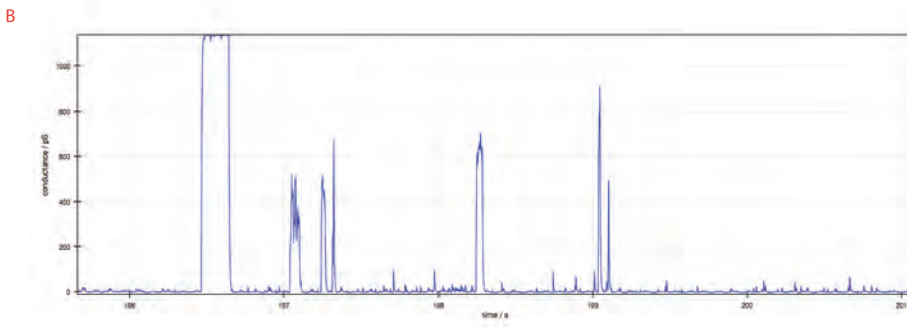
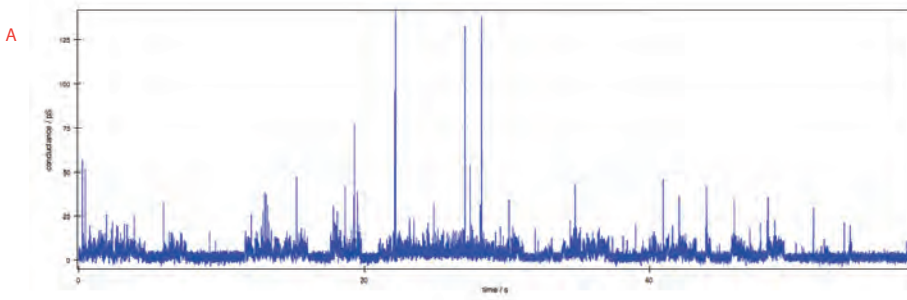
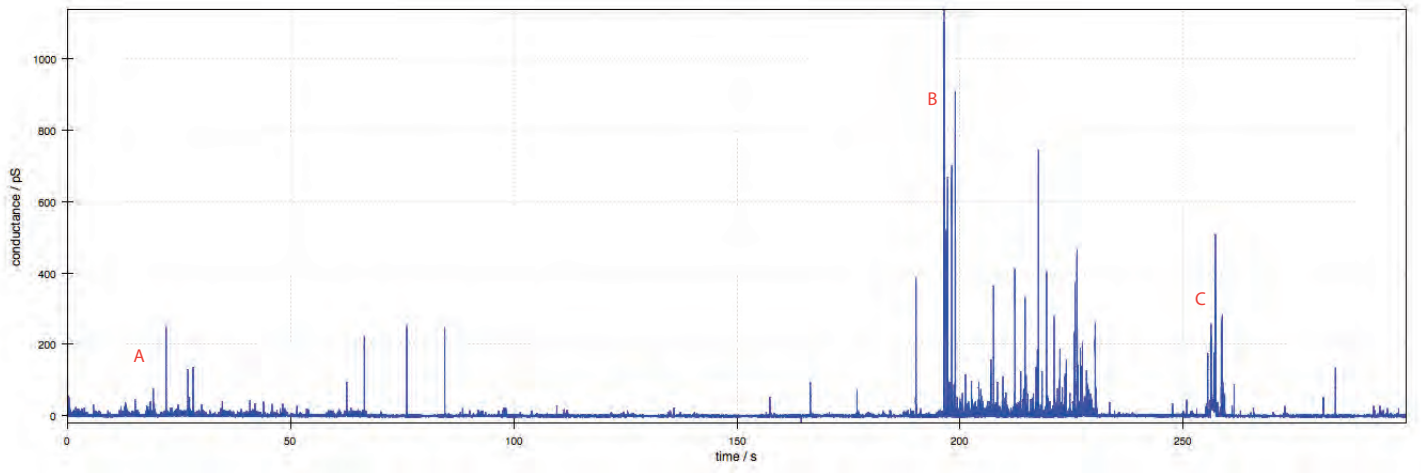




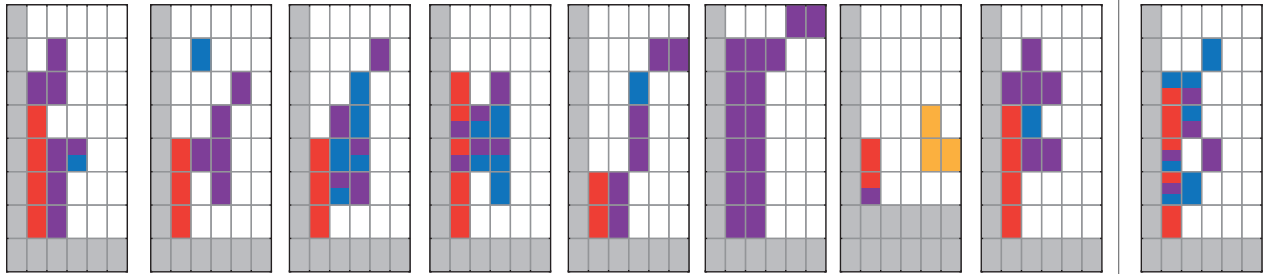
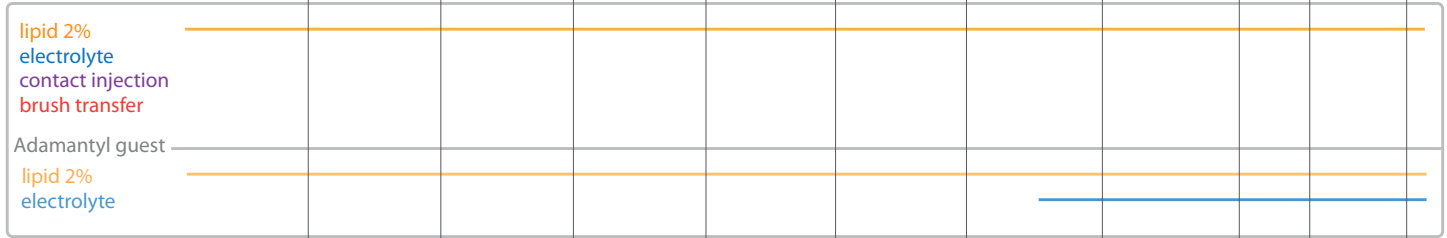
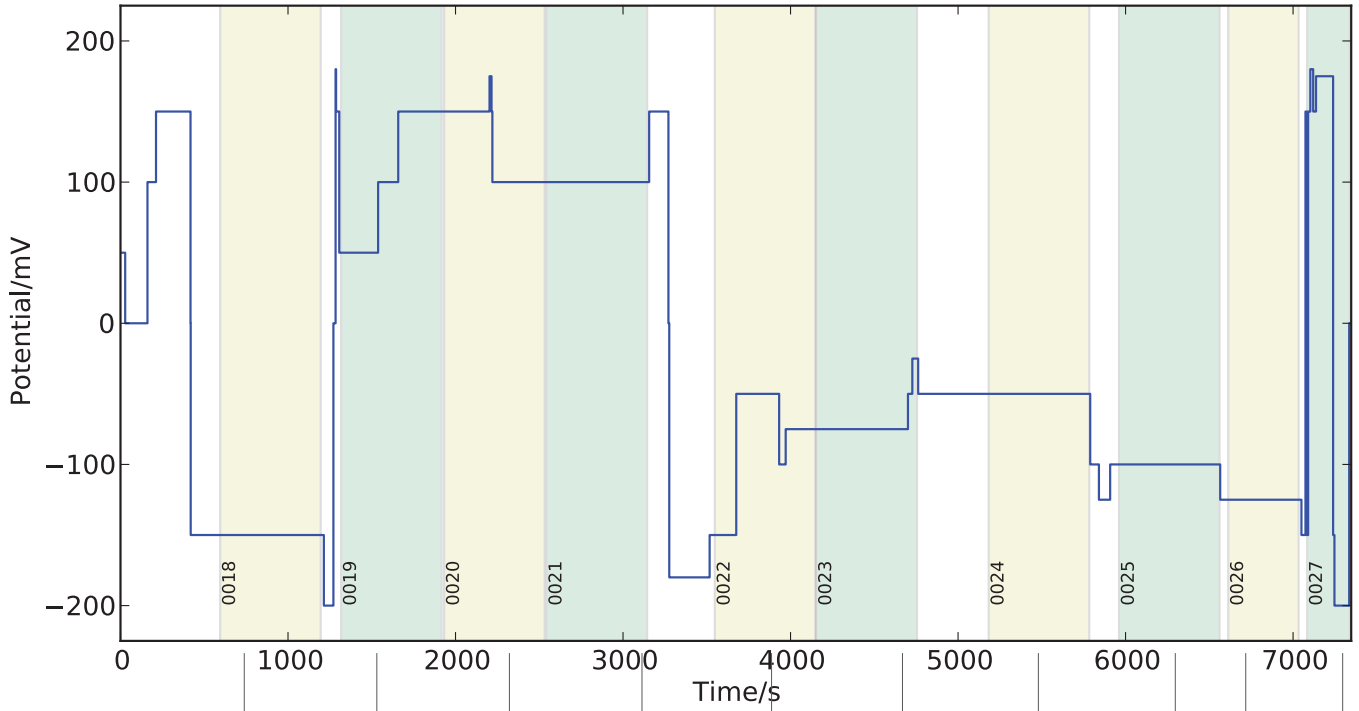




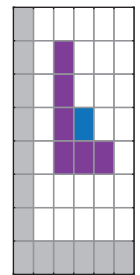


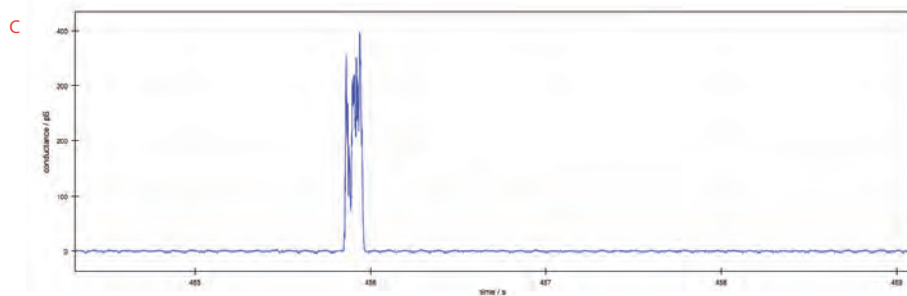
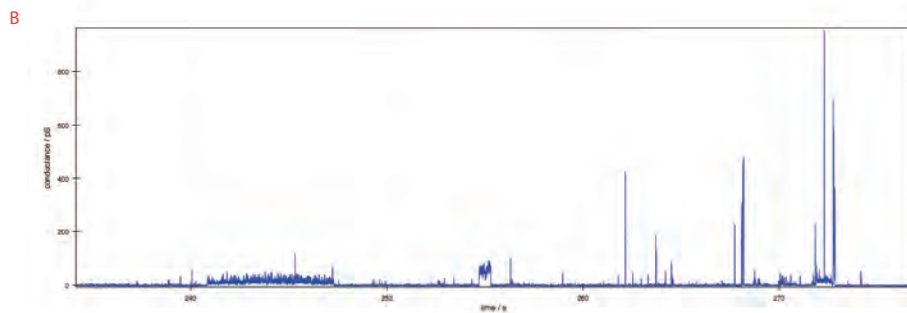
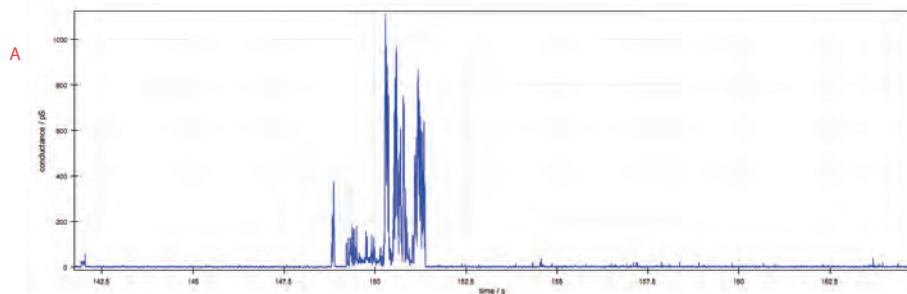
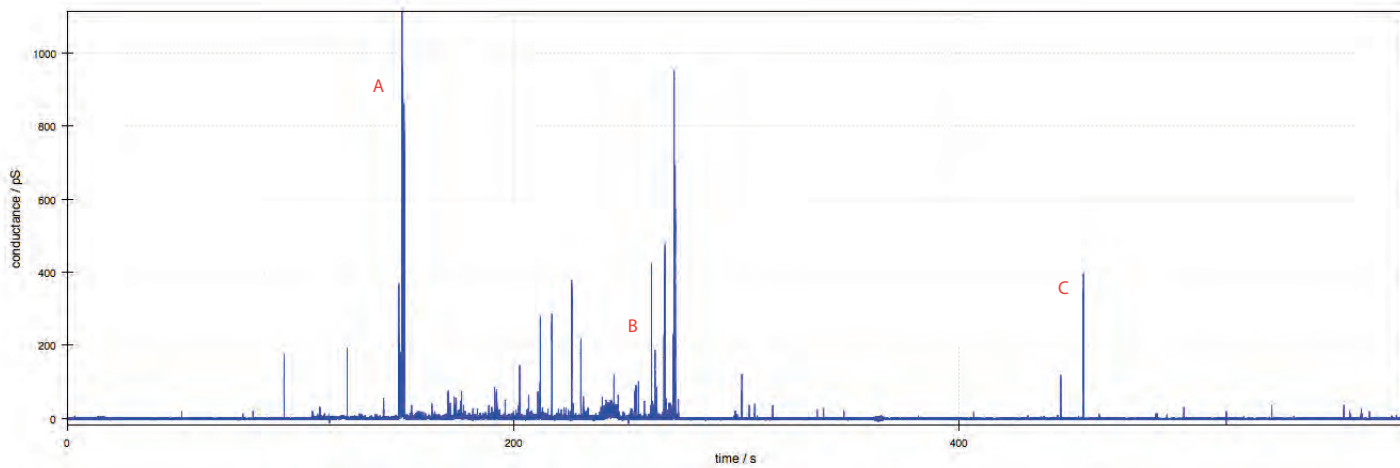


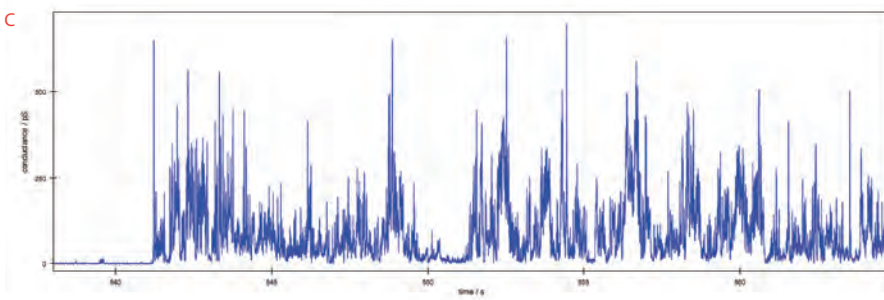
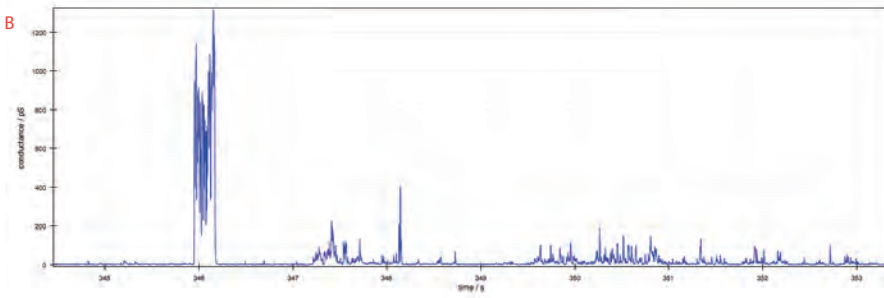
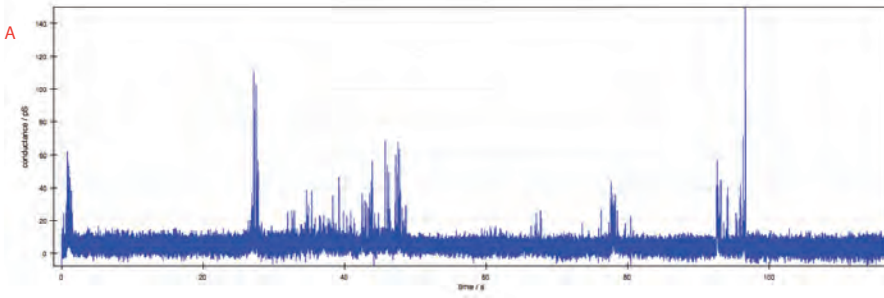
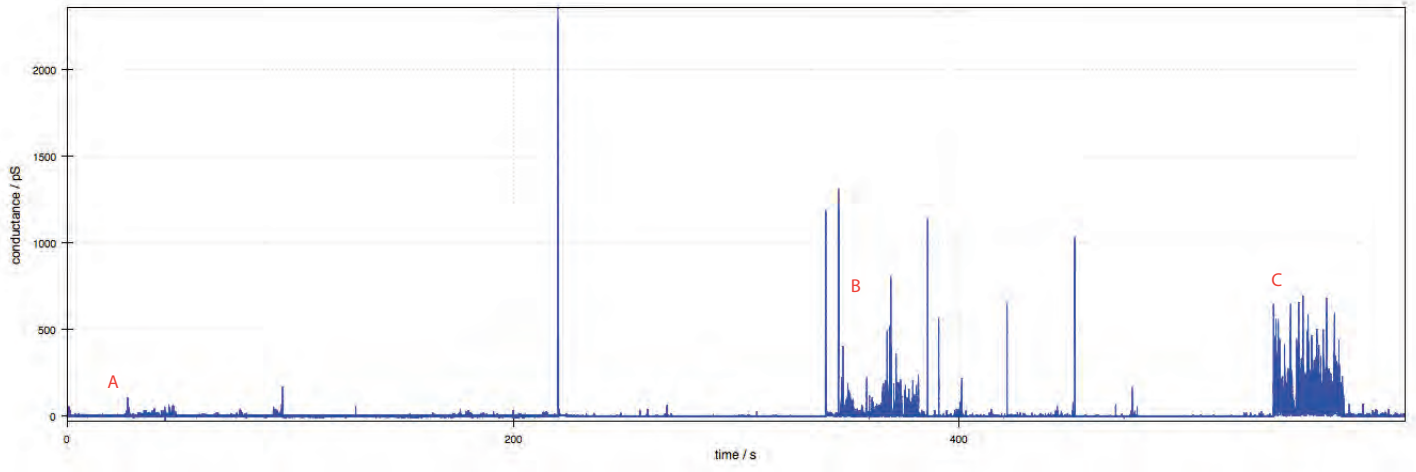
# JC-159 bCD-CholateAmide 2percent 1M CsCl AdCOOH pH 4

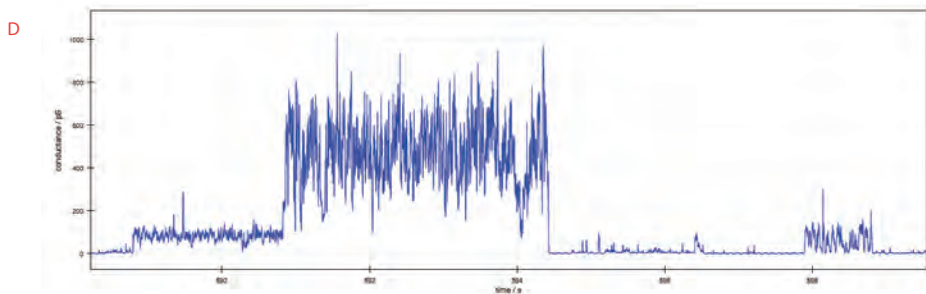
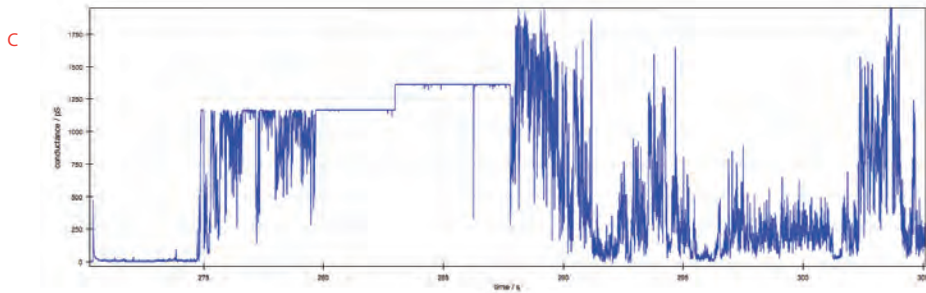
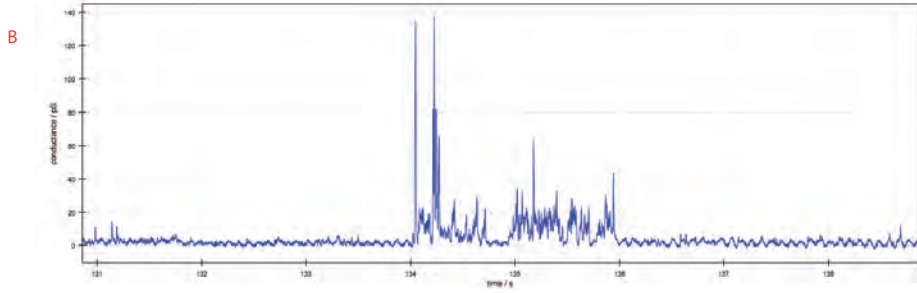
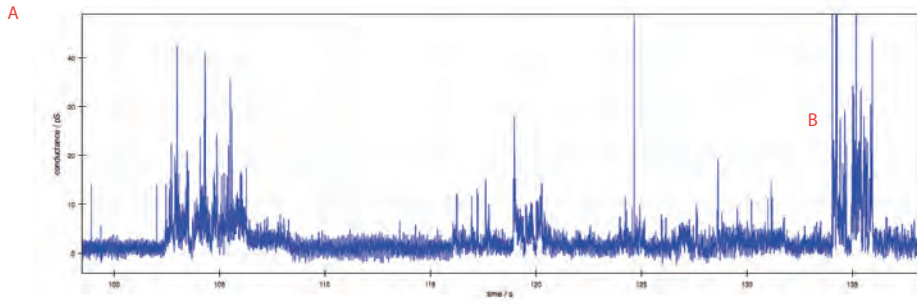
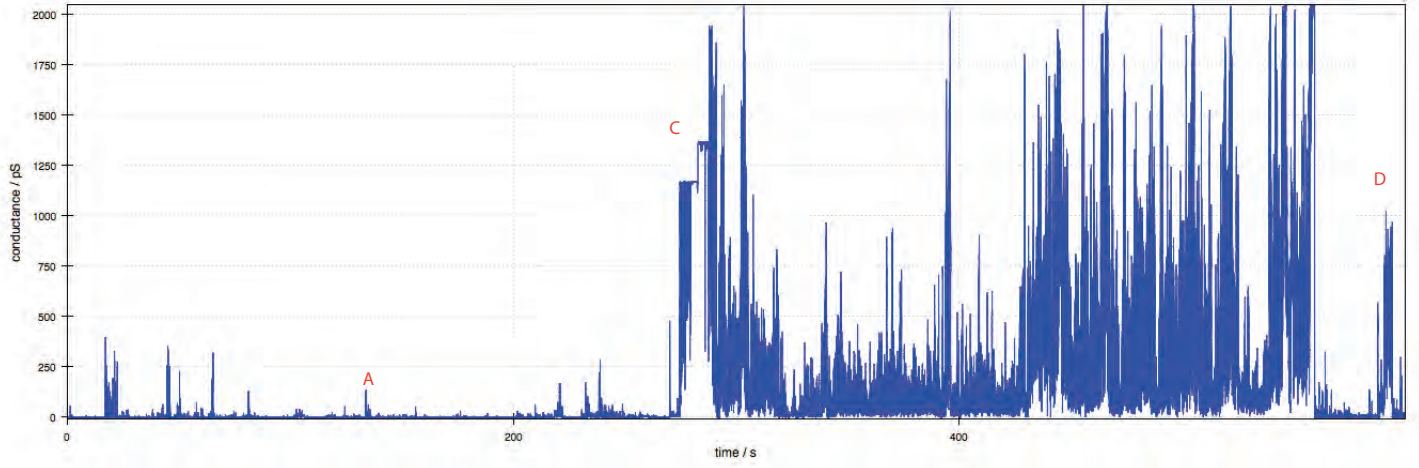


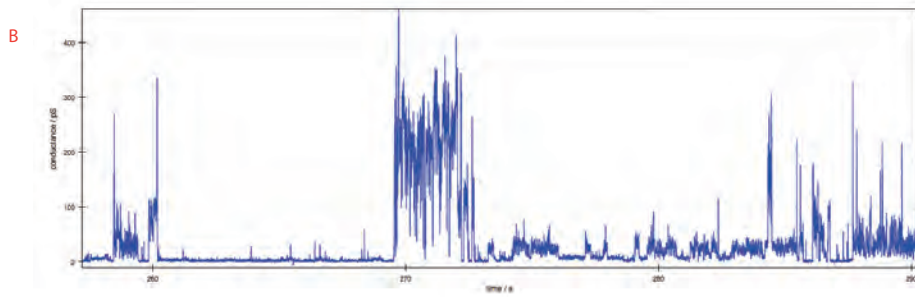
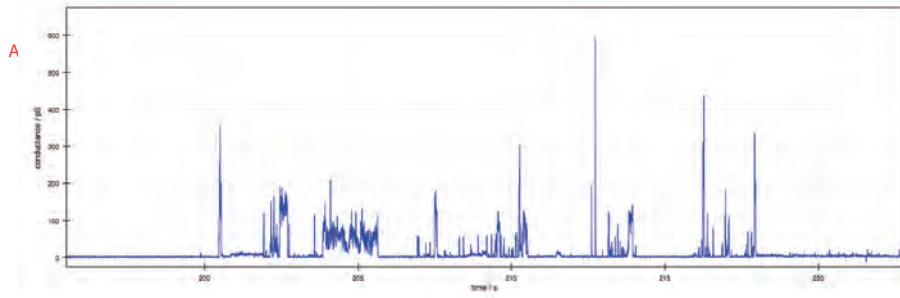
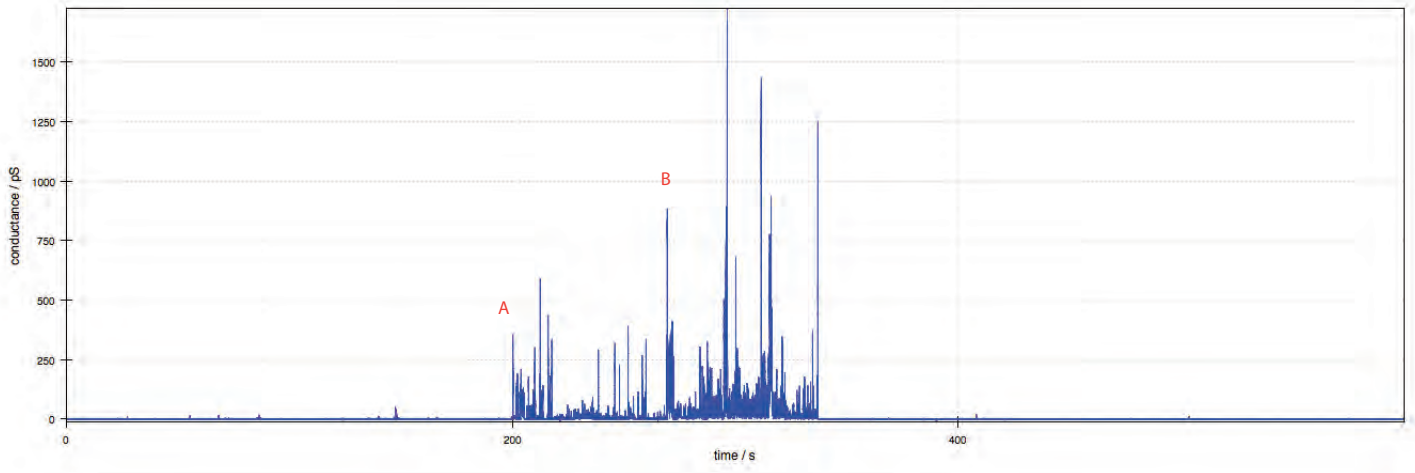
inverse flicker?

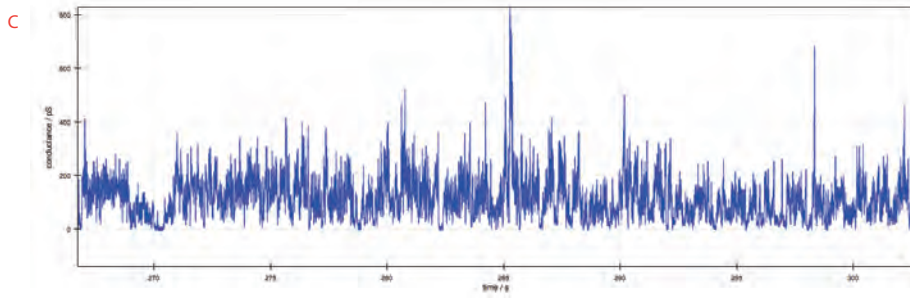
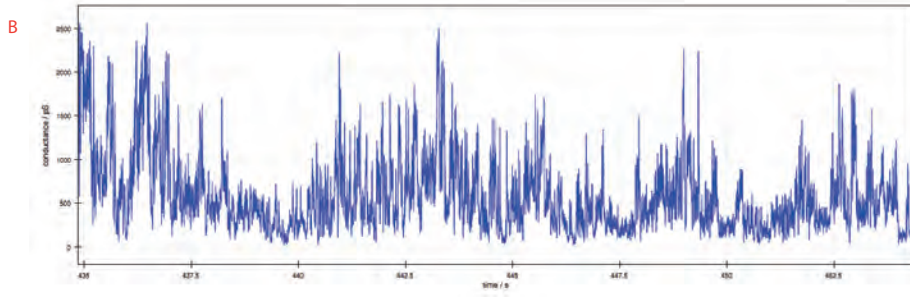
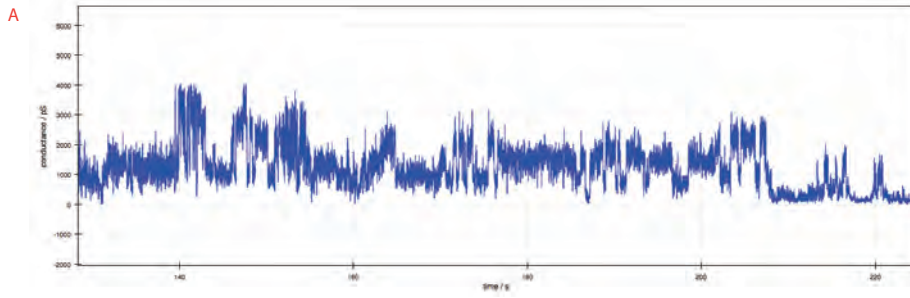
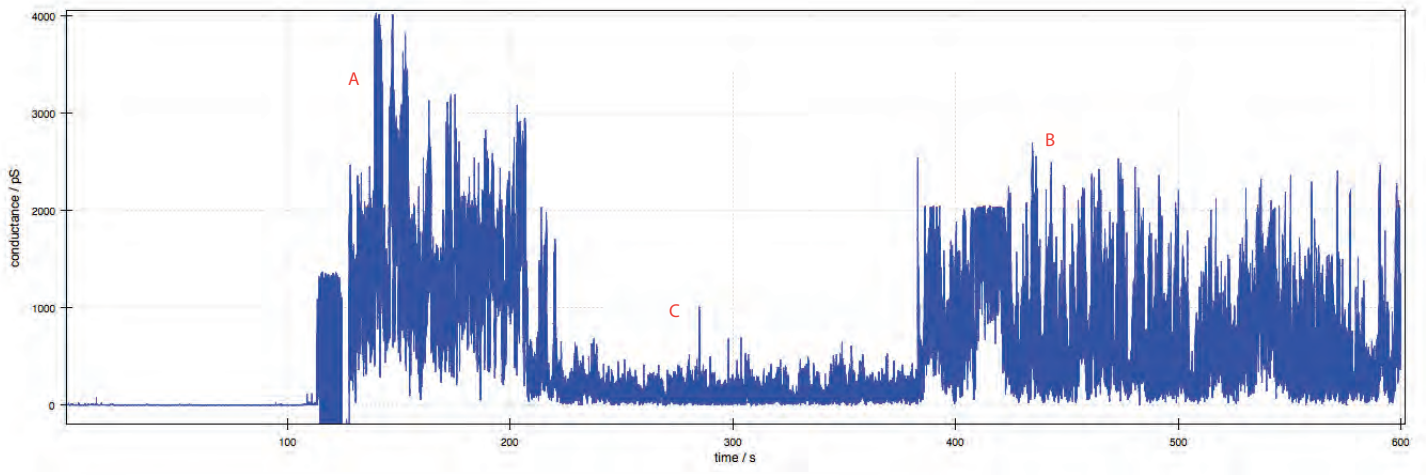


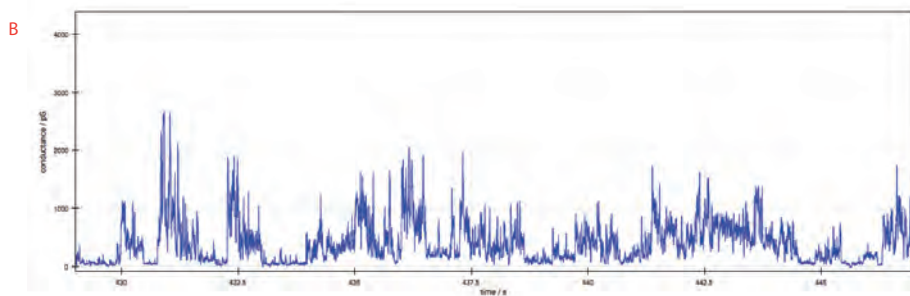
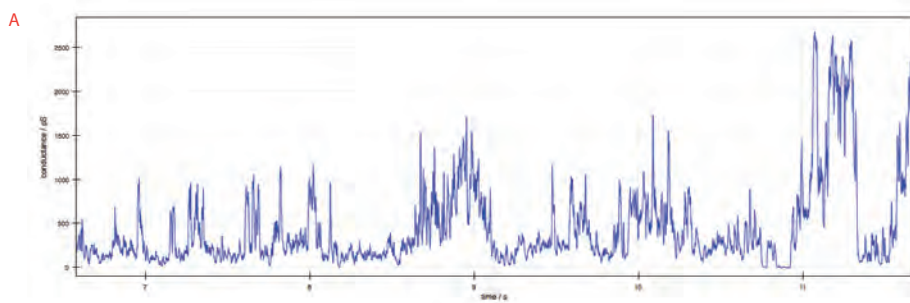
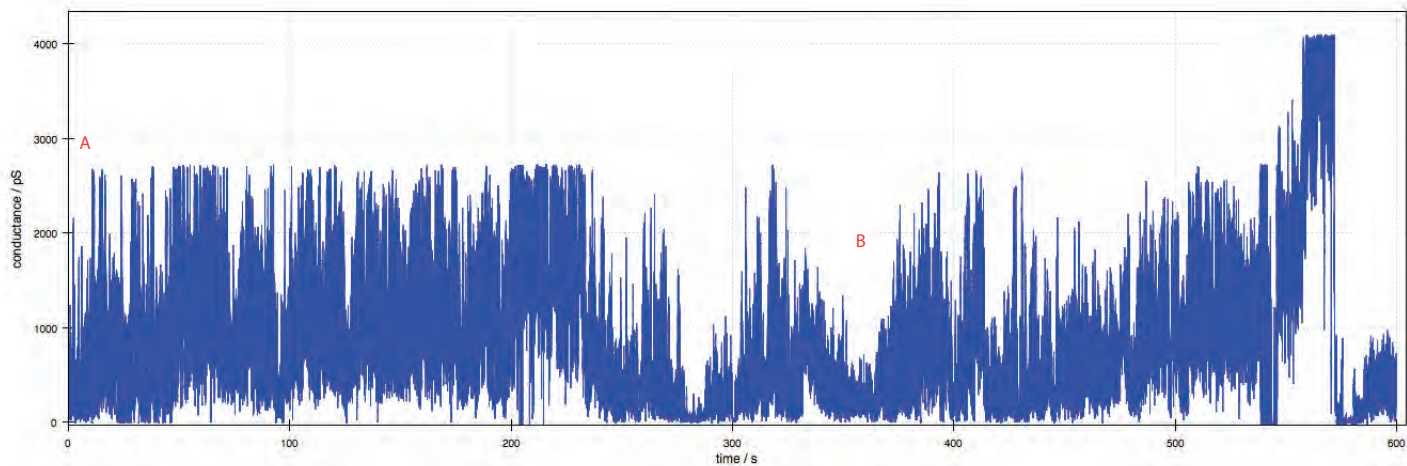


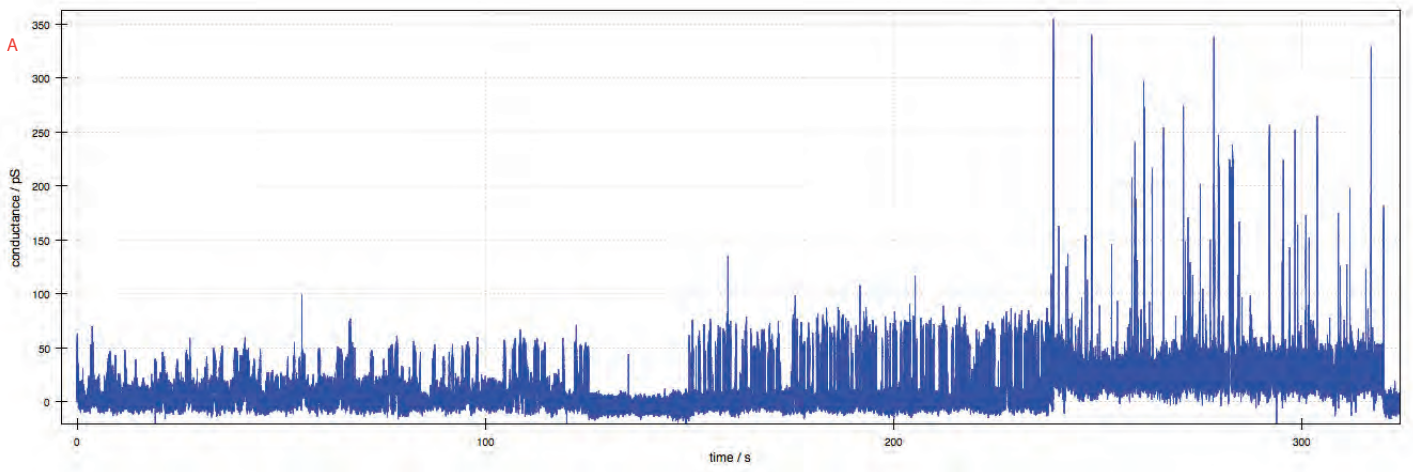
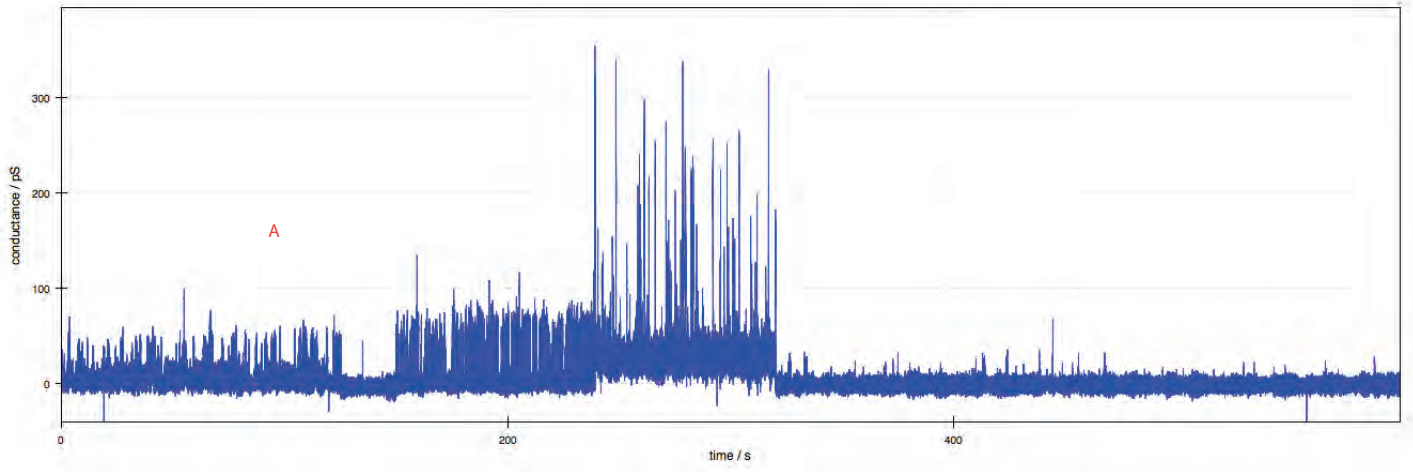




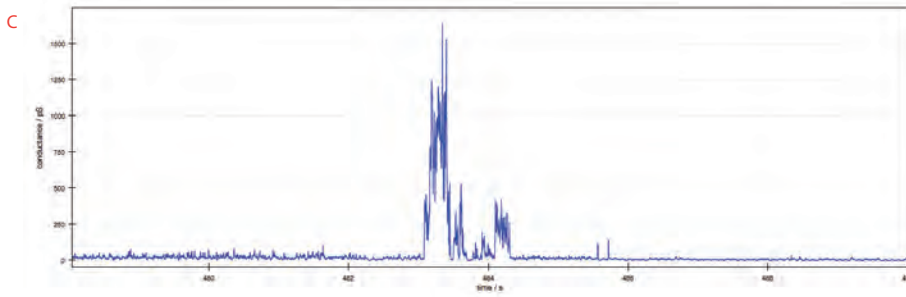
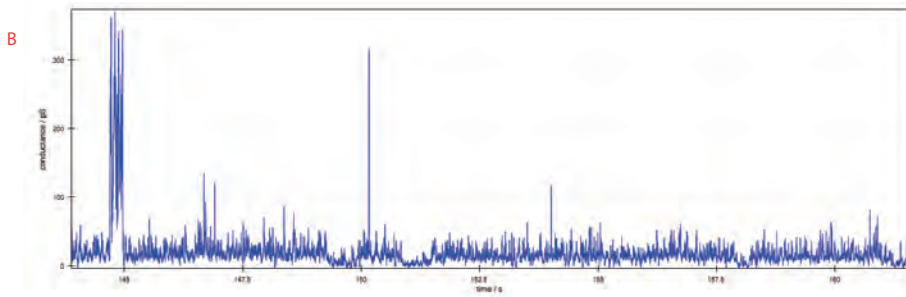
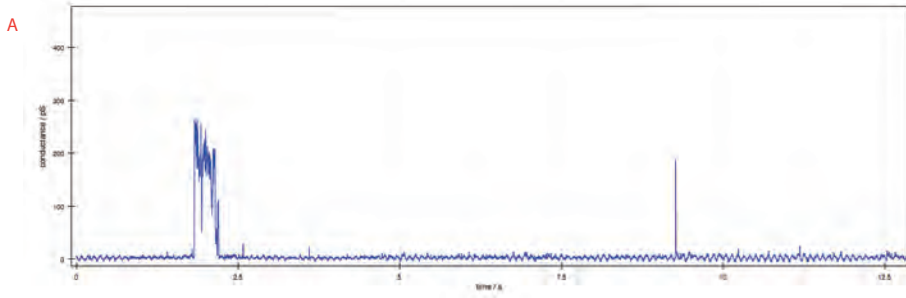
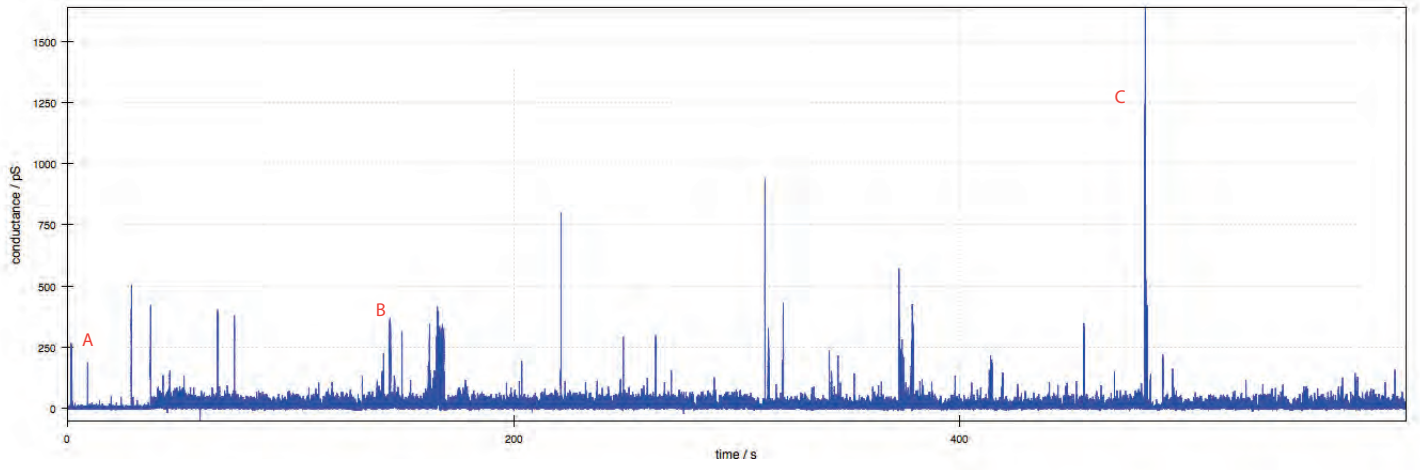


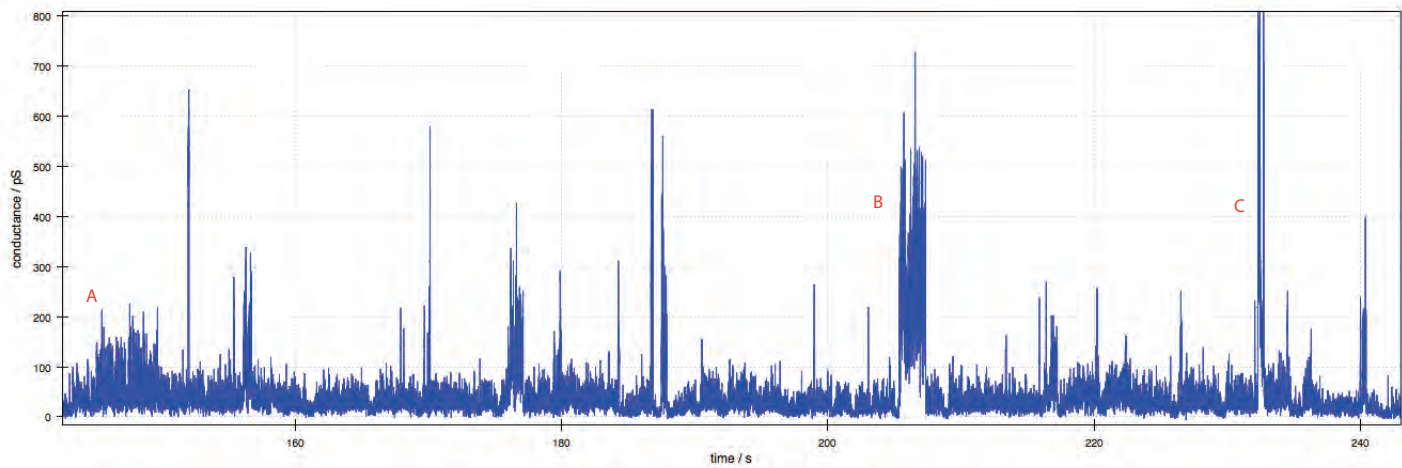




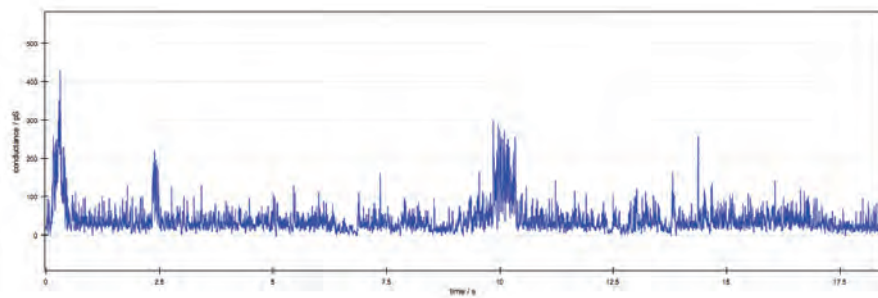


inverse flicker? No potential changes throughout.

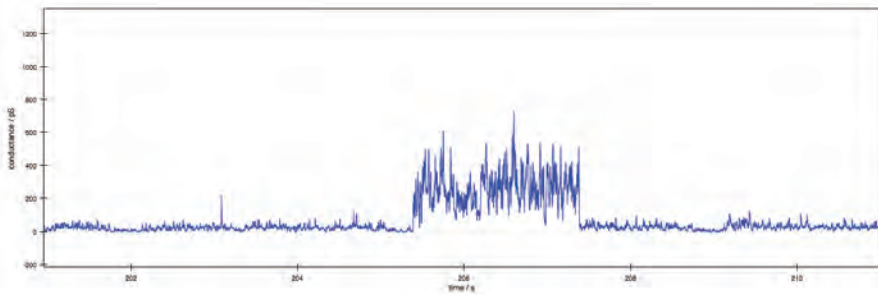




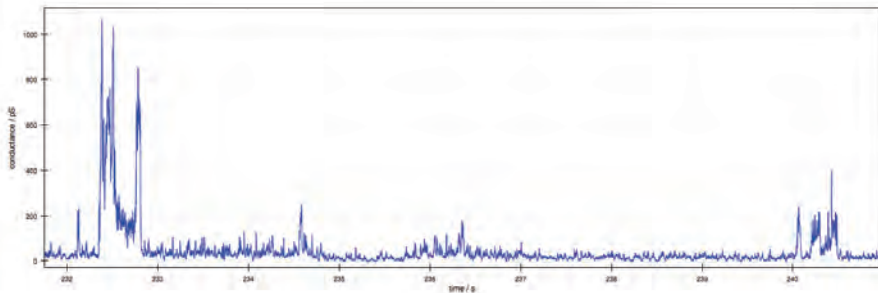
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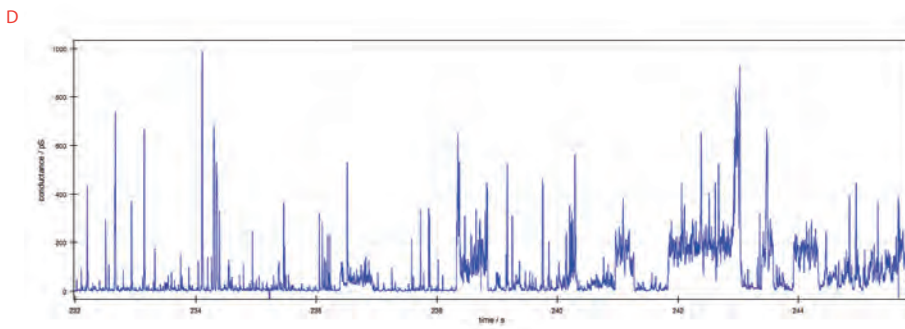
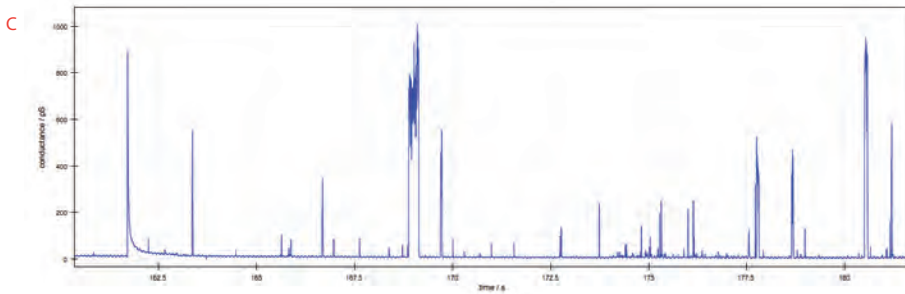
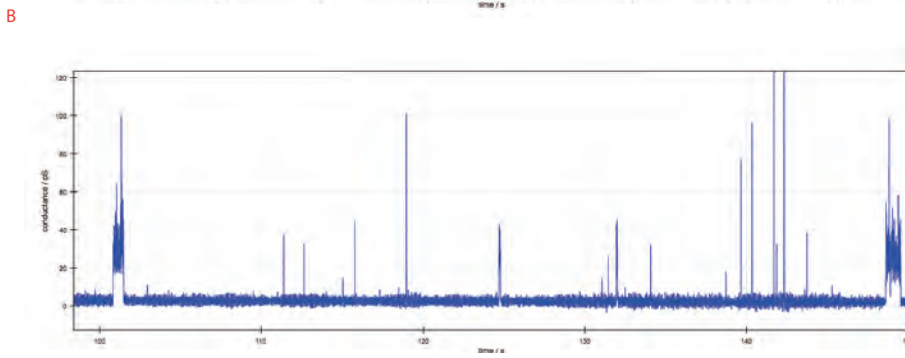
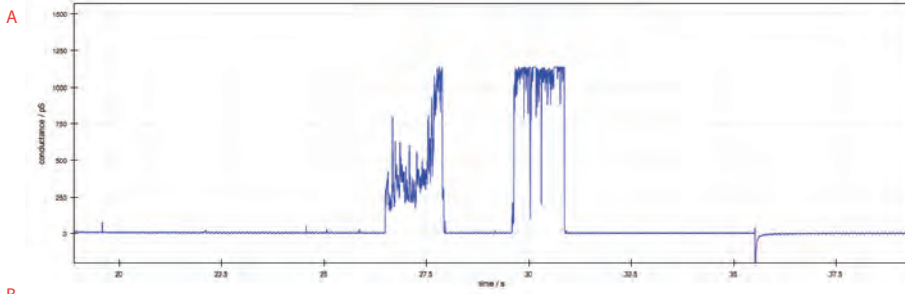
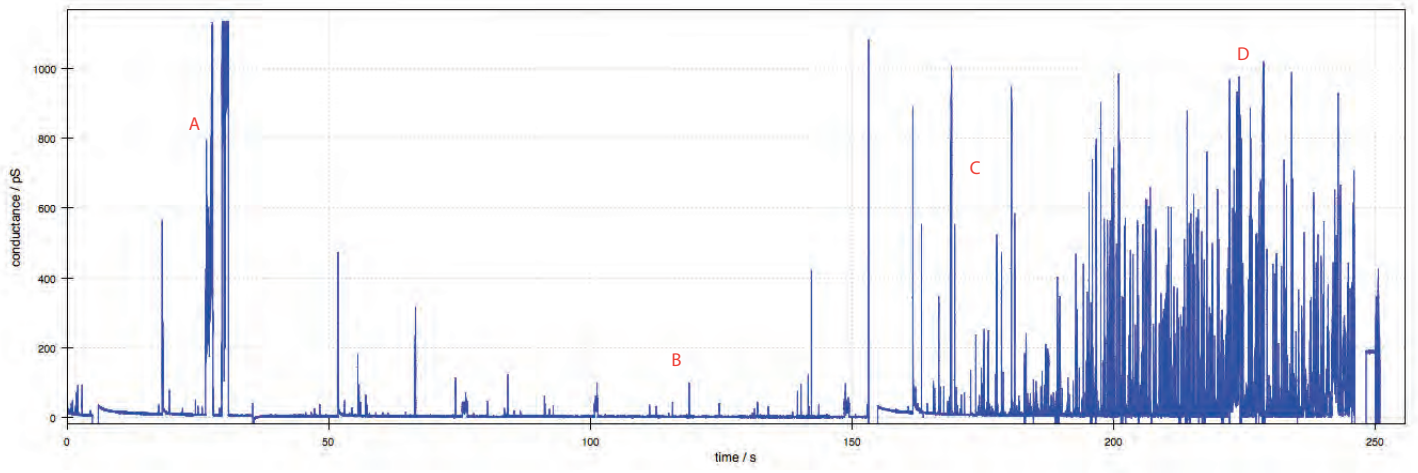


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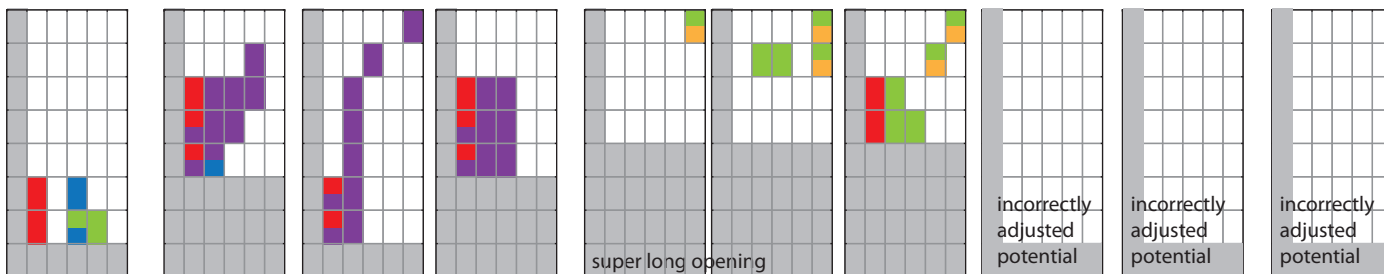
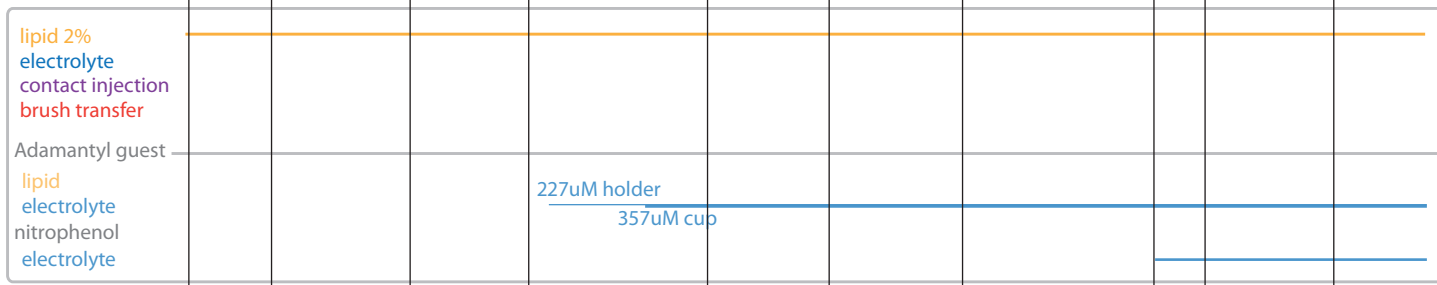
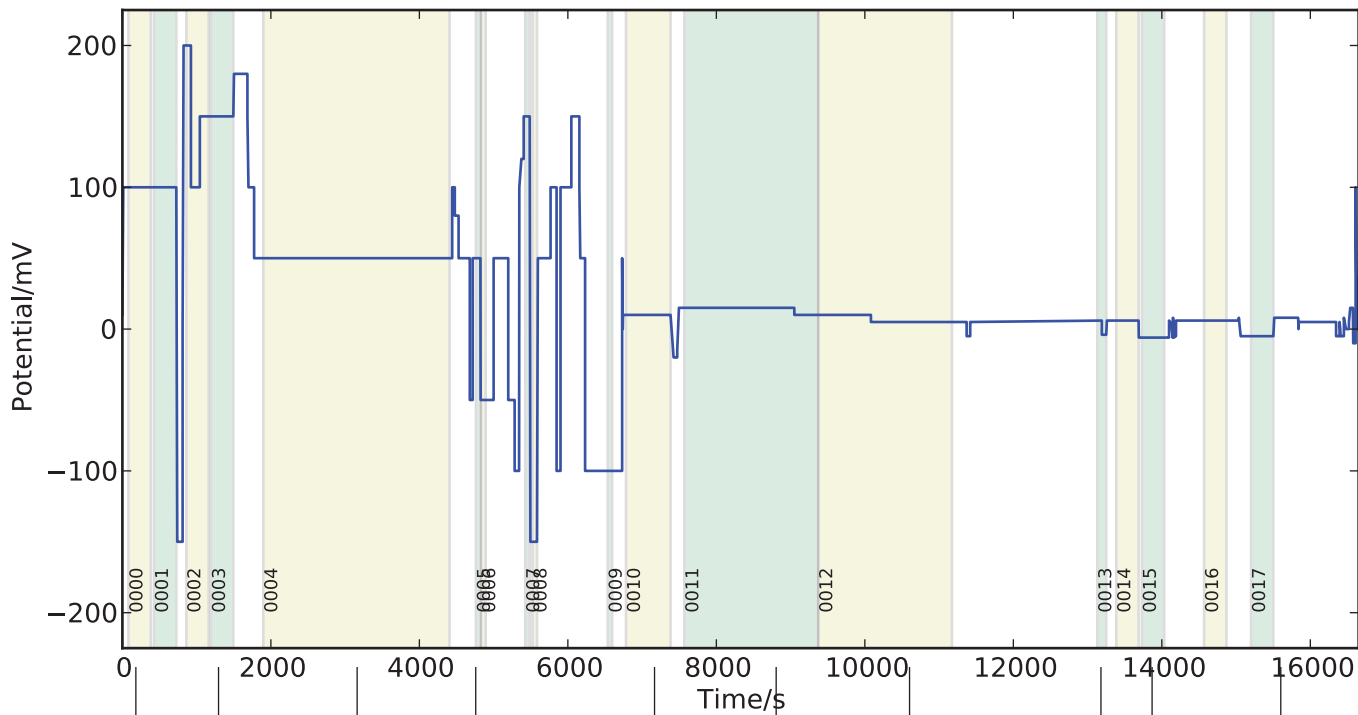


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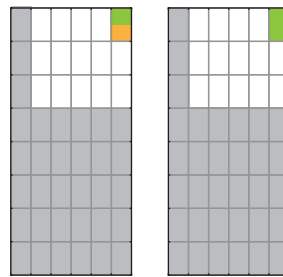
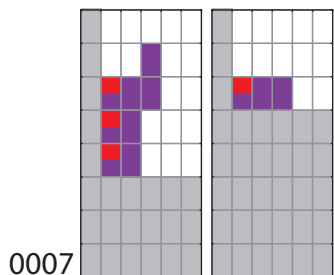
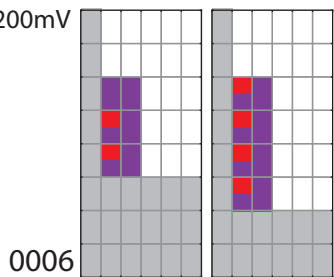
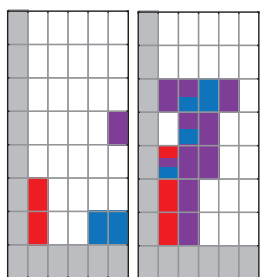




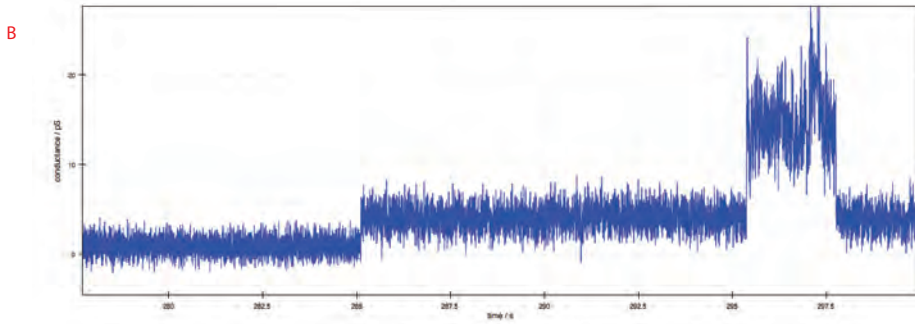
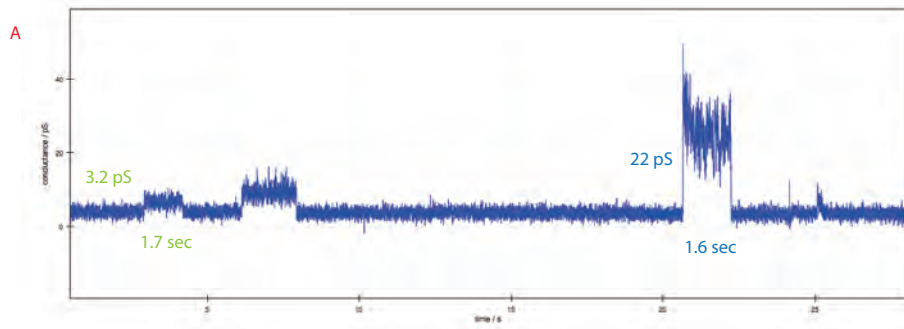
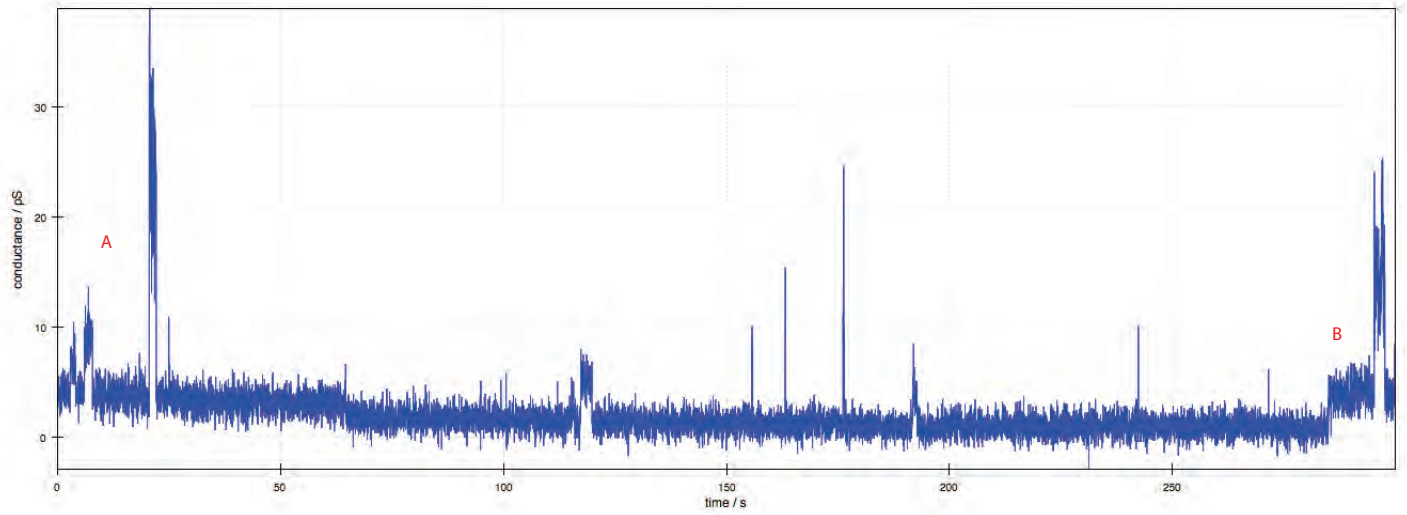
# JC-160 aCD-CholateAmide 2percent 1M CsCl pH 7

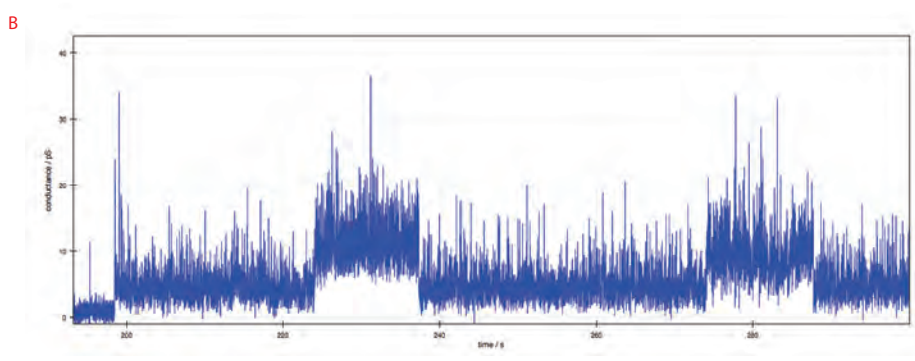
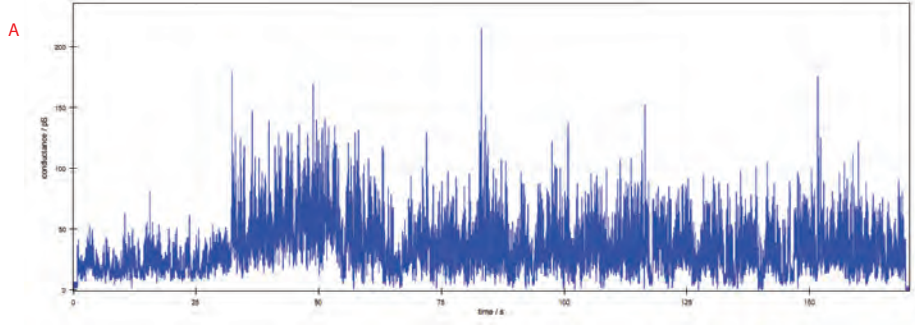
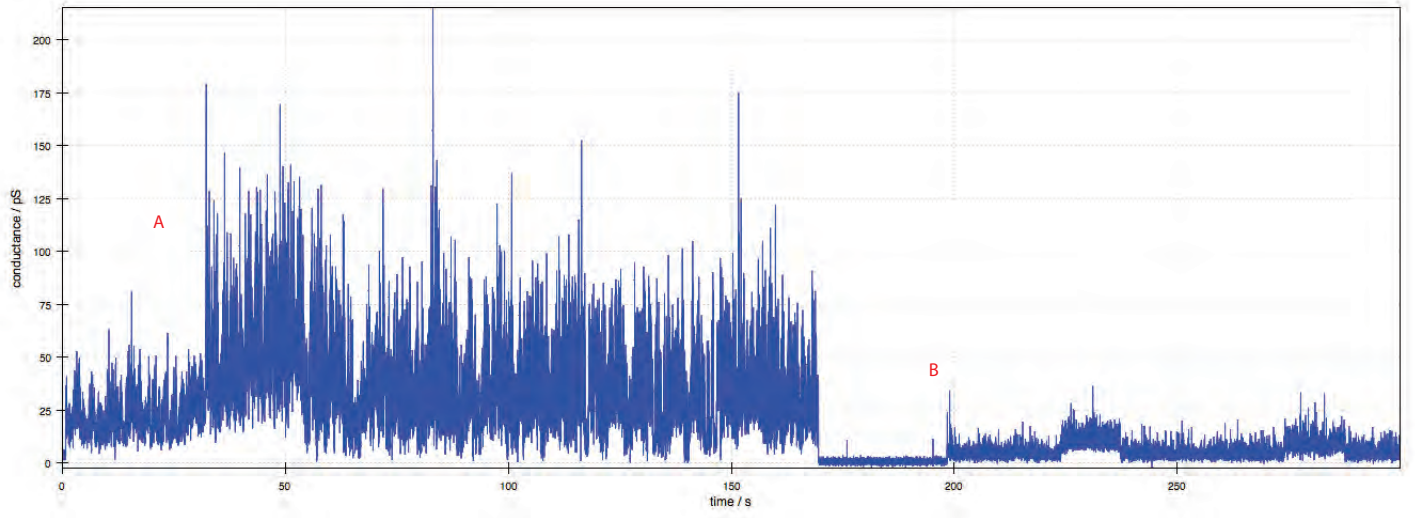


IV 0->200mV

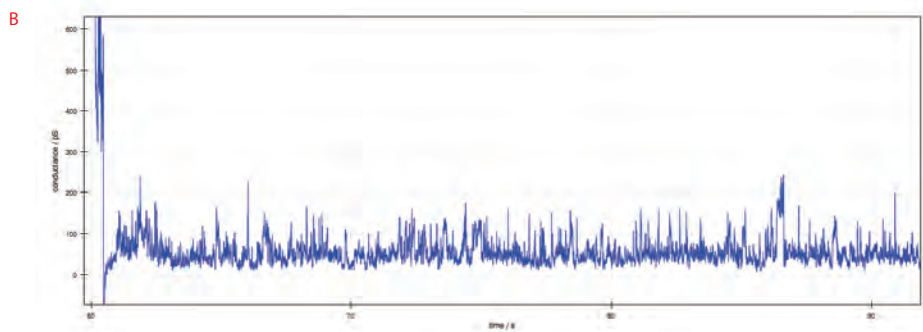
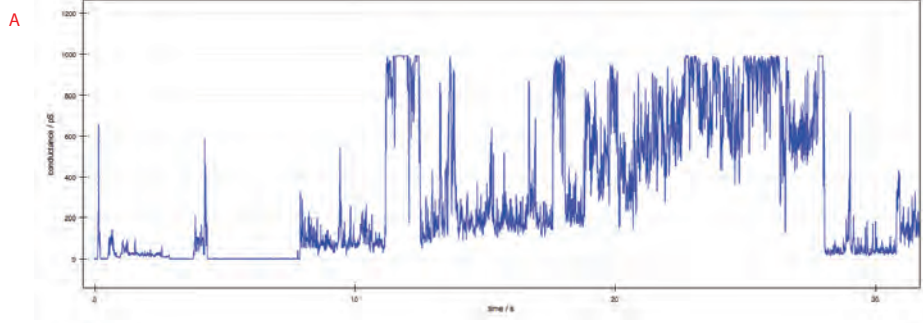
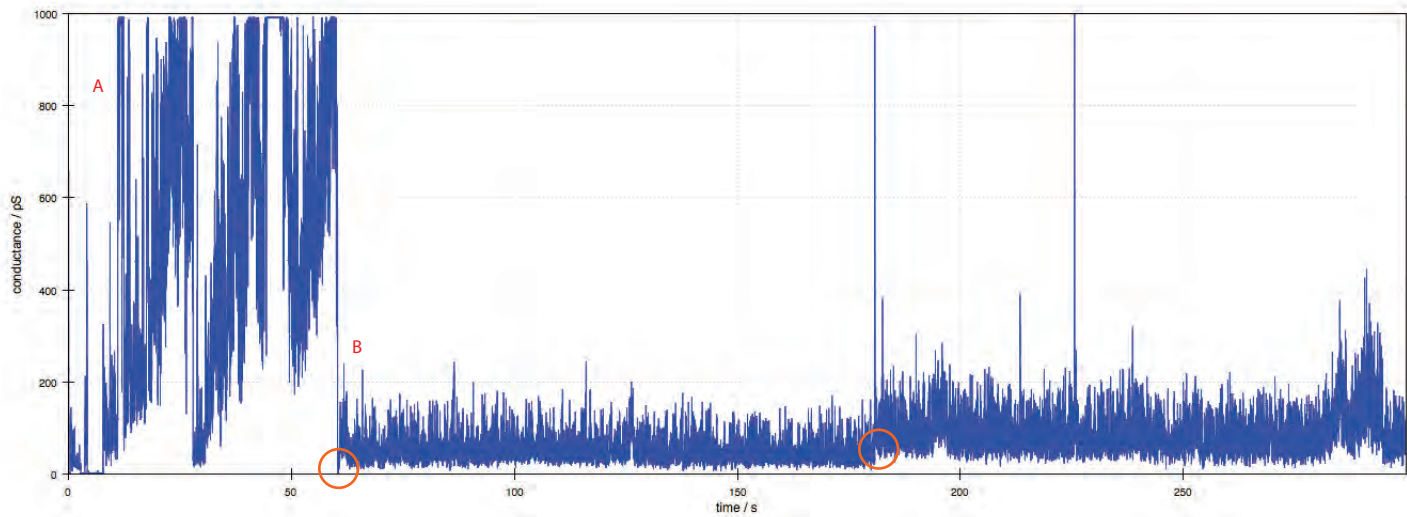


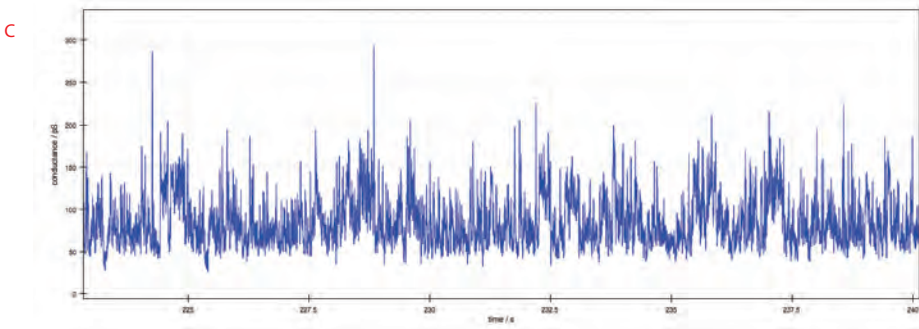
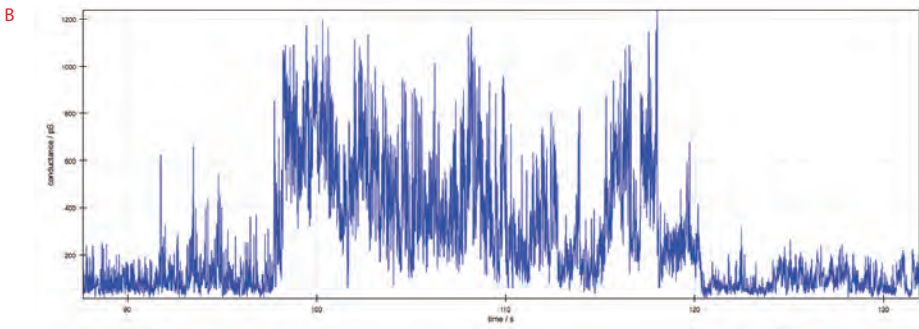
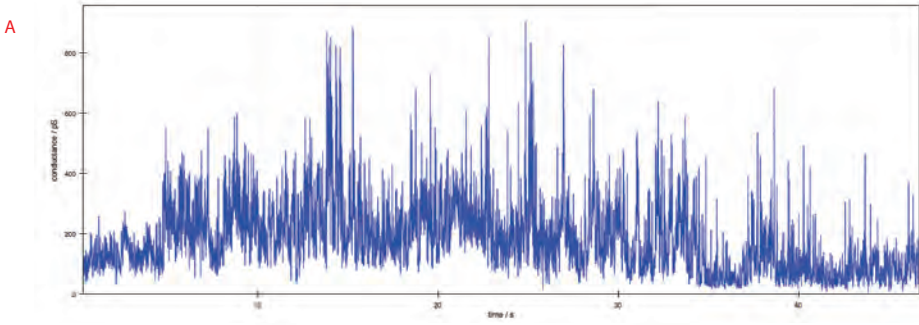
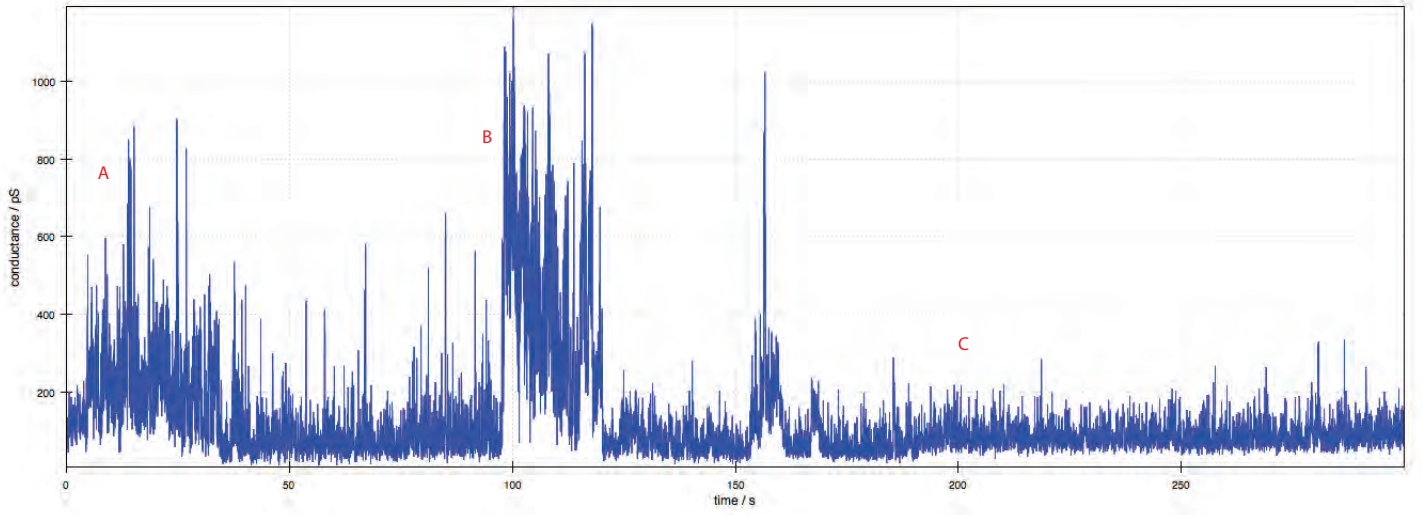
0014 0016

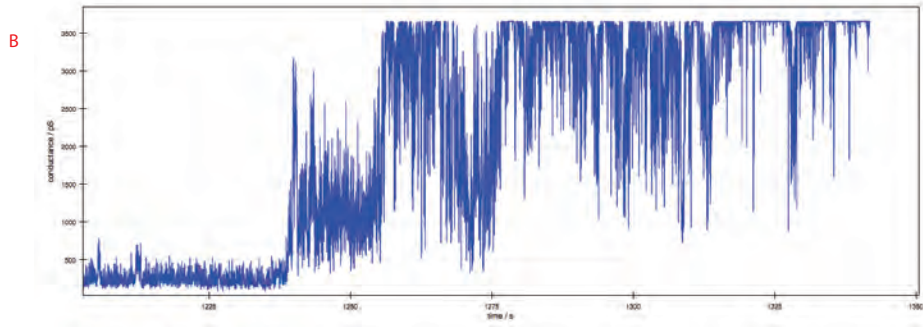
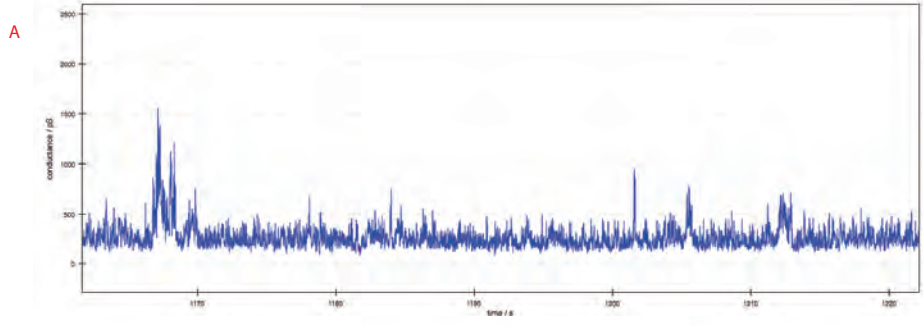
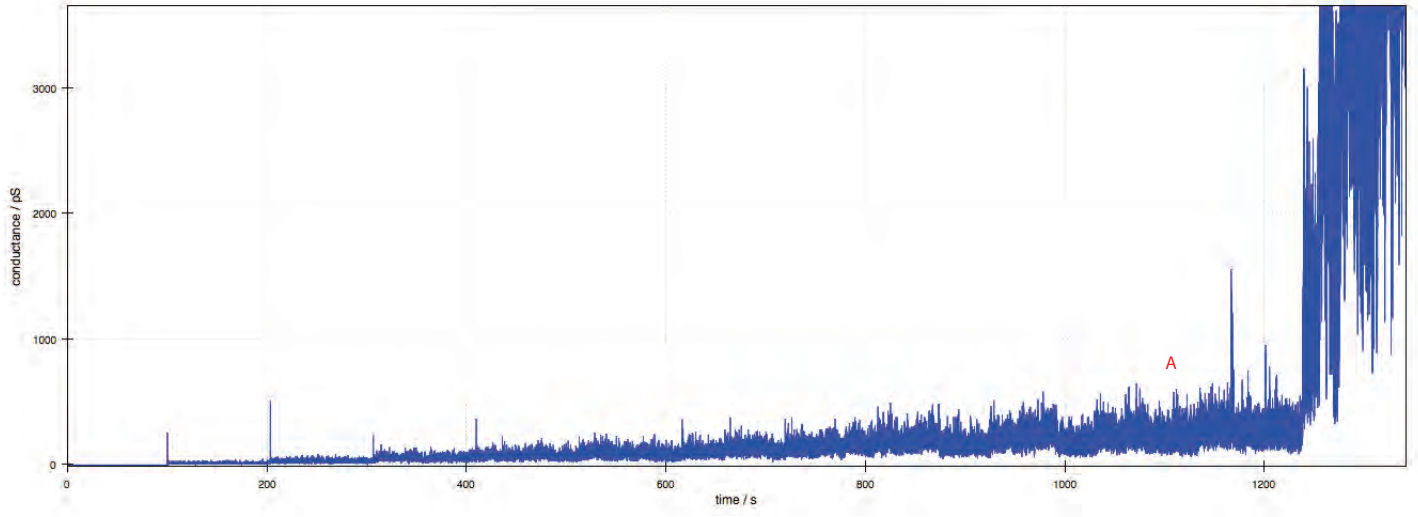




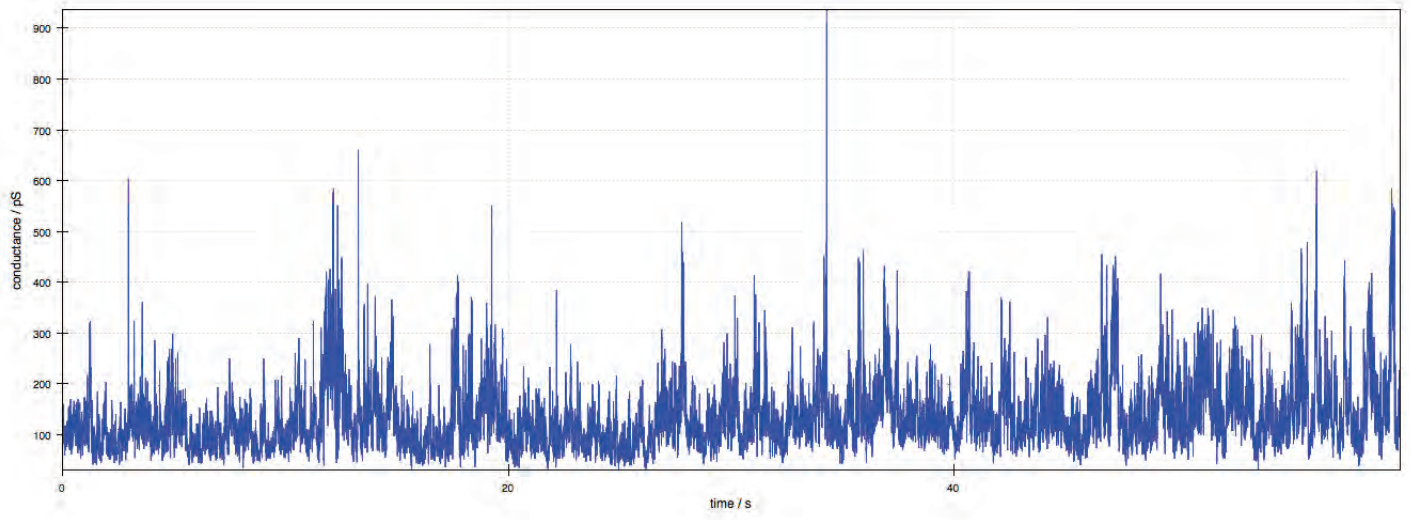
160-0002



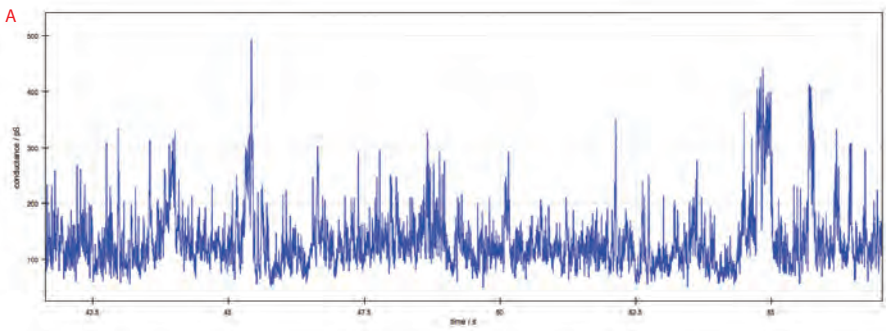
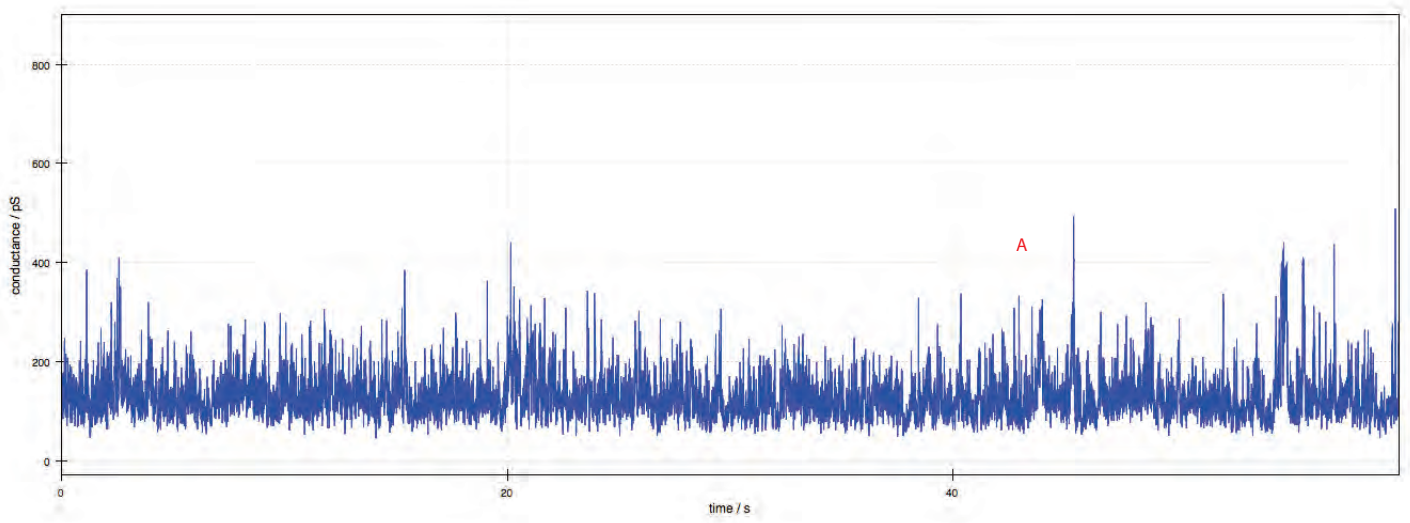


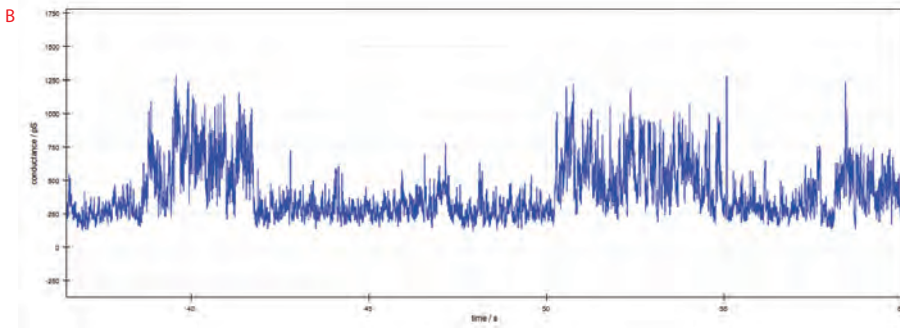
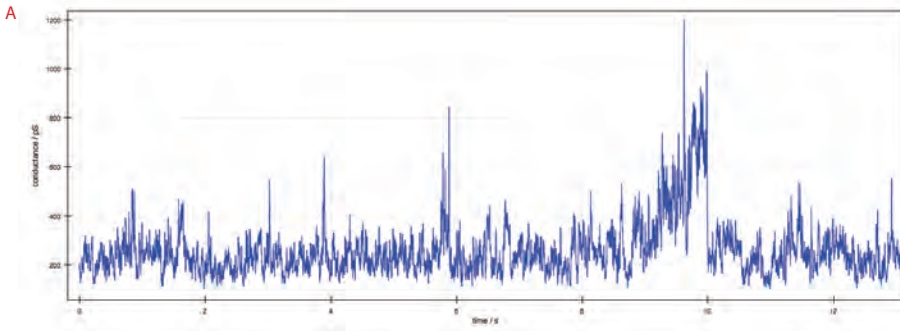
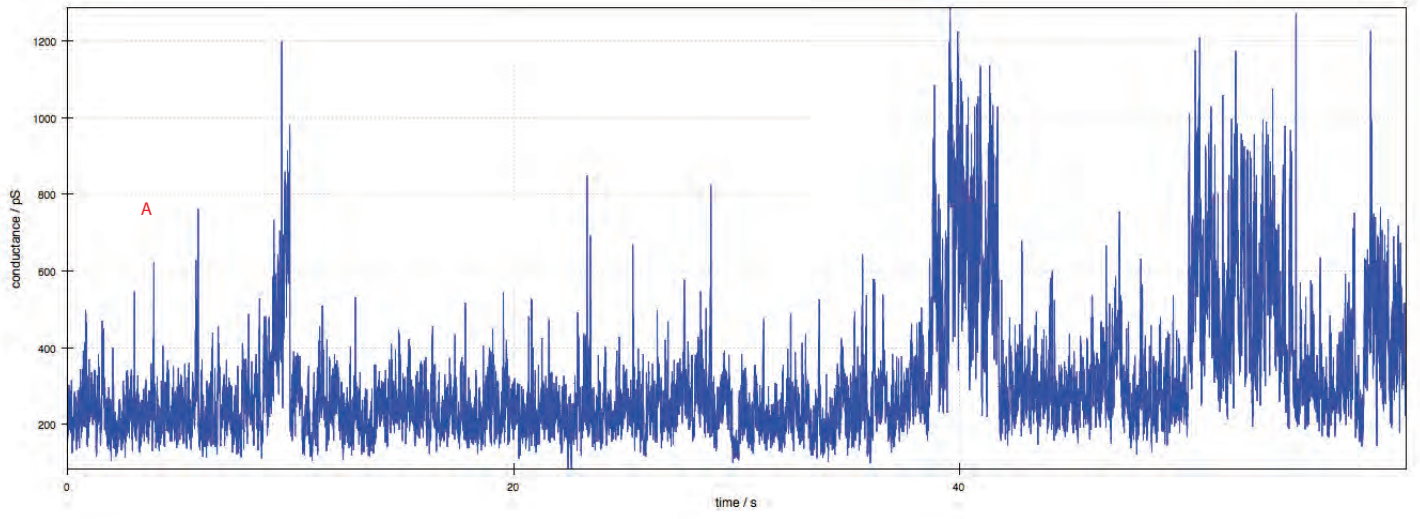


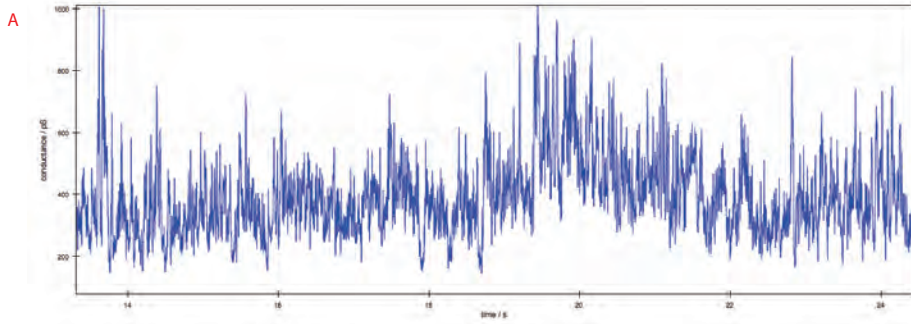
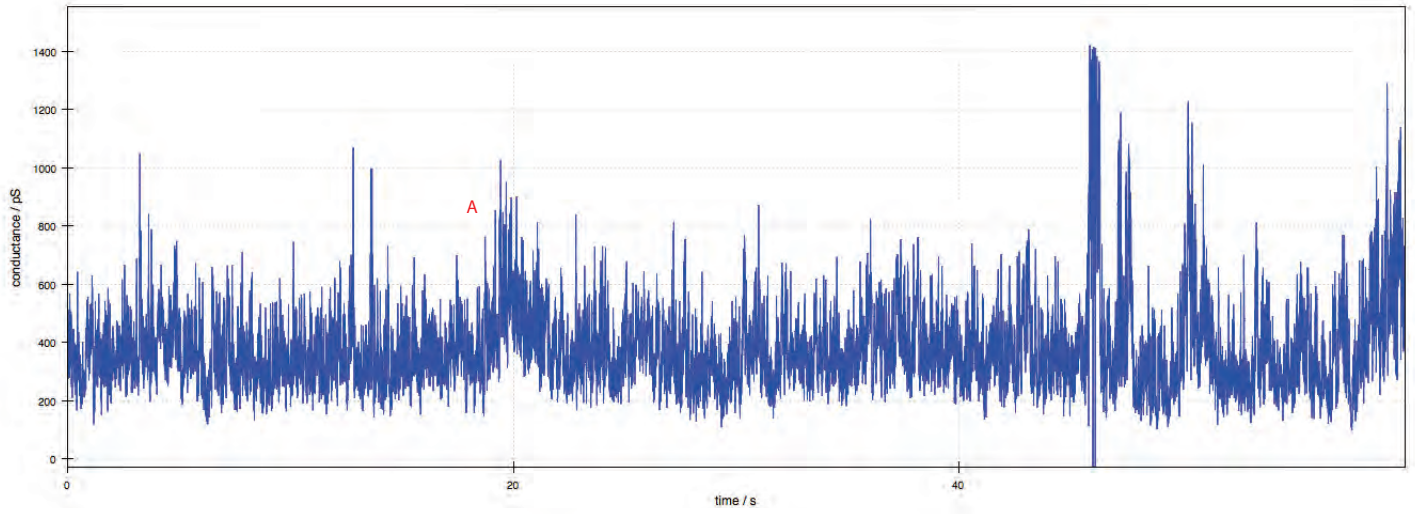
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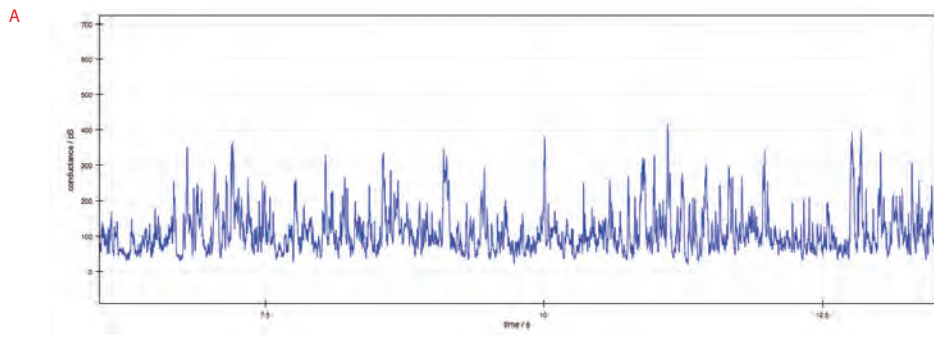
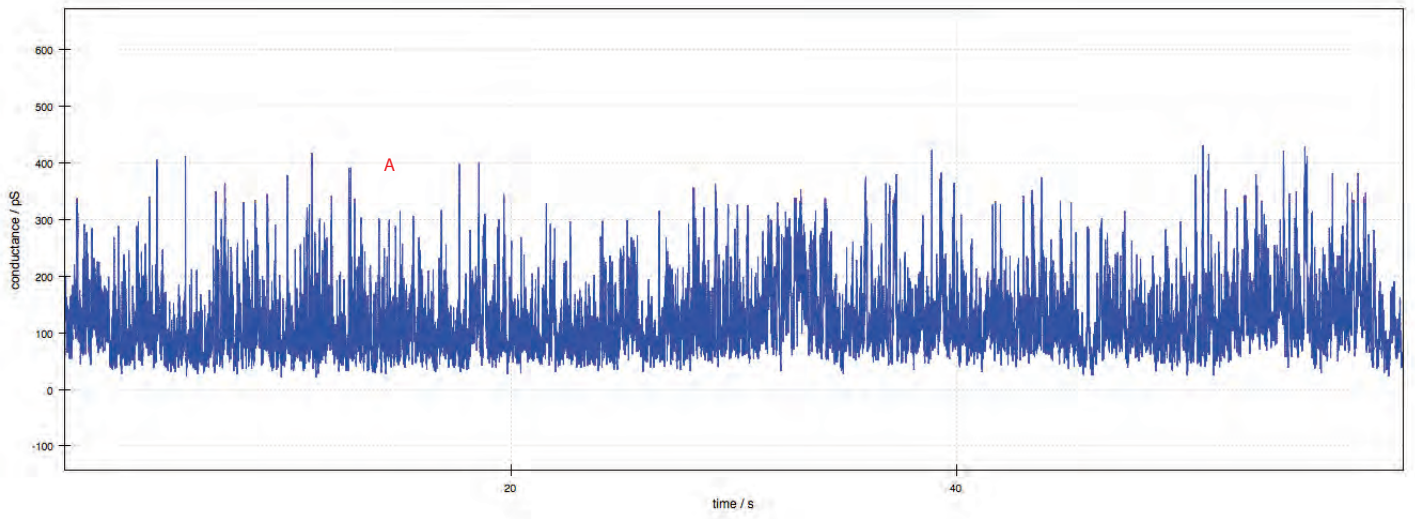


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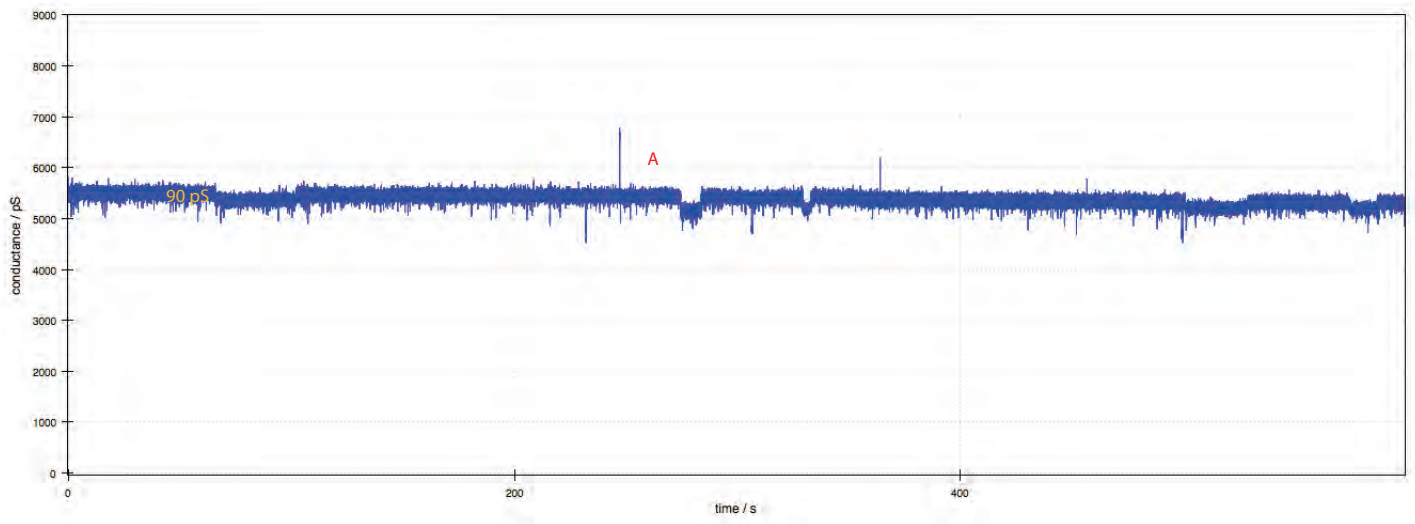




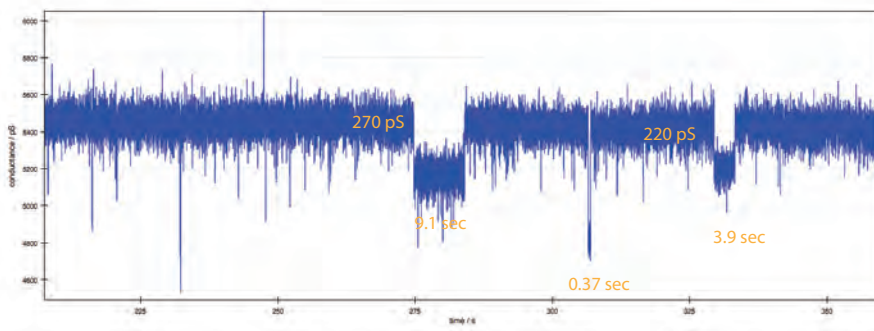




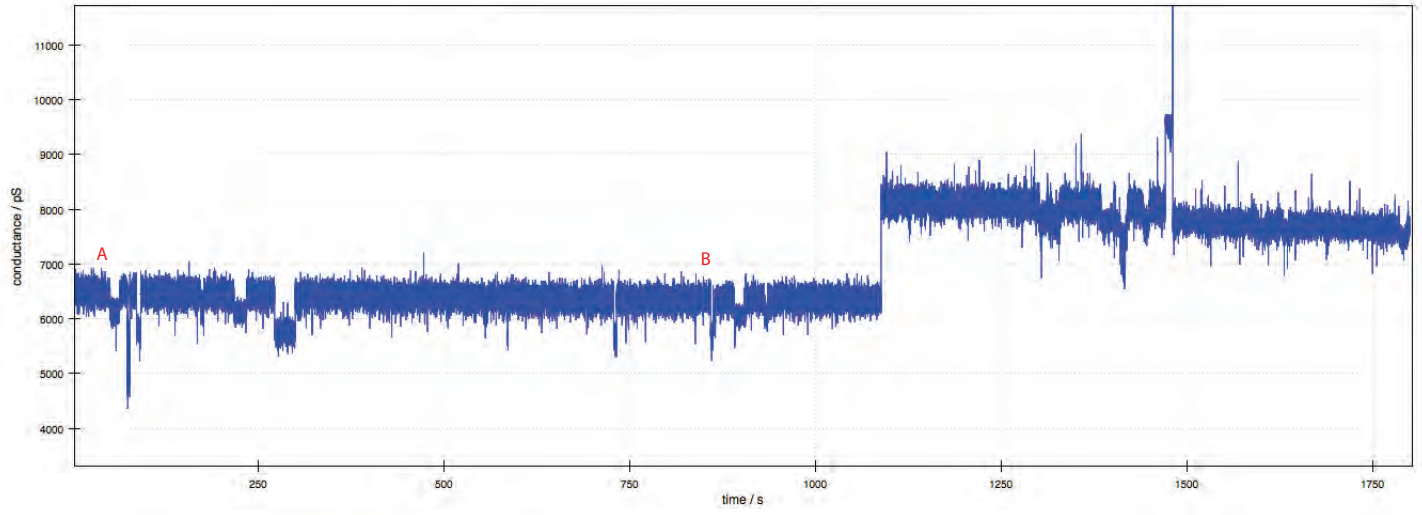
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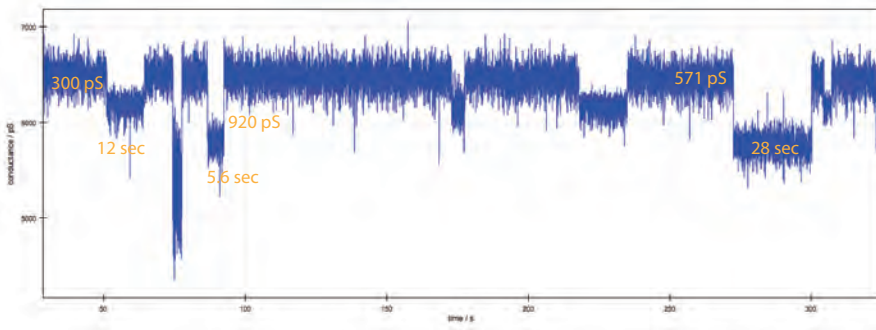
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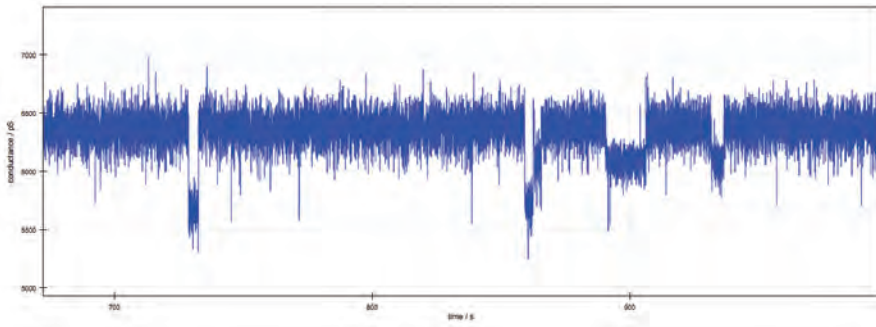
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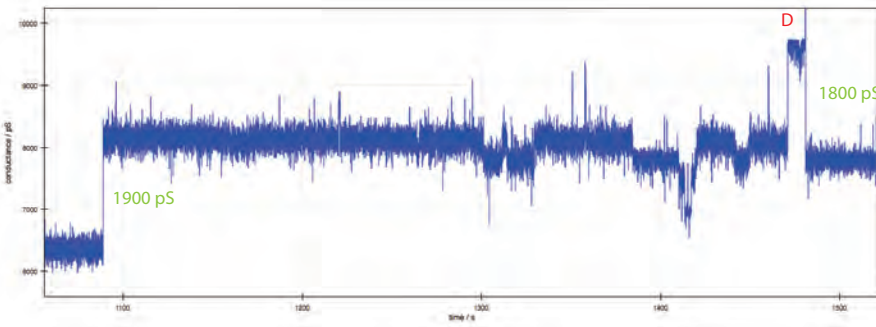
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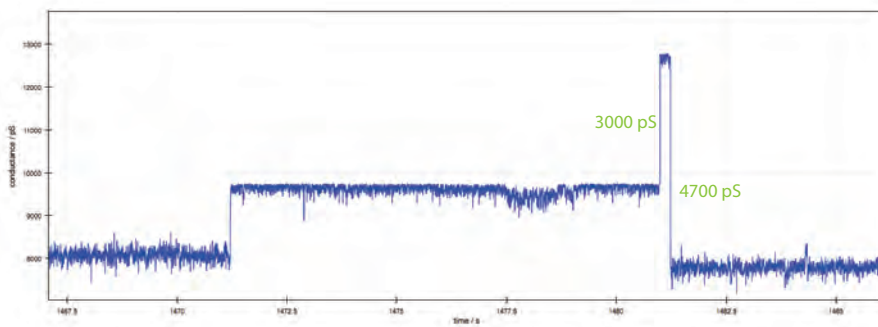
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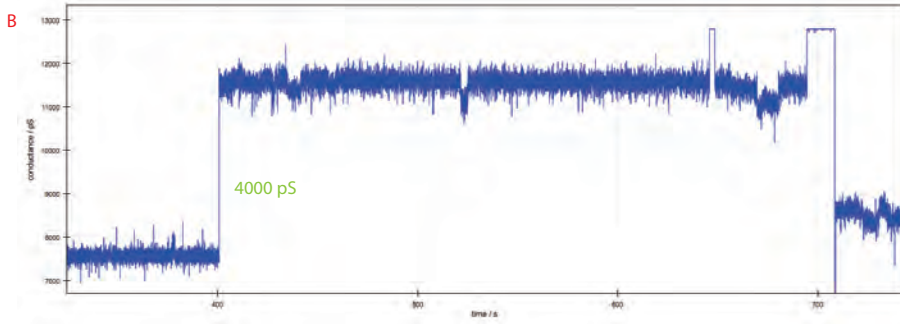
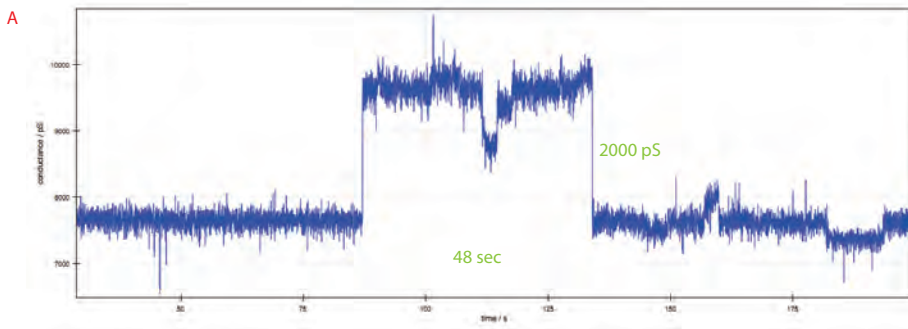
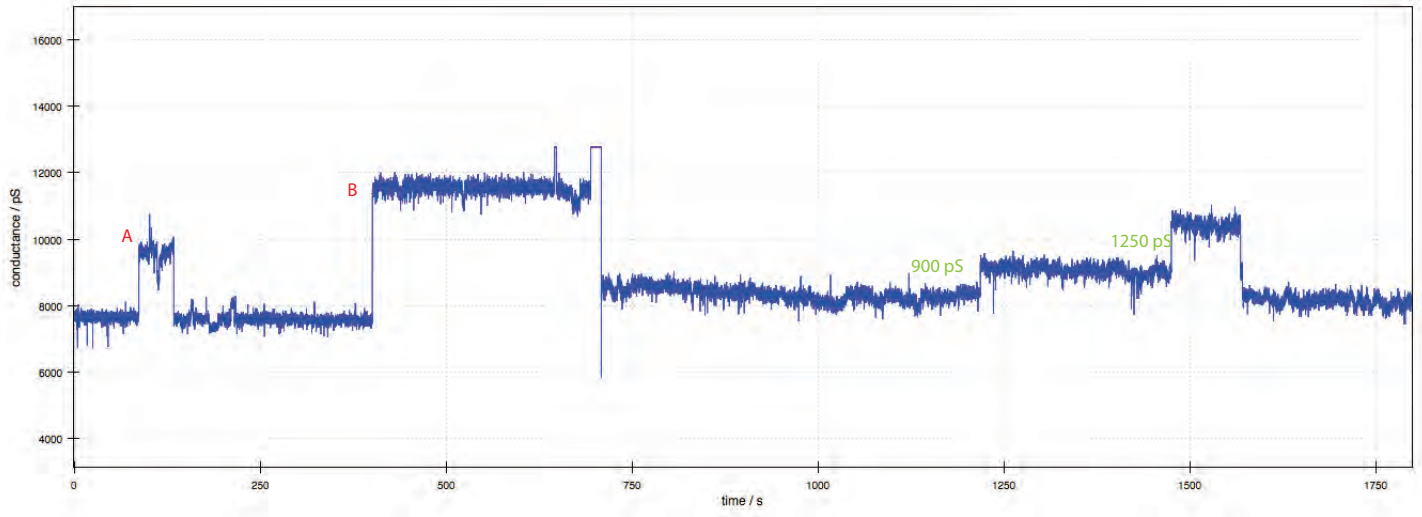
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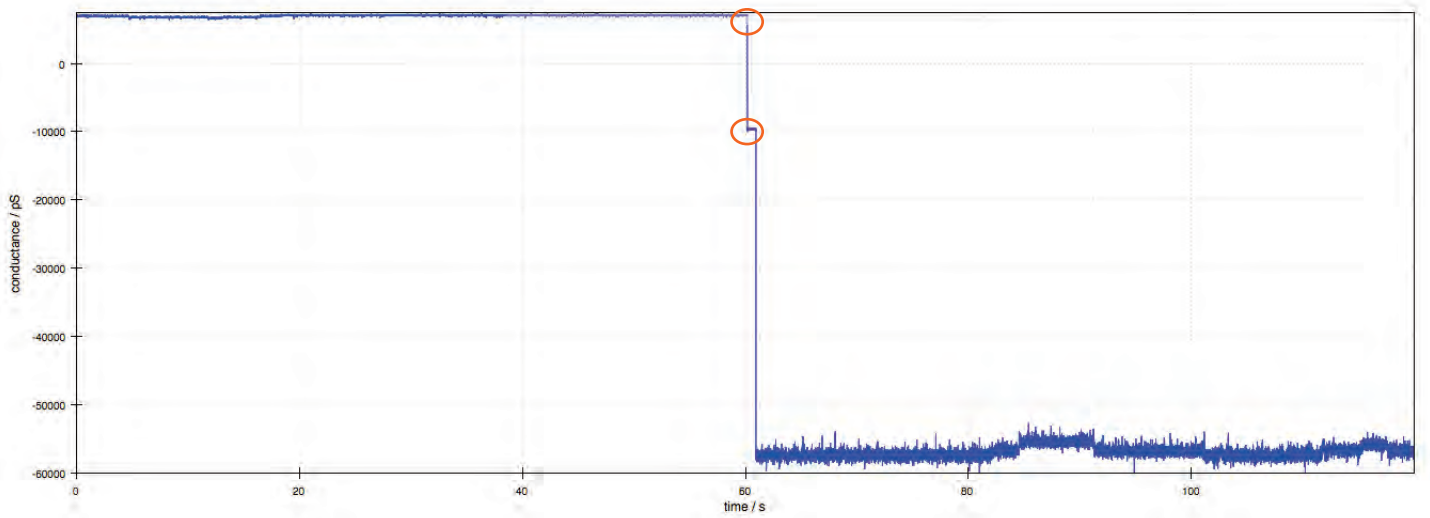
D



160-0012

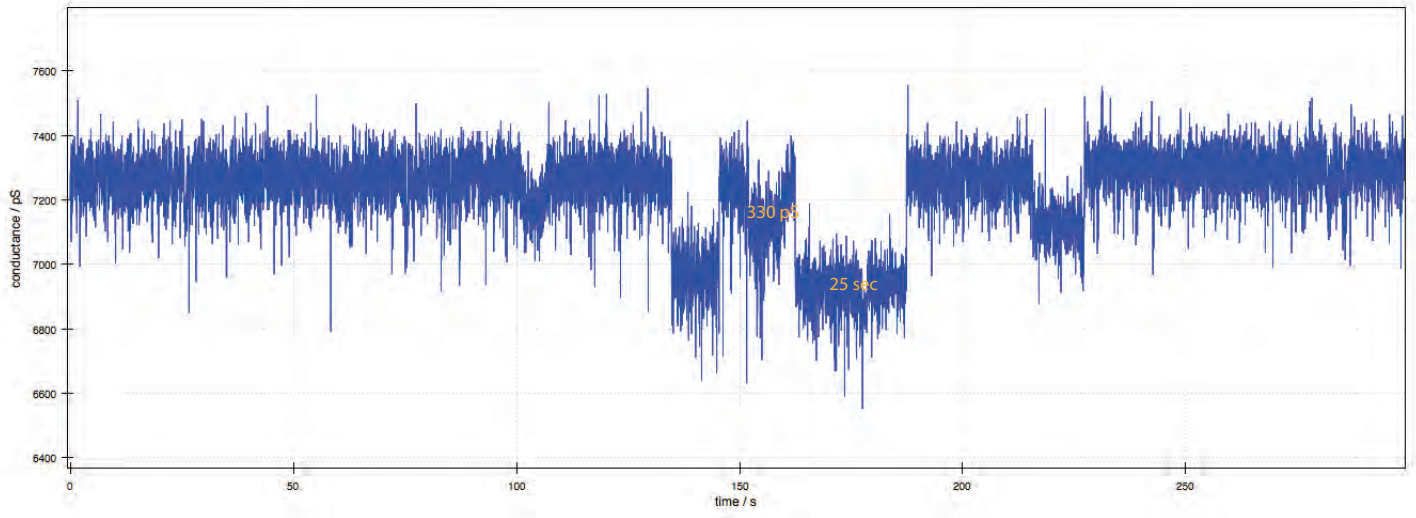


160-0013

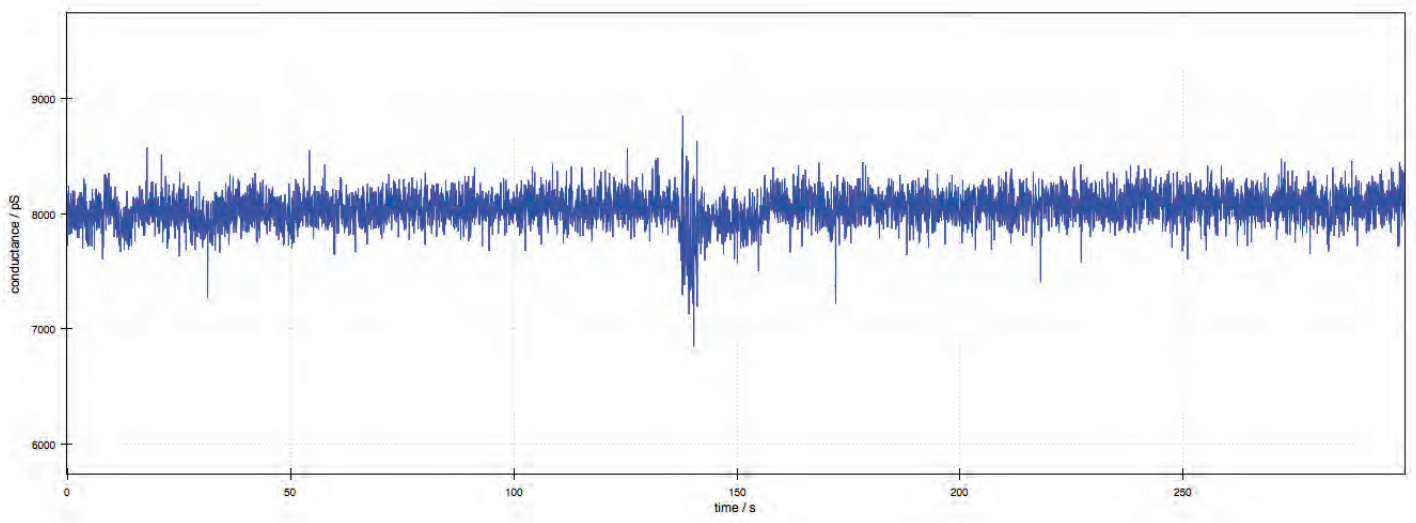


Incorrectly corrected junction potentials

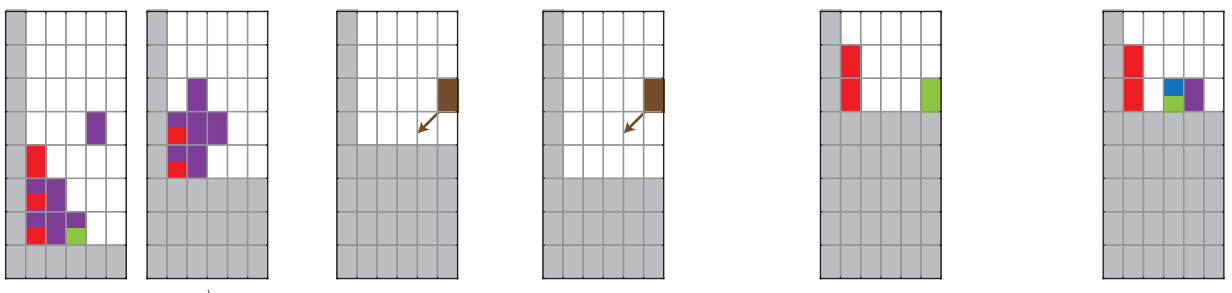
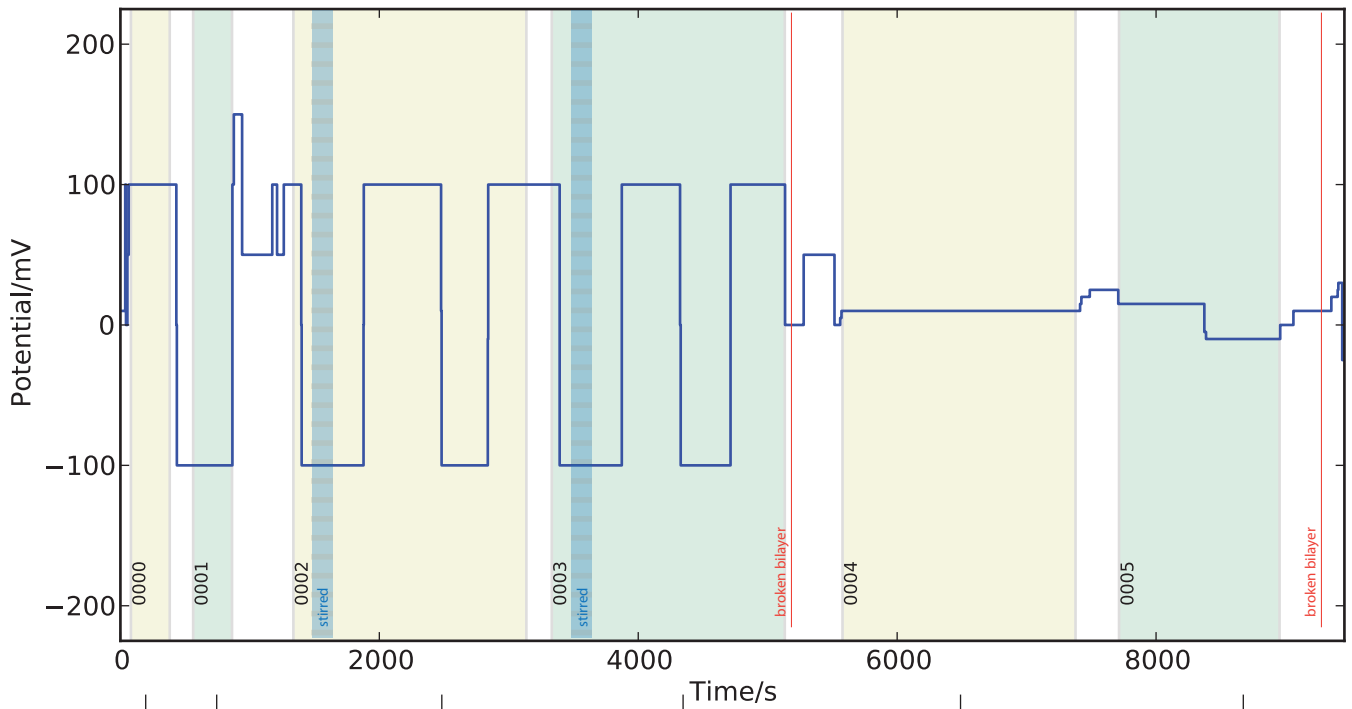
160-0014



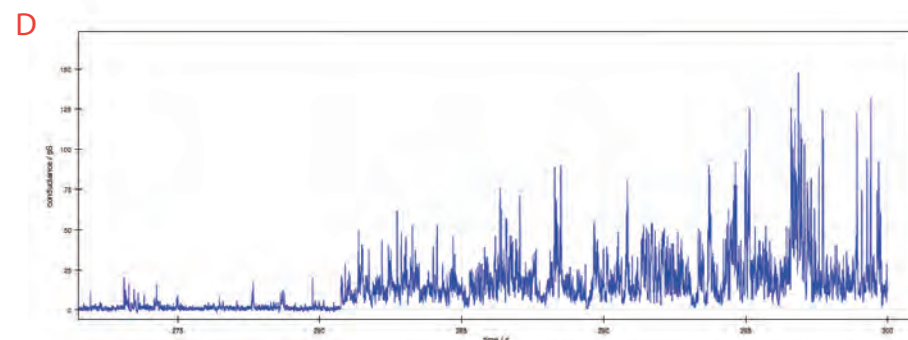
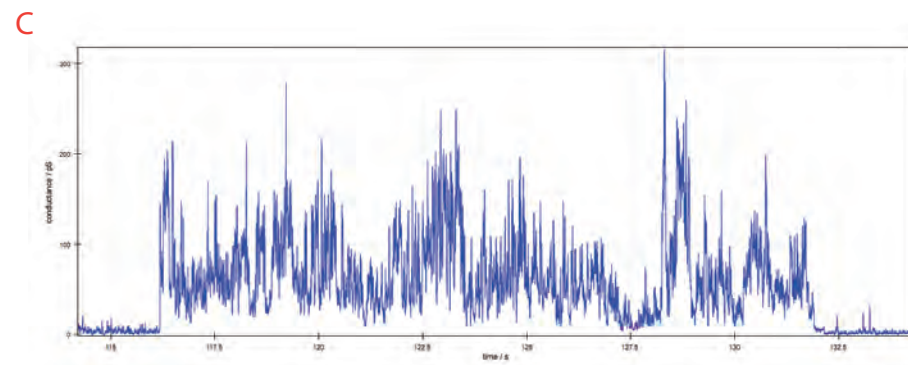
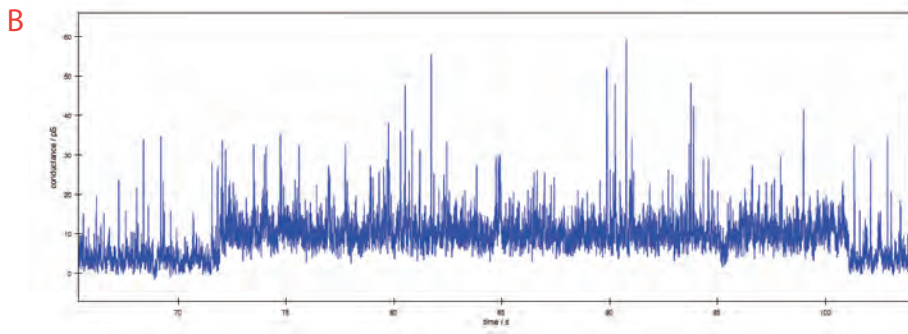
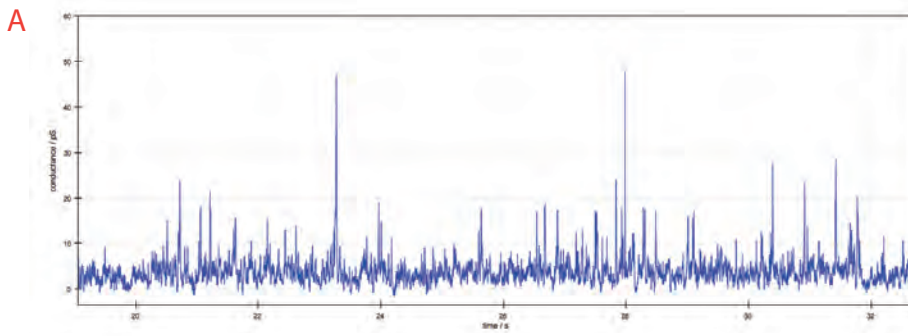
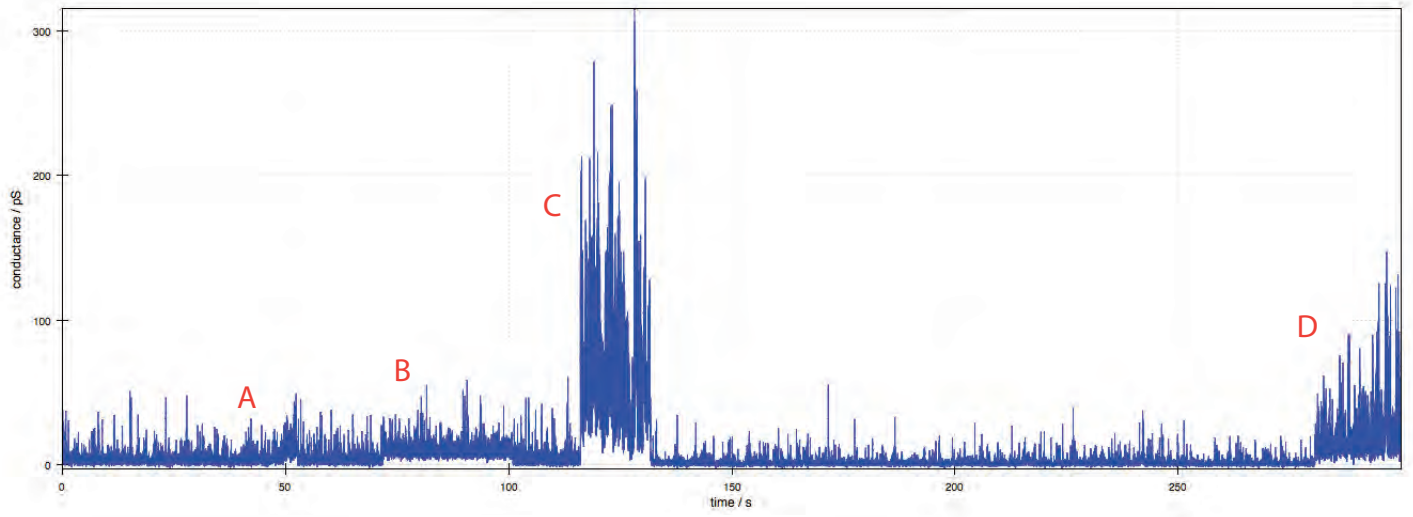
160-0016



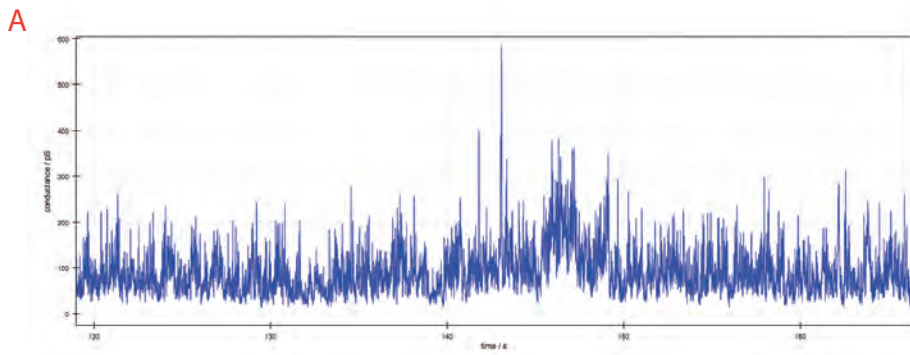
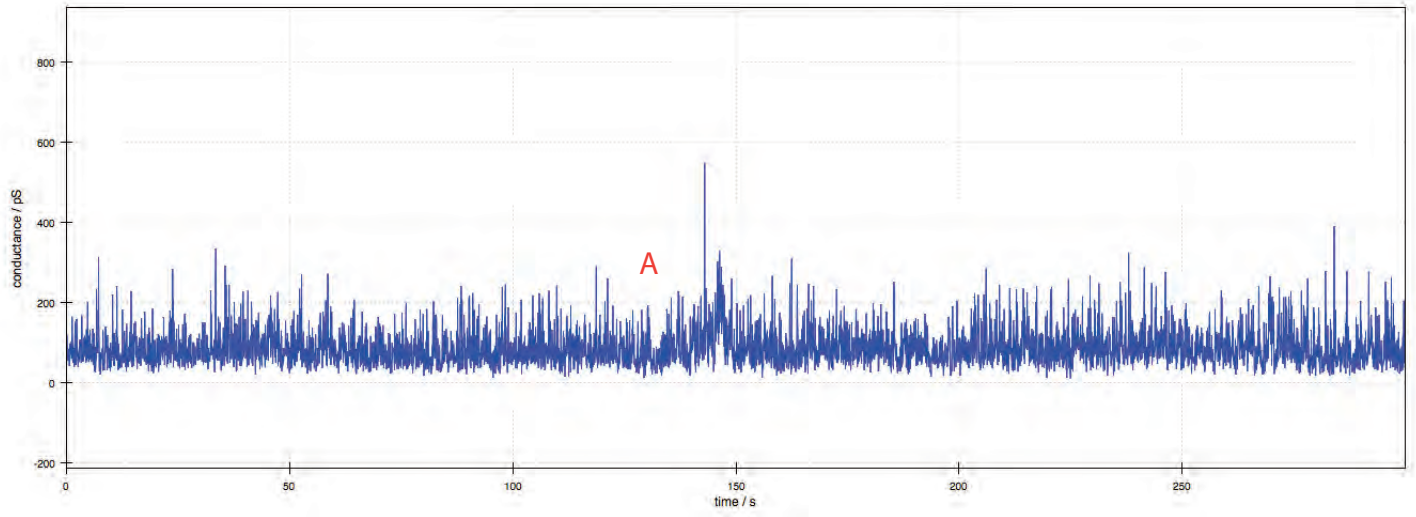
# JC-161 aCD-CholateAmide 2percent 1M KCl pH 7



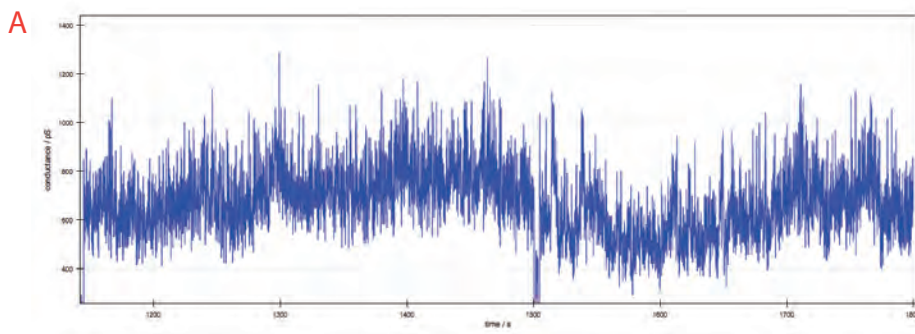
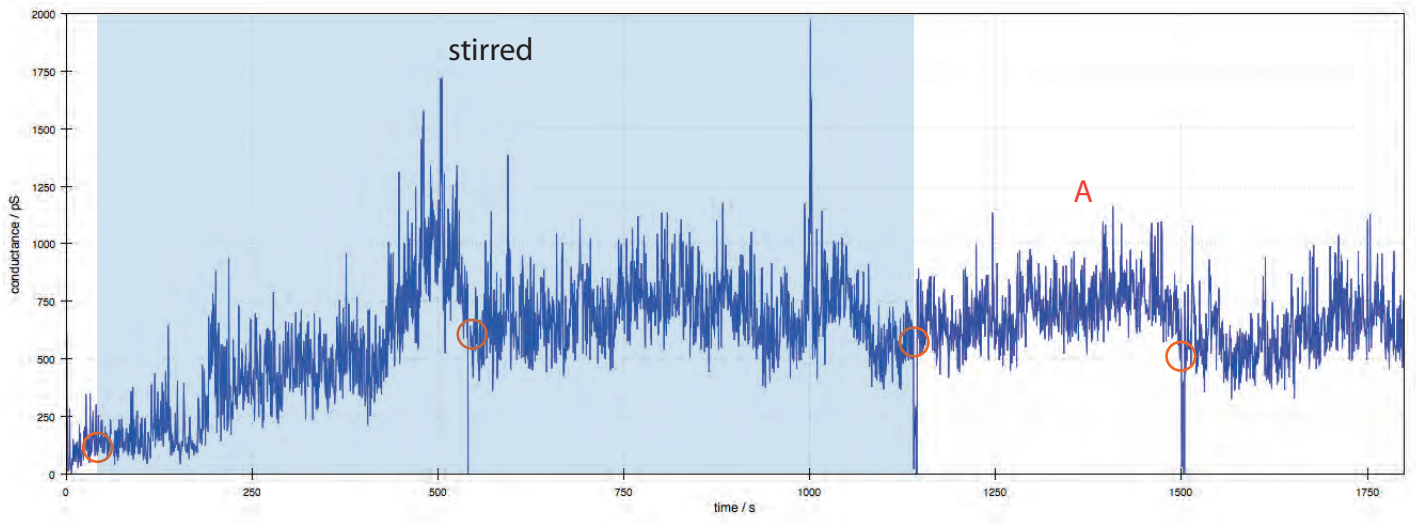
There is definitely some of this exponential potential dependence thing going on that's worth checking out at some point.



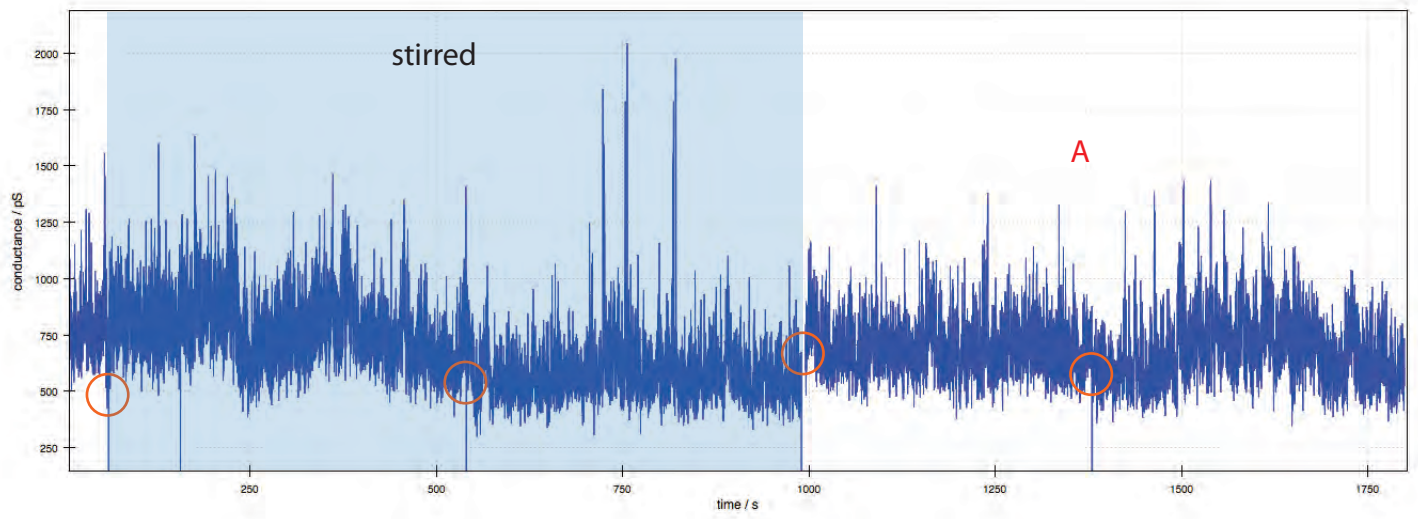
161-0001



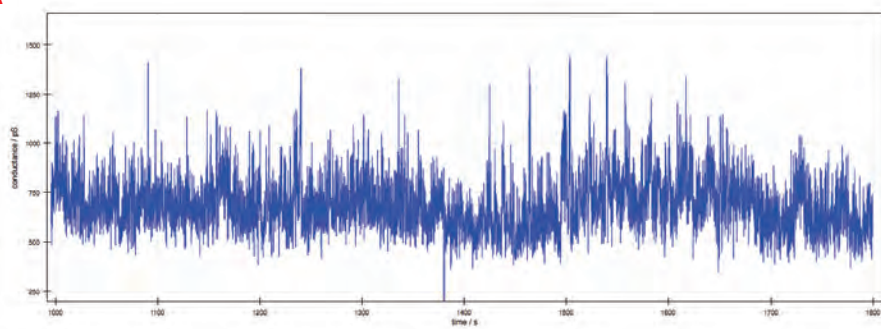
161-0002



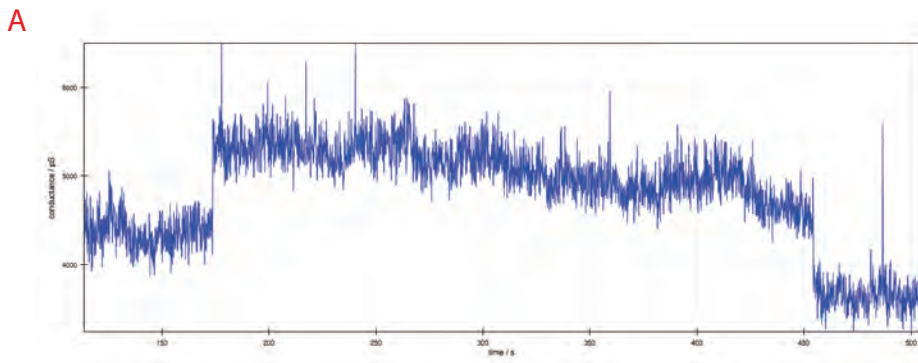
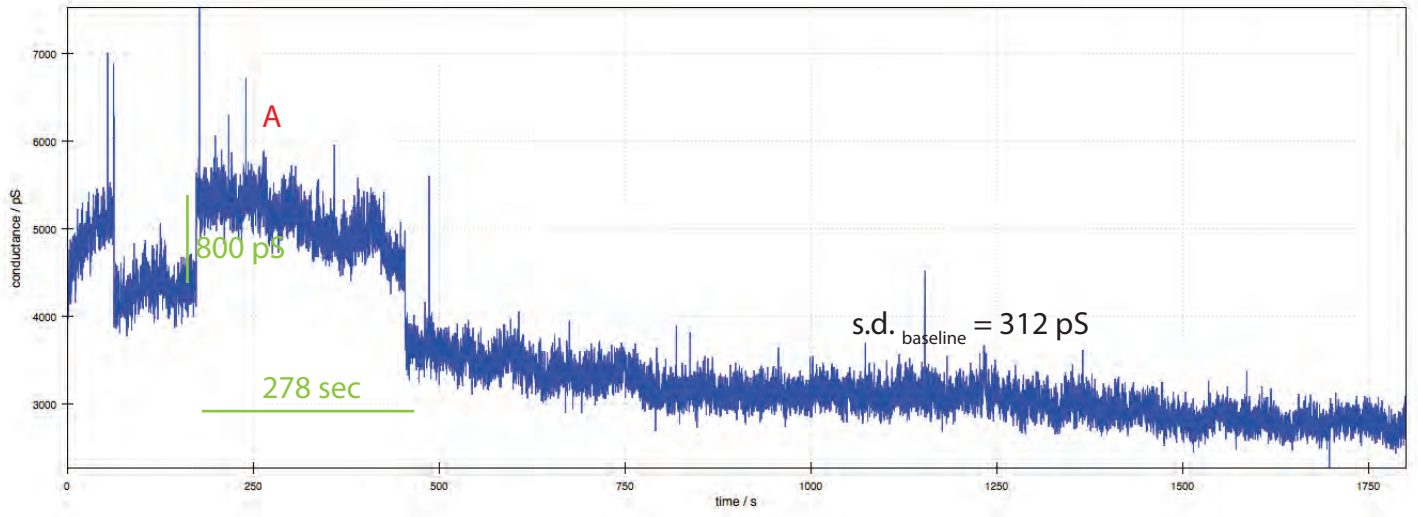
161-0003

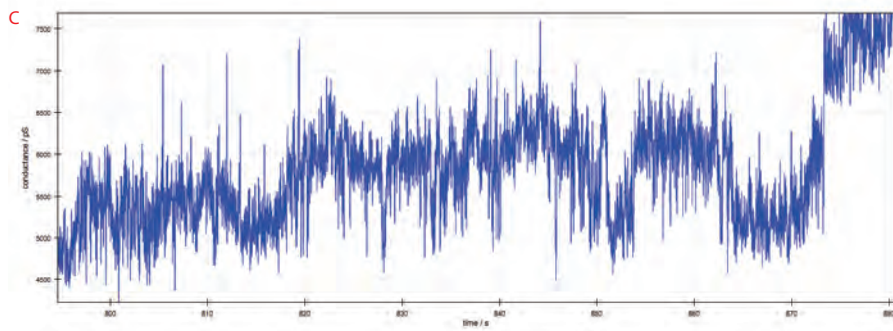
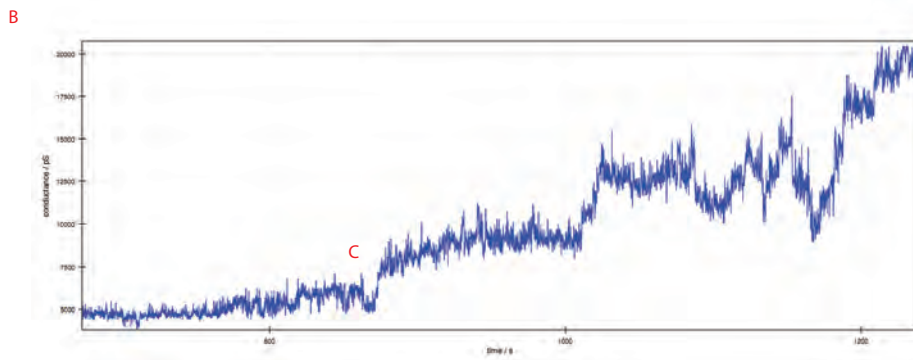
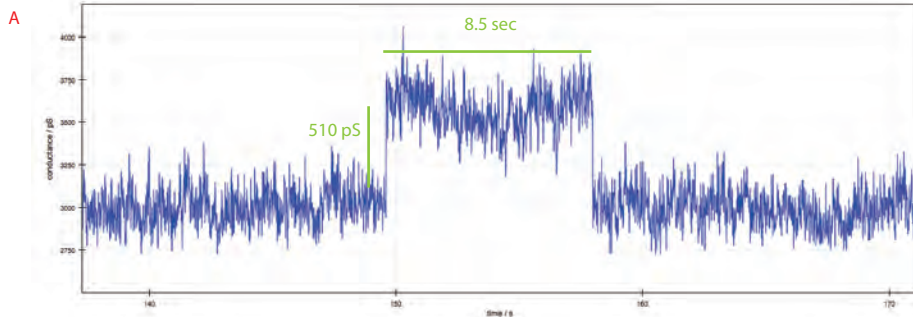
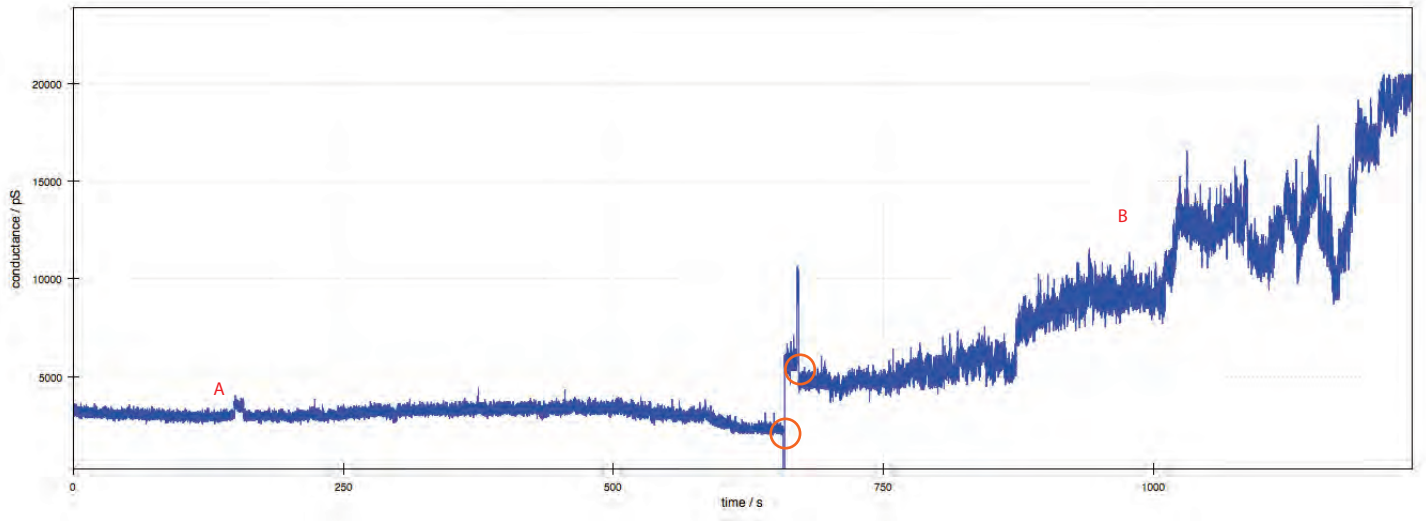


A

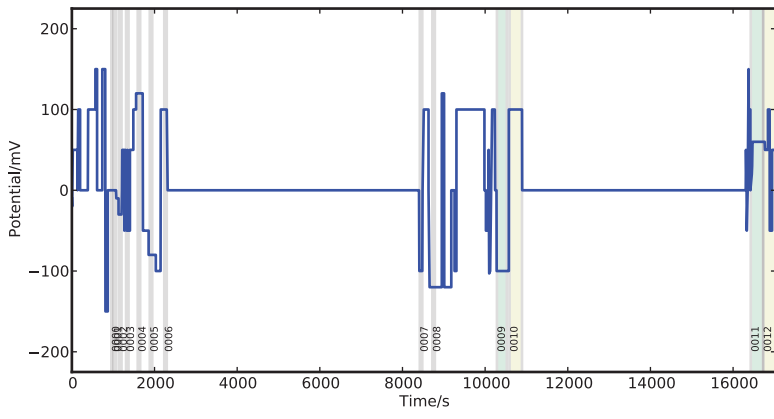


161-0004



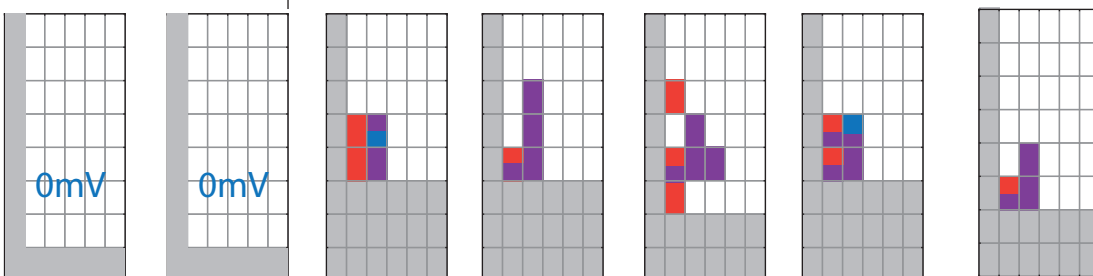
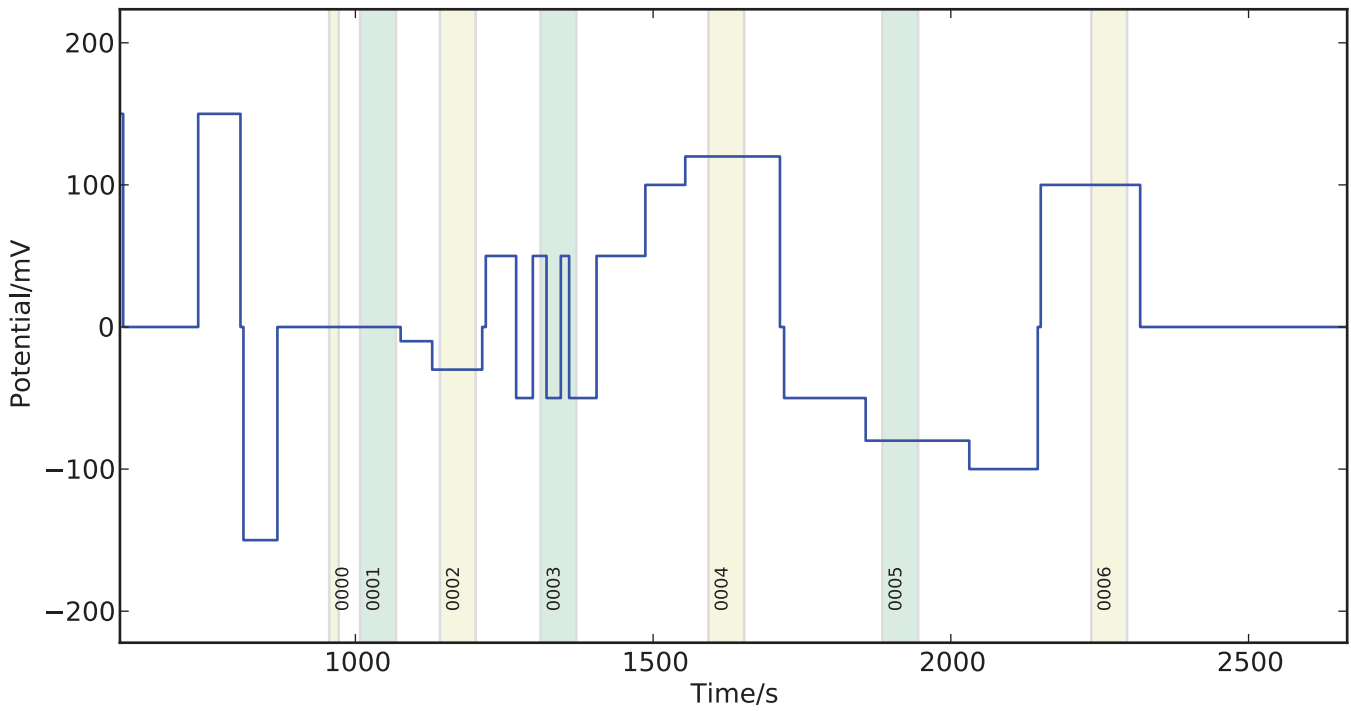


JC-127 bCD-Ethisterone JC-V-23 1percent - 1M CsCl pH 7

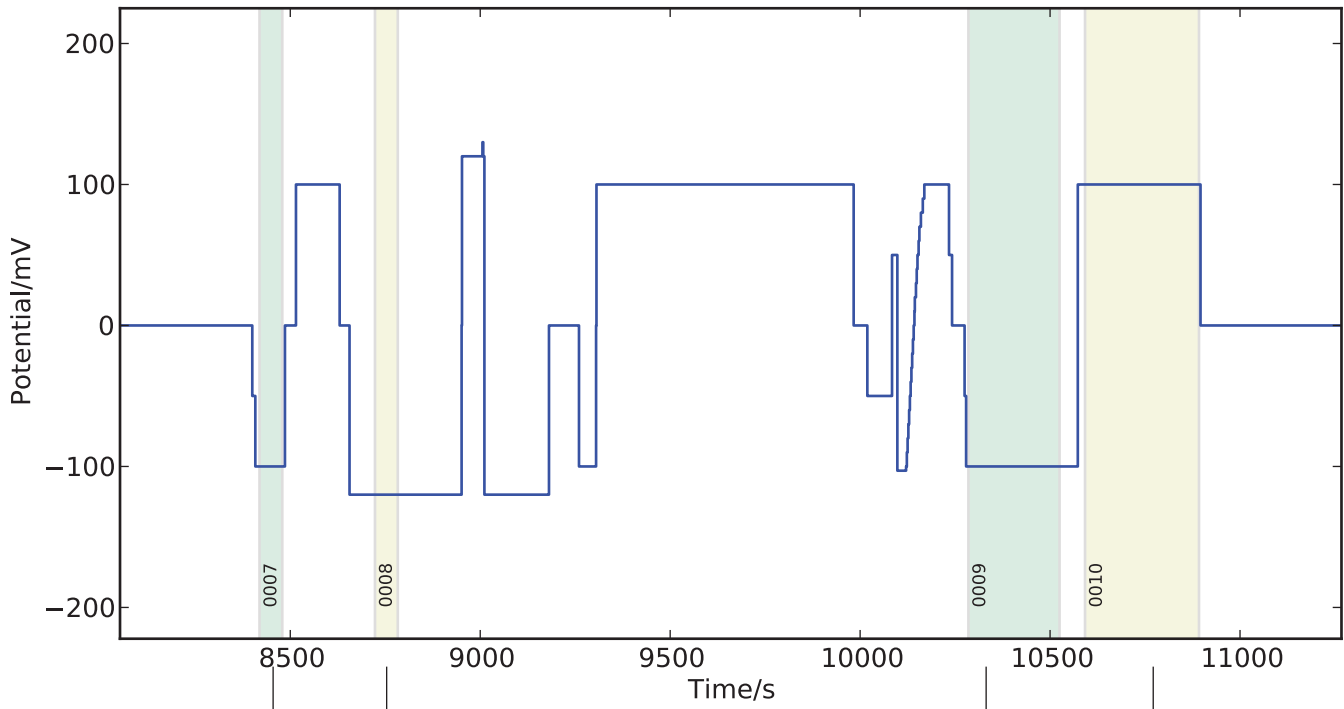


The lab book is corrupted and contain no expt descriptions

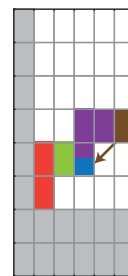
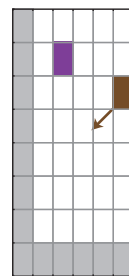
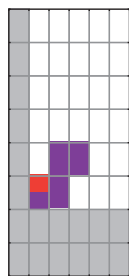
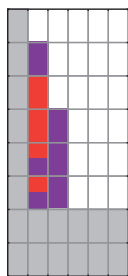
JC-127 bCD-Ethisterone JC-V-23 1percent - 1M CsCl pH 7



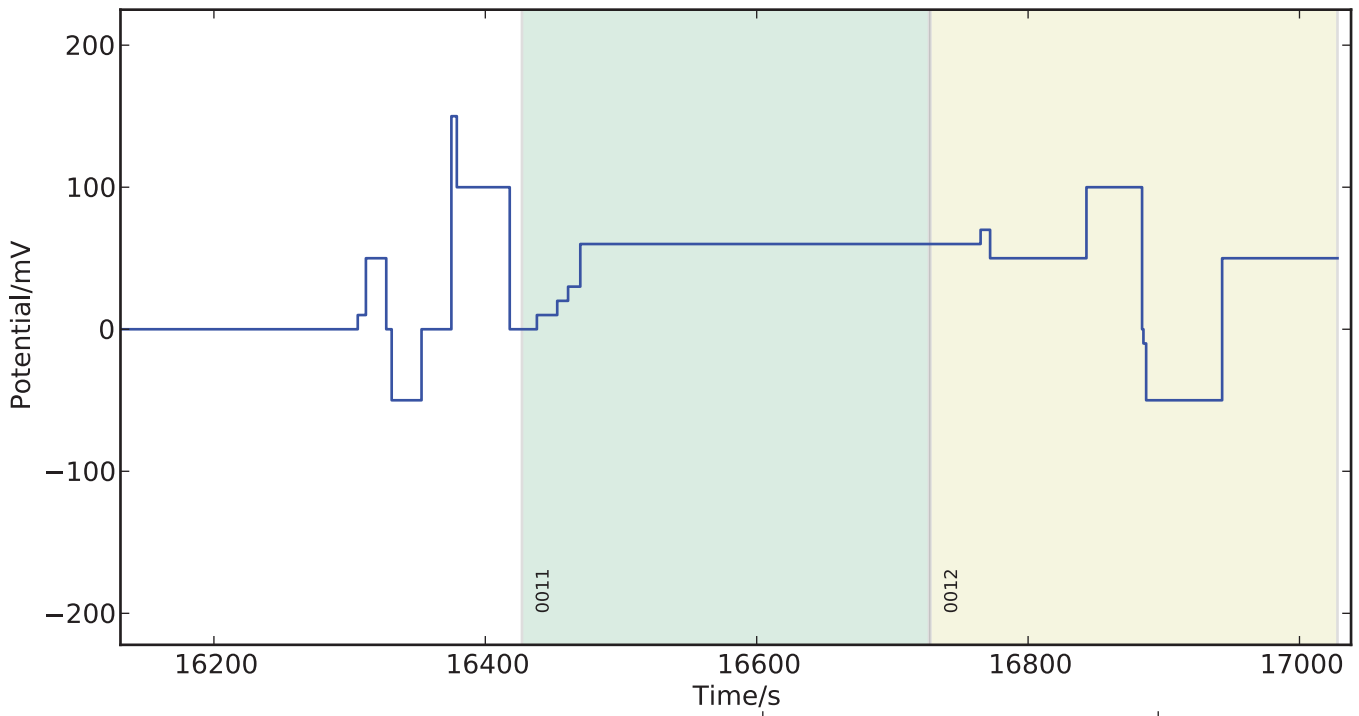
JC-127 bCD-Ethisterone JC-V-23 1percent - 1M CsCl pH 7



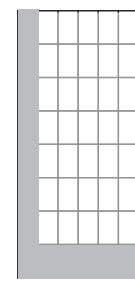
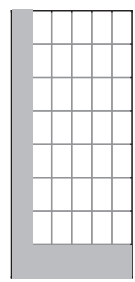
lipid 1%  
electrolyte  
contact injection  
brush transfer



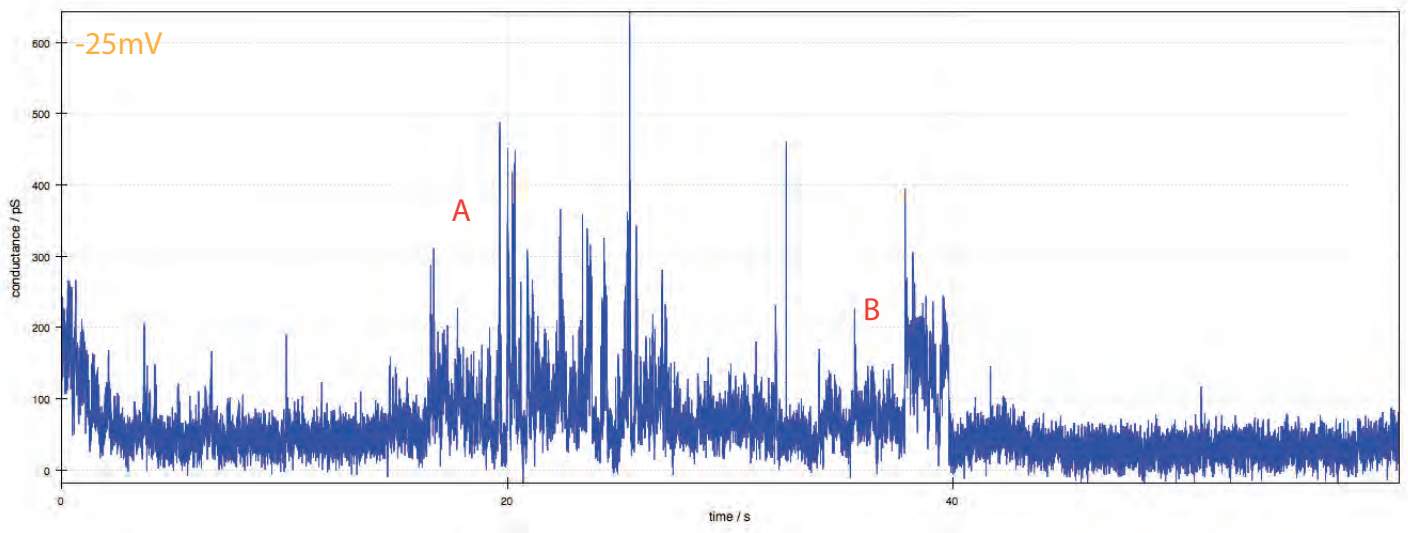
JC-127 bCD-Ethisterone JC-V-23 1percent - 1M CsCl pH 7



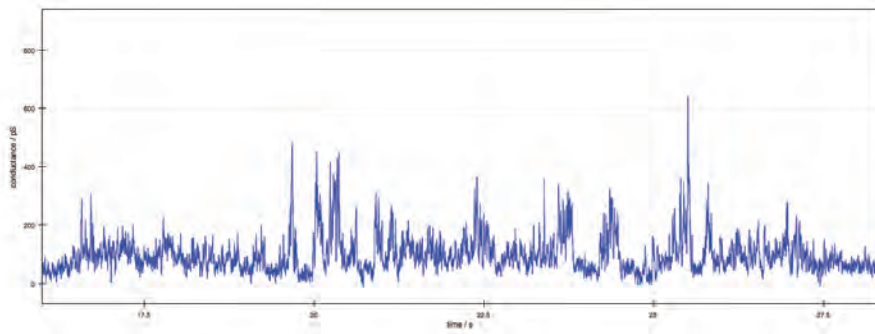
lipid 1%  
electrolyte  
contact injection  
brush transfer



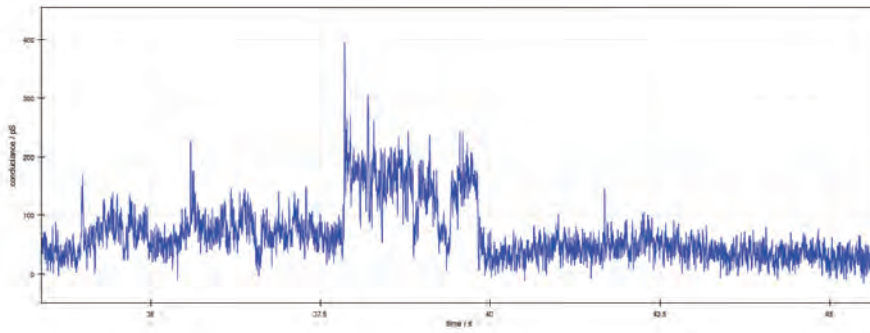
No idea what is going on with this trace?

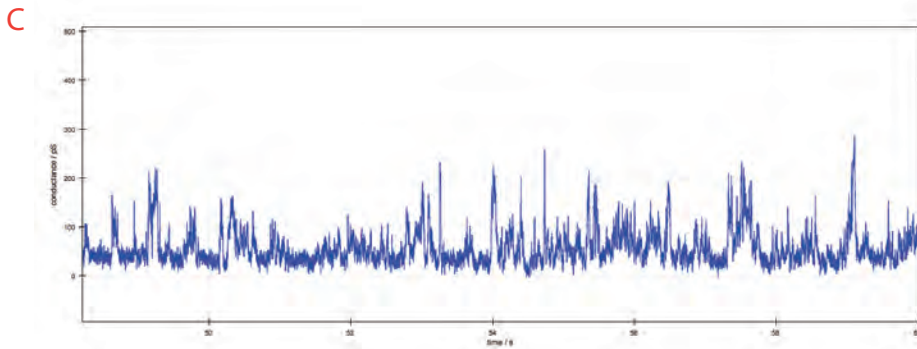
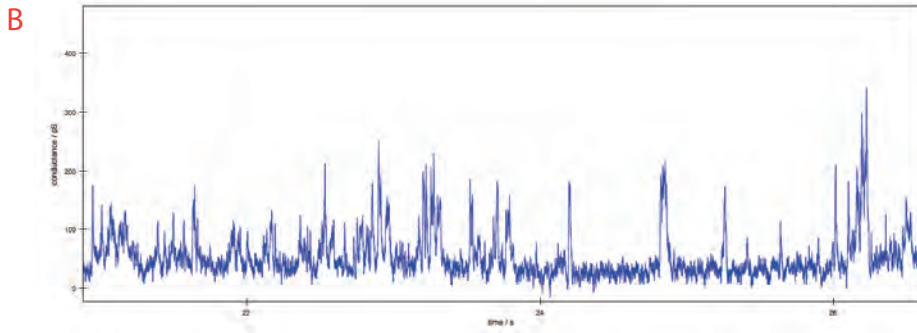
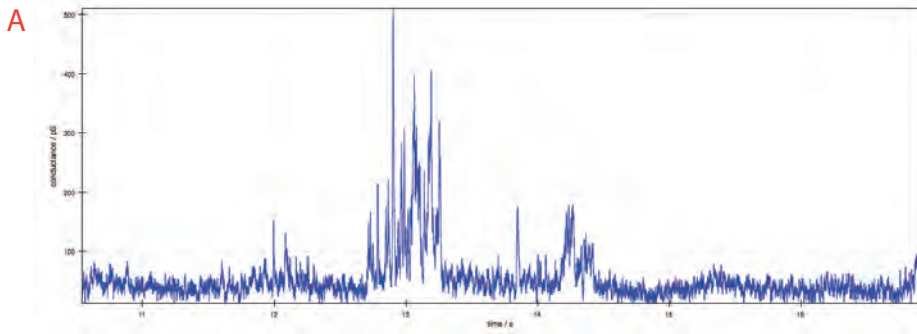
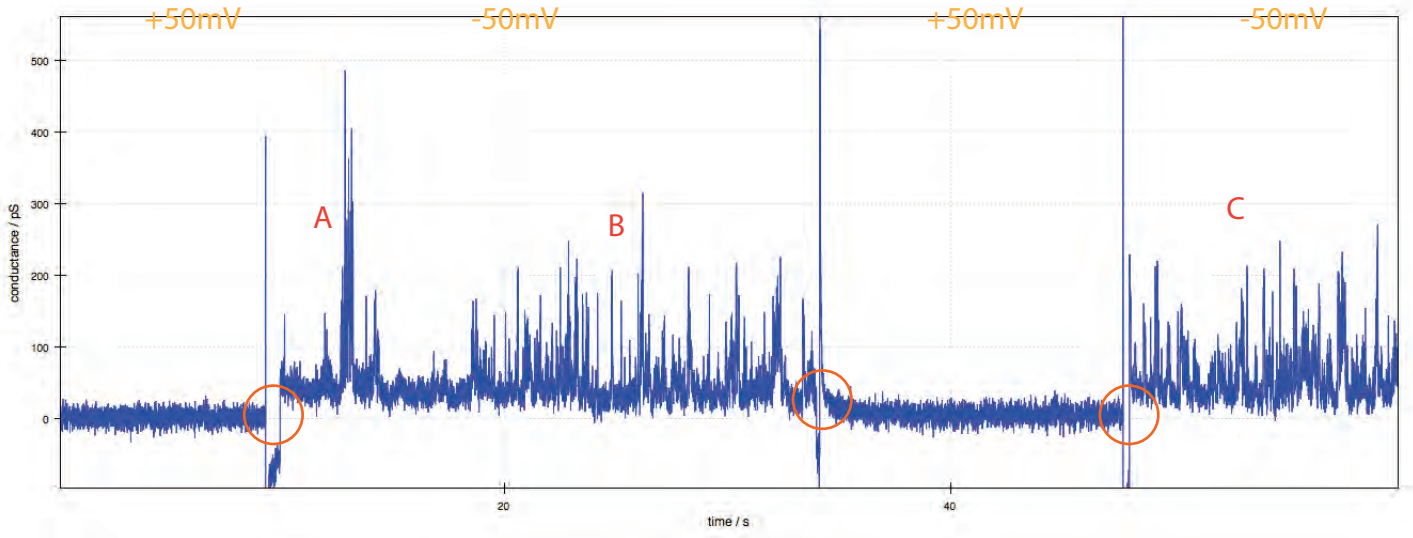


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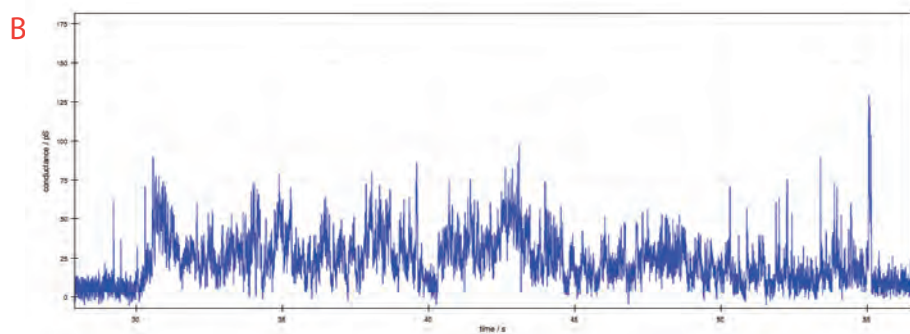
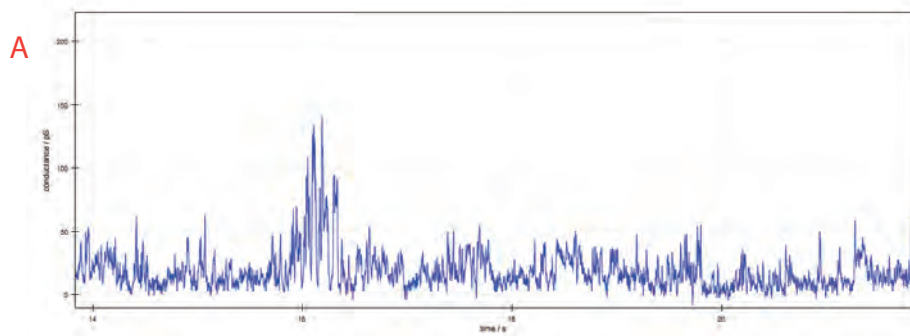
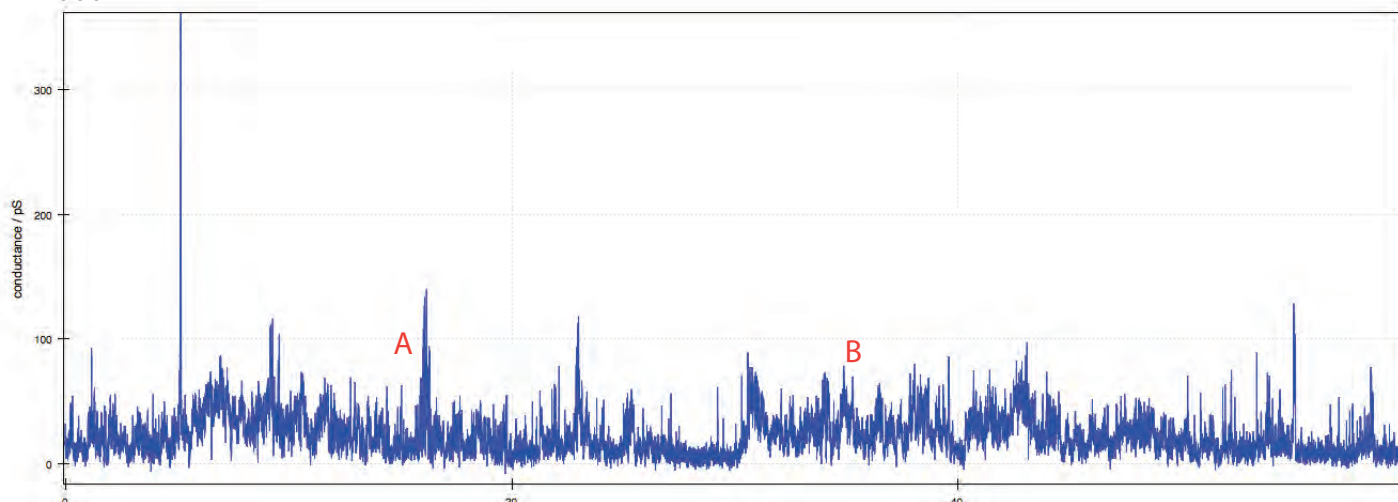


B

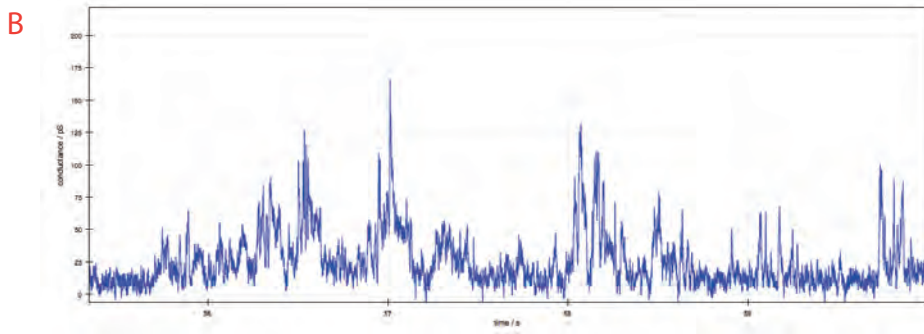
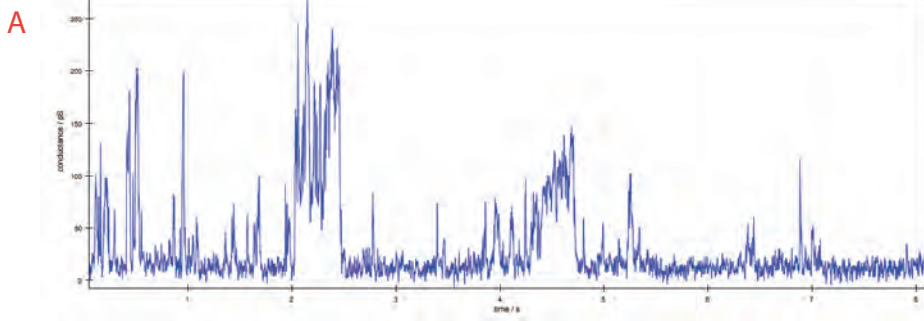
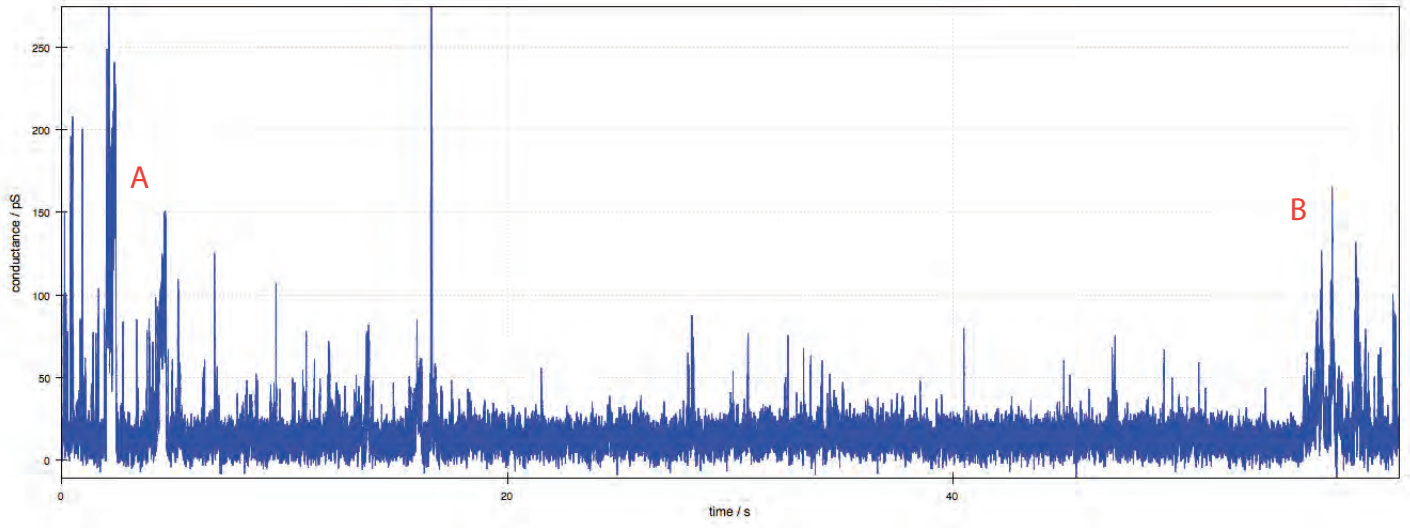




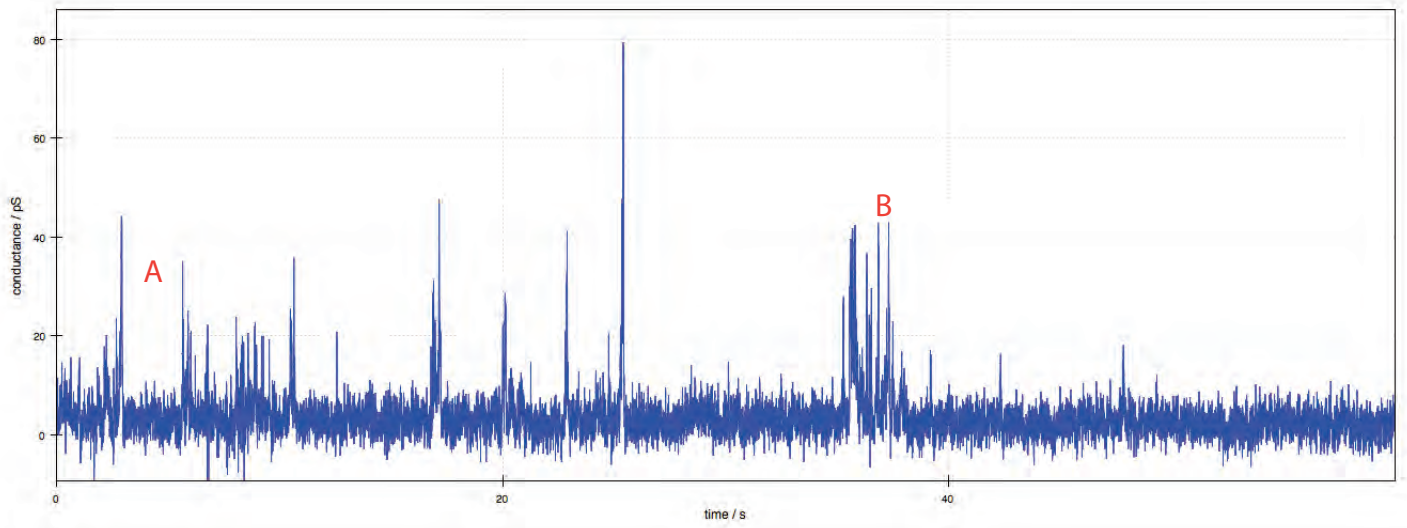
127-0004



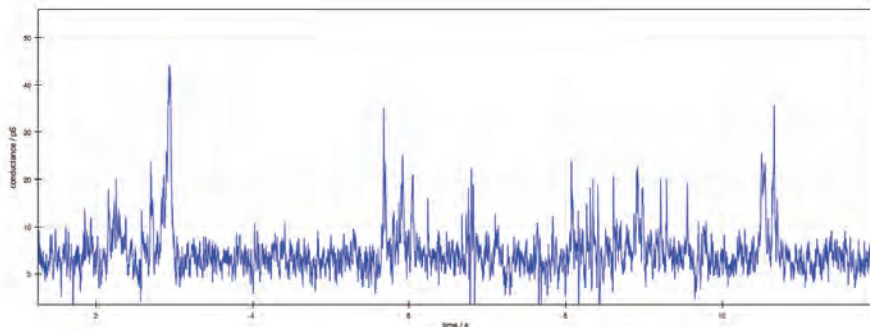
127-0005



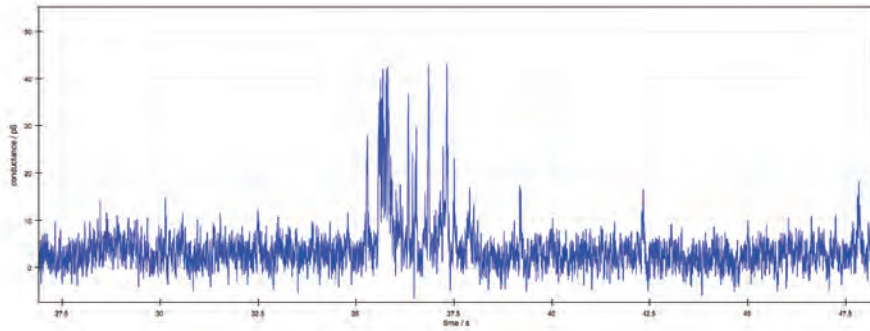
127-0006



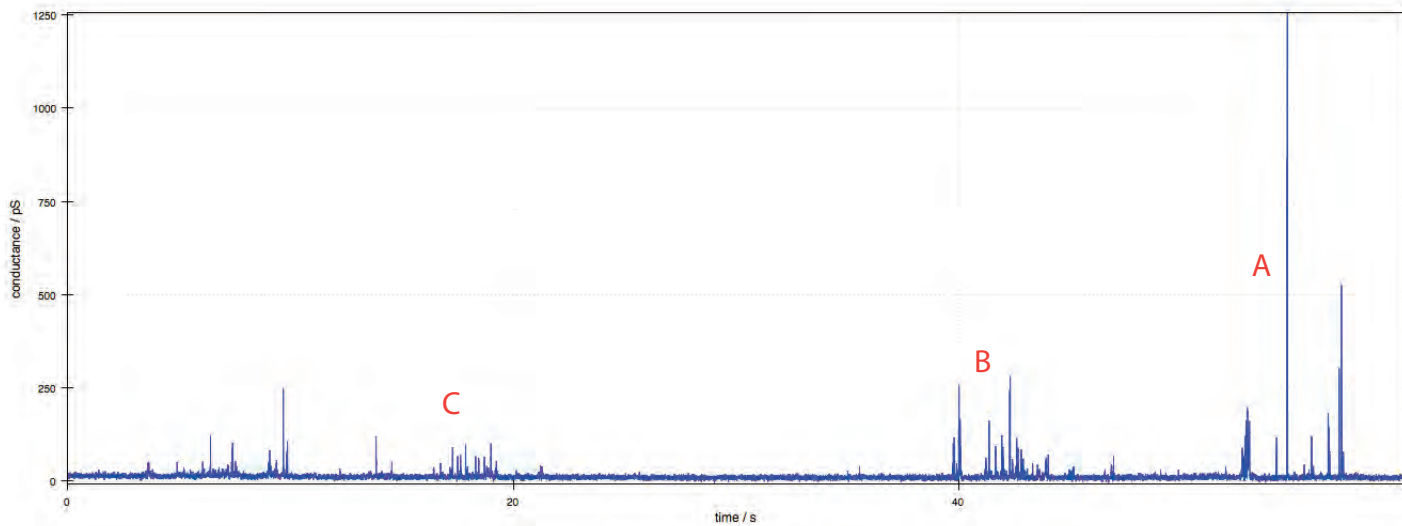
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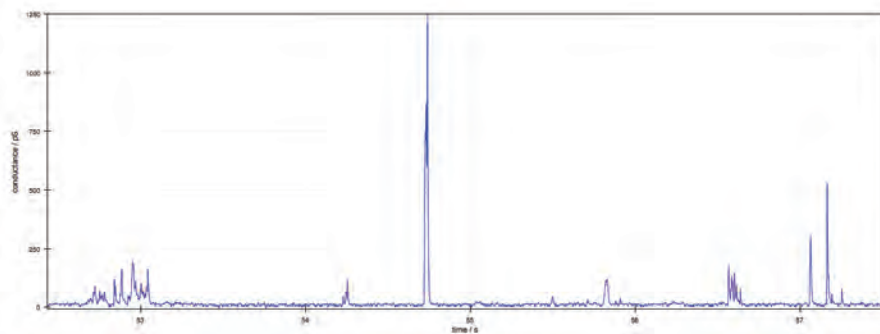
B



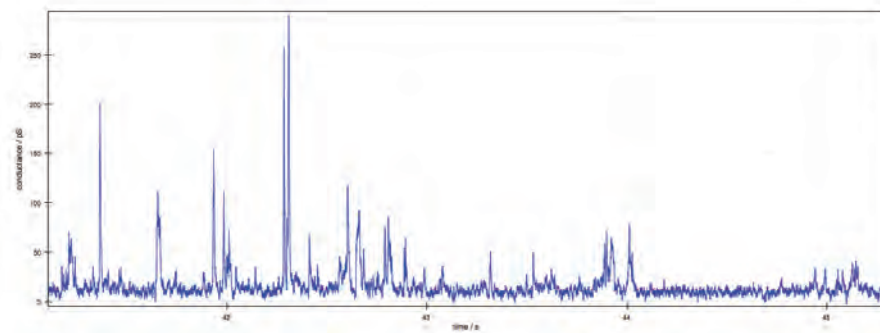
127-0007



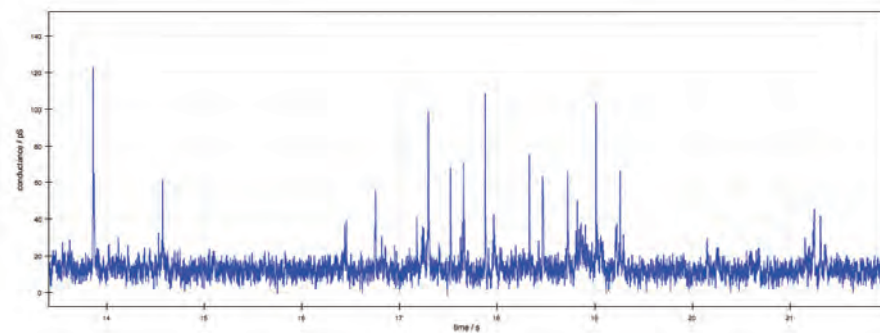
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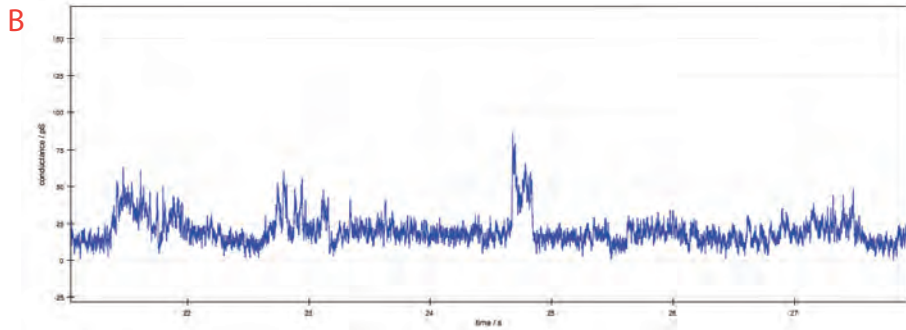
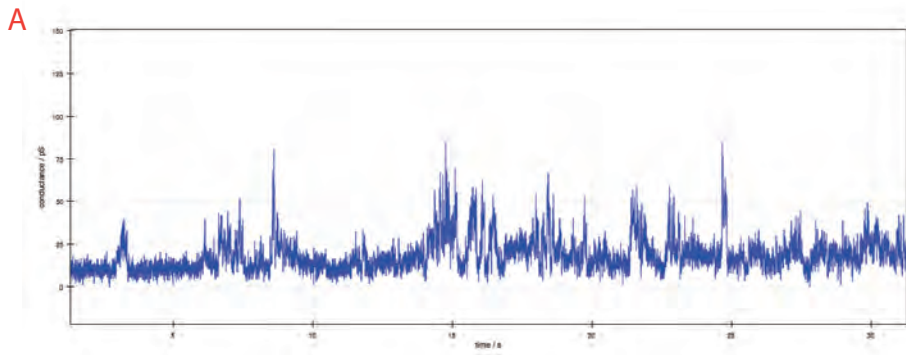
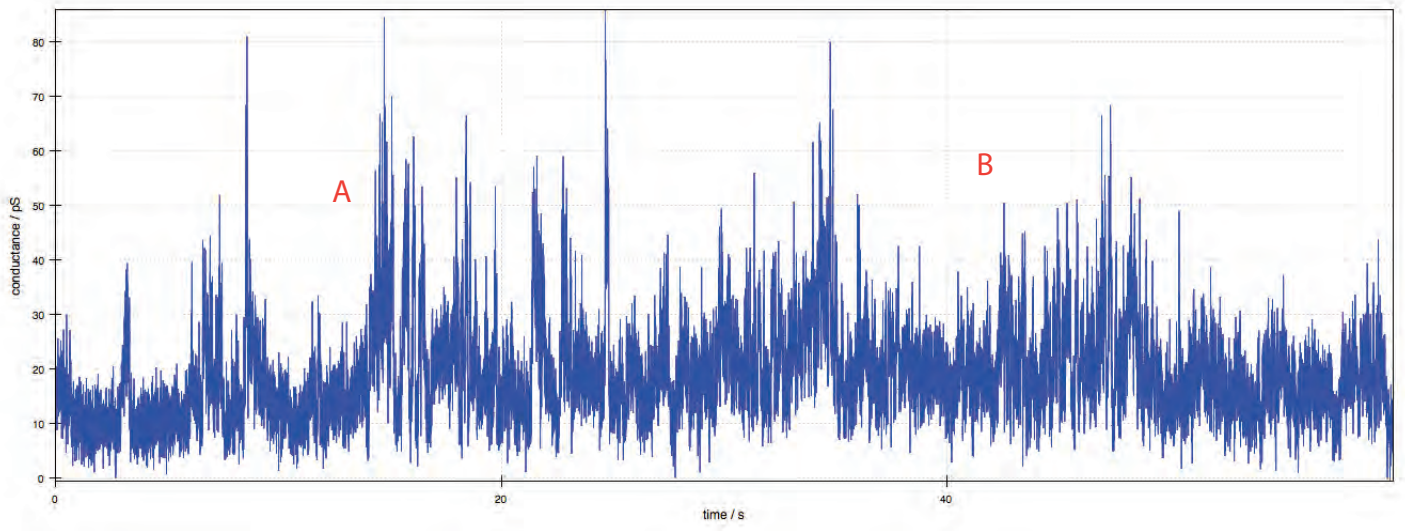
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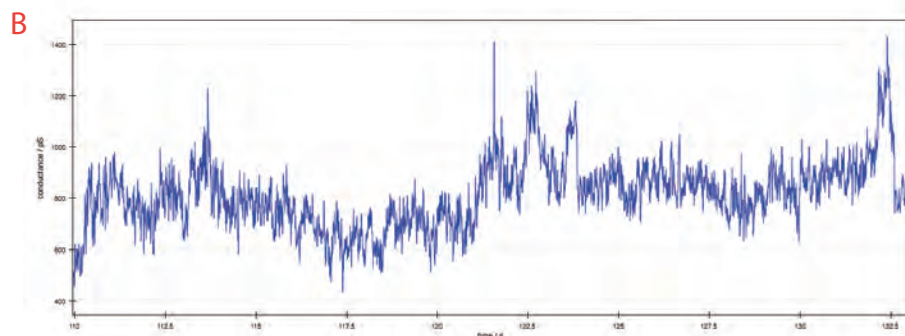
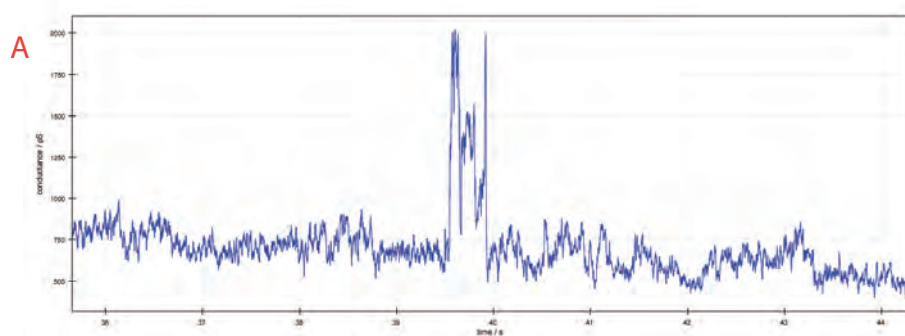
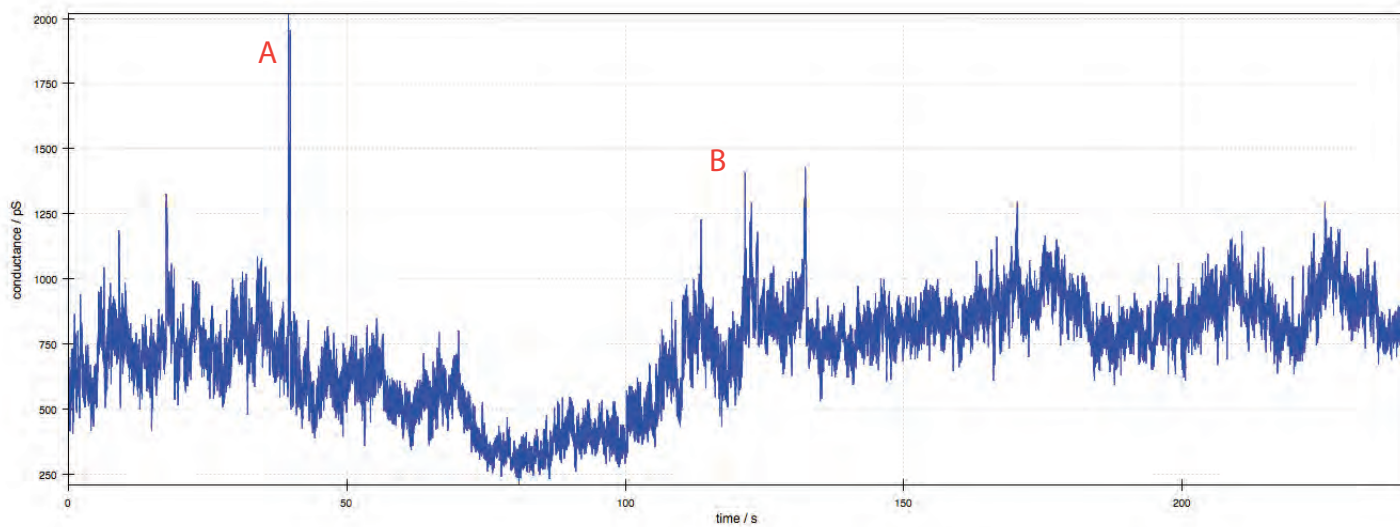
C

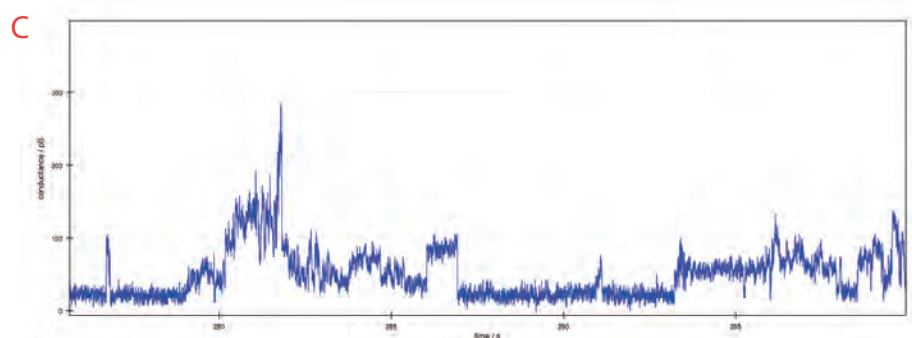
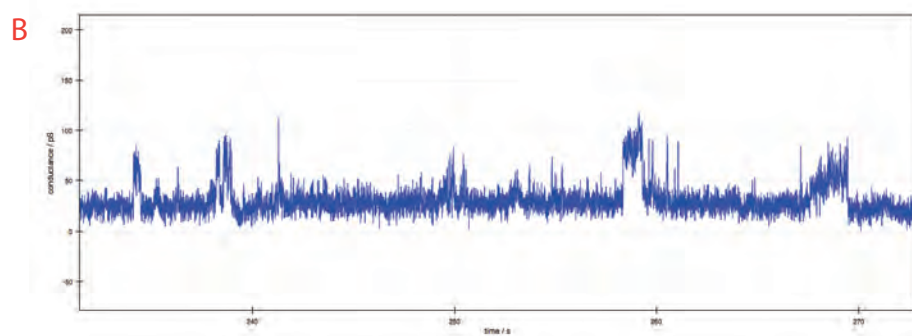
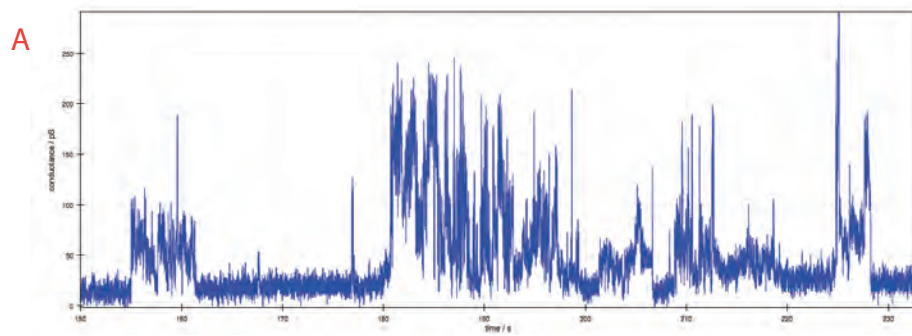
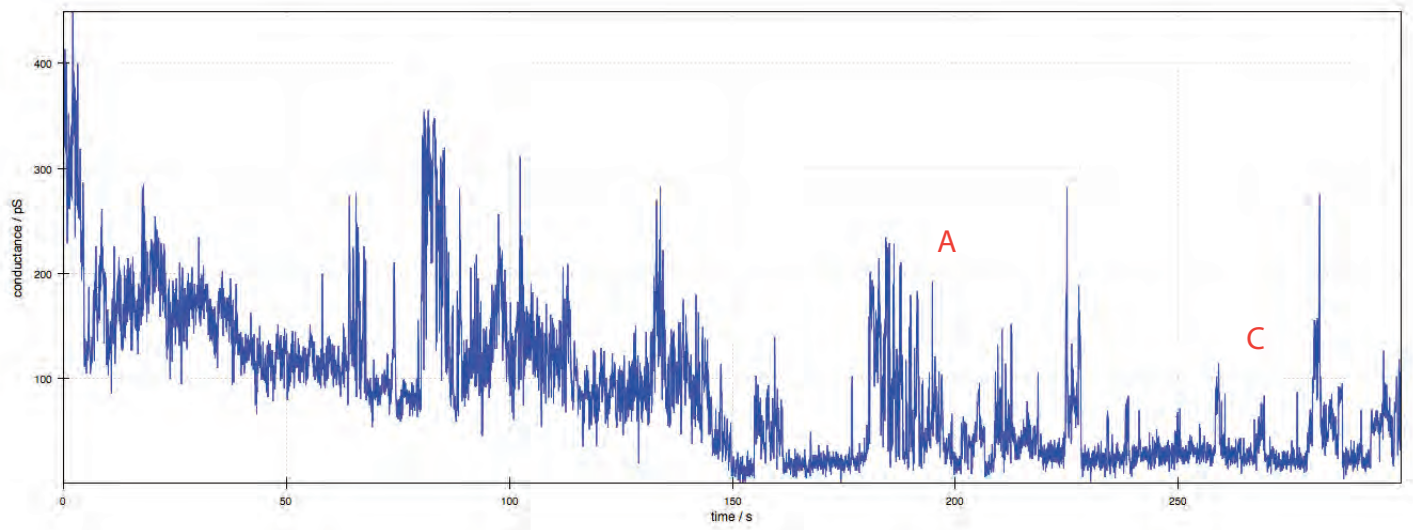


127-0008

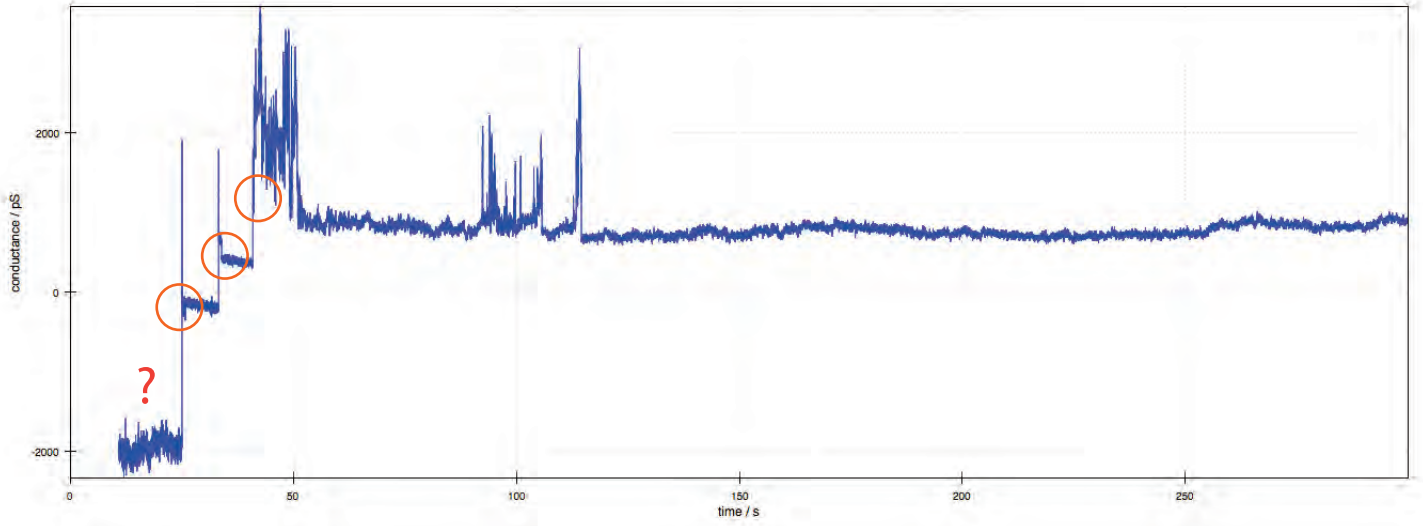


127-0009



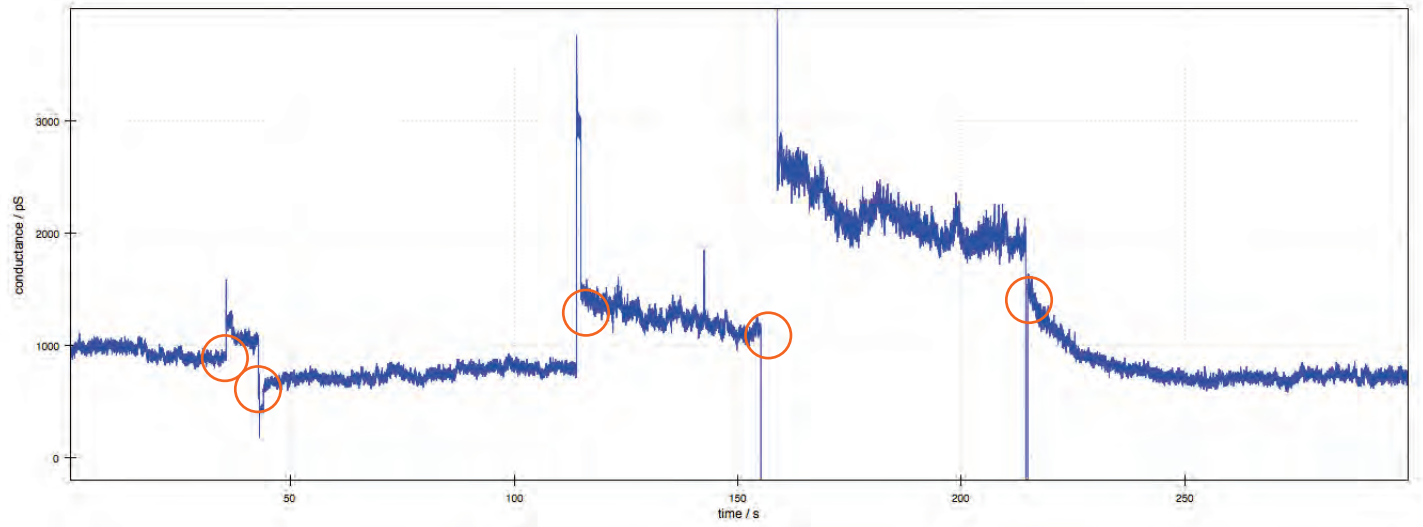


127-0011

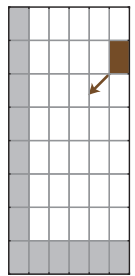
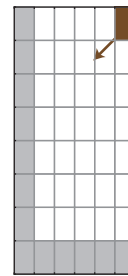
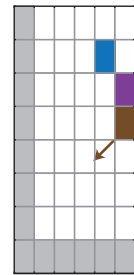
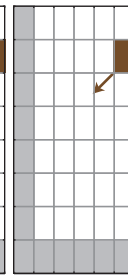
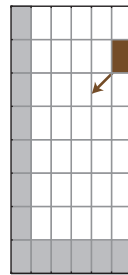
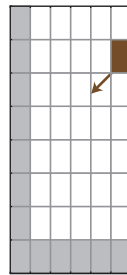
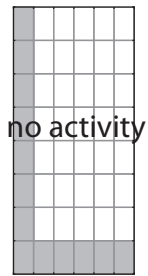
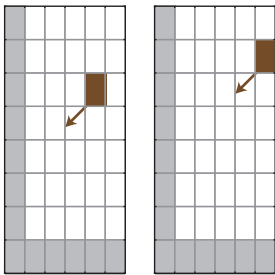
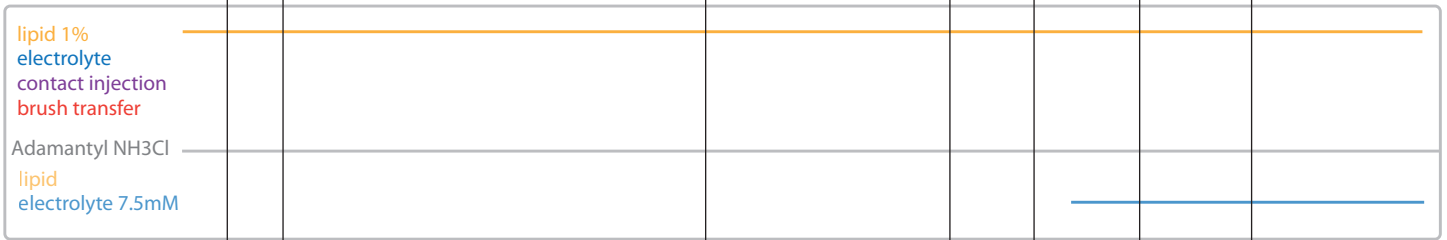
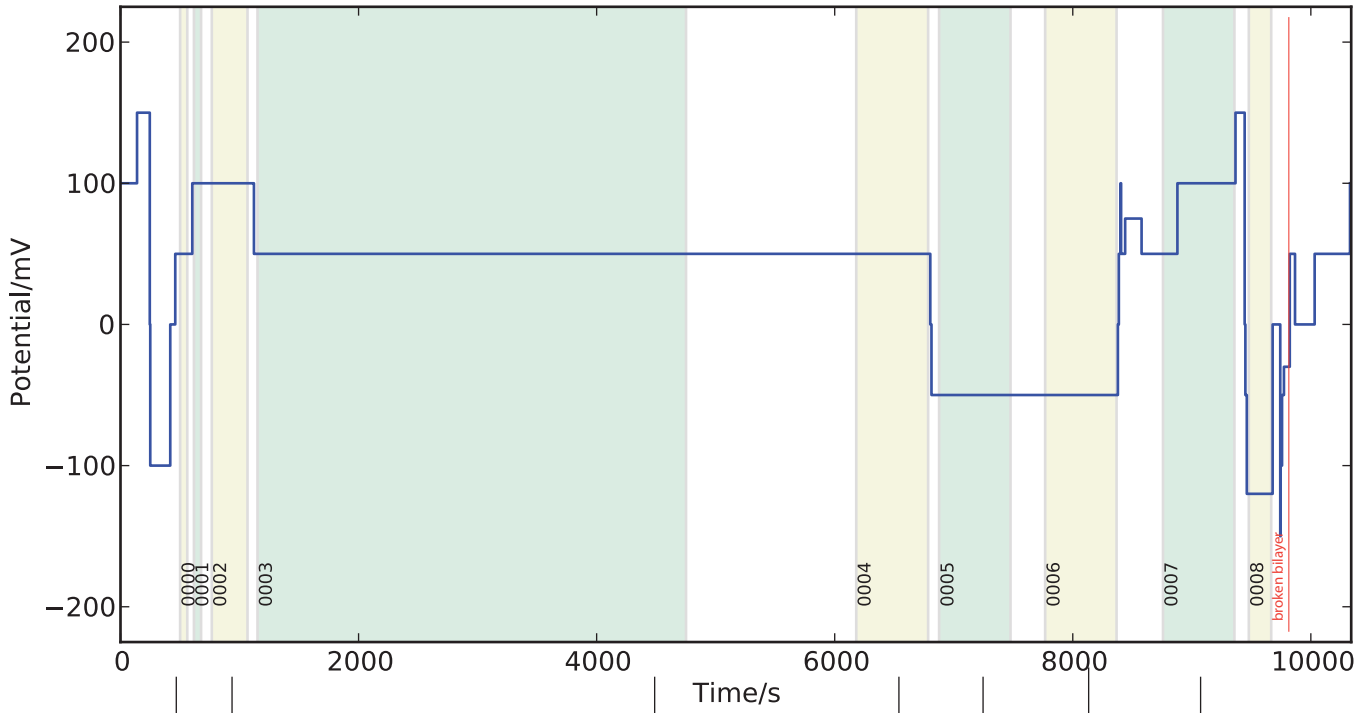


I don't know what is going on with this trace.

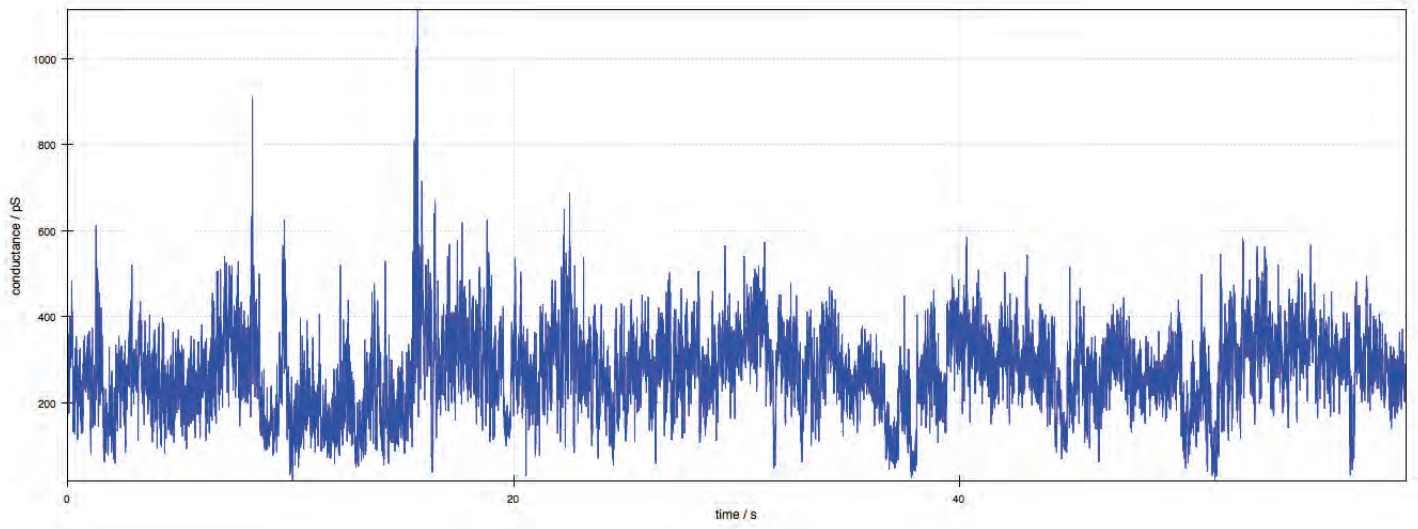
127-0012



# JC-134 bCD-Ethisterone JC-V-23 1percent - 1MMe4NO3

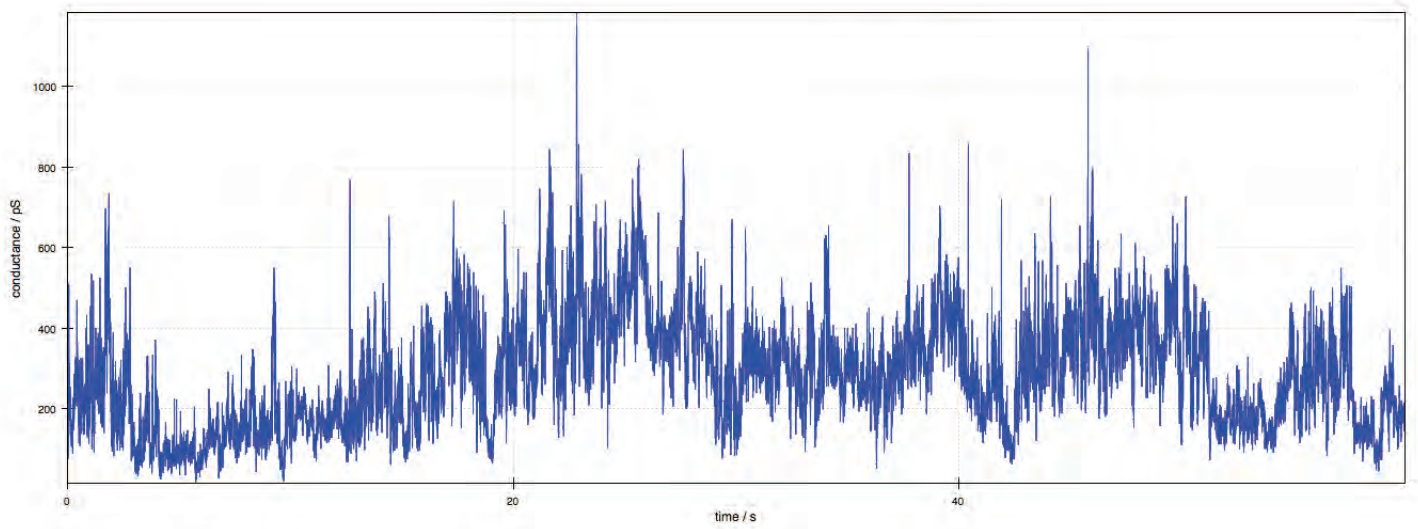


134-0000



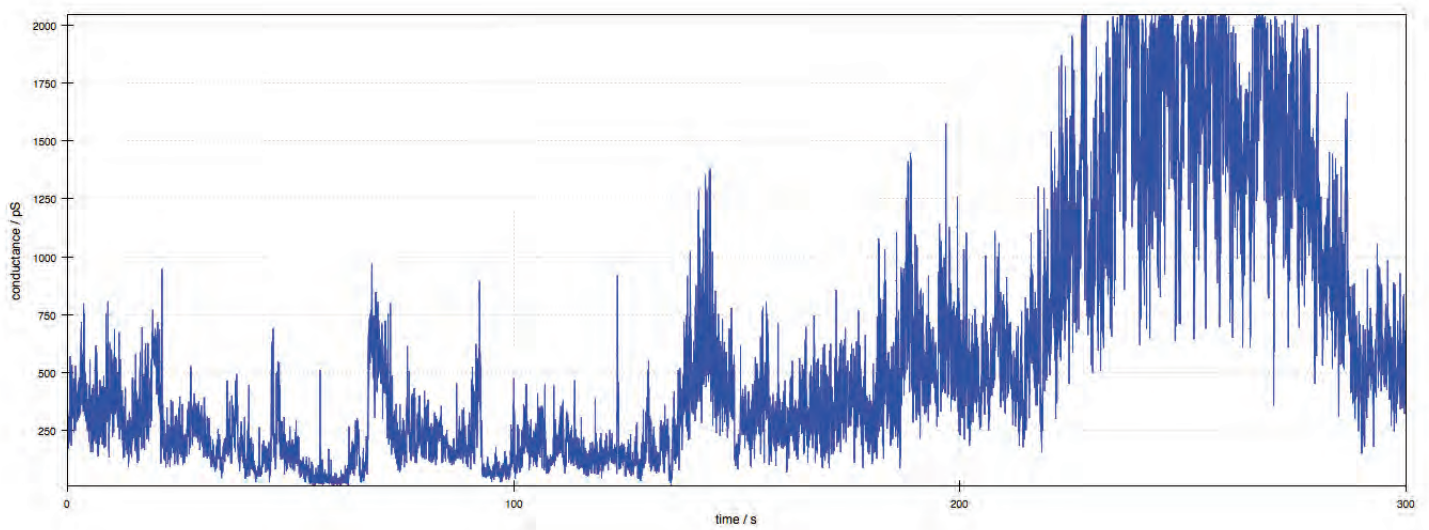
fractal?

134-0001

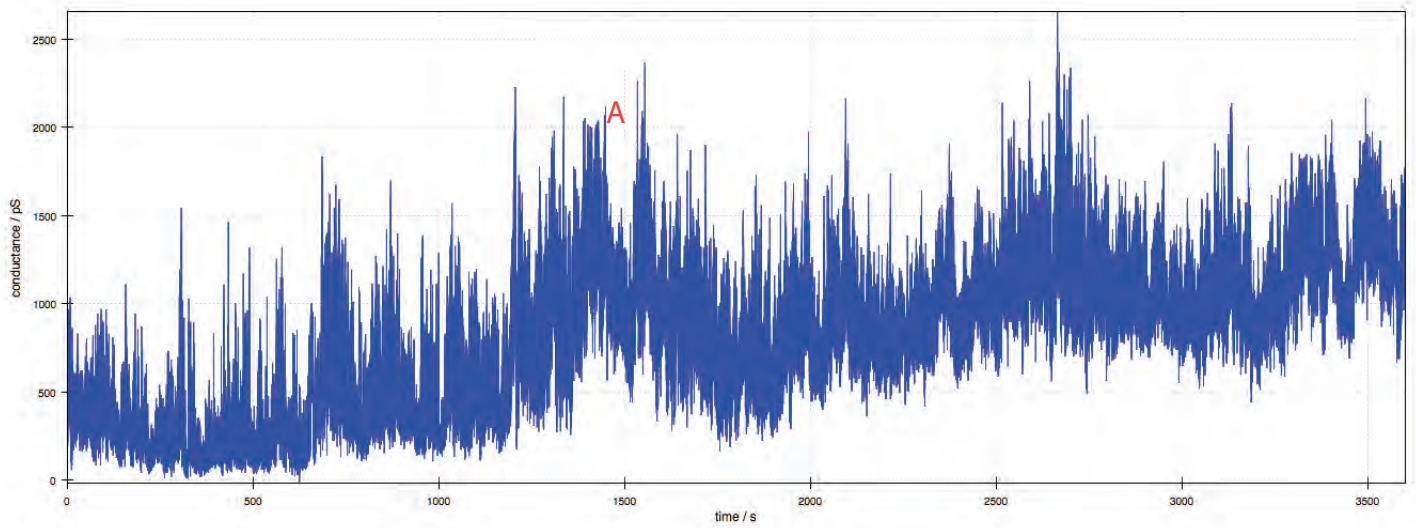


fractal?

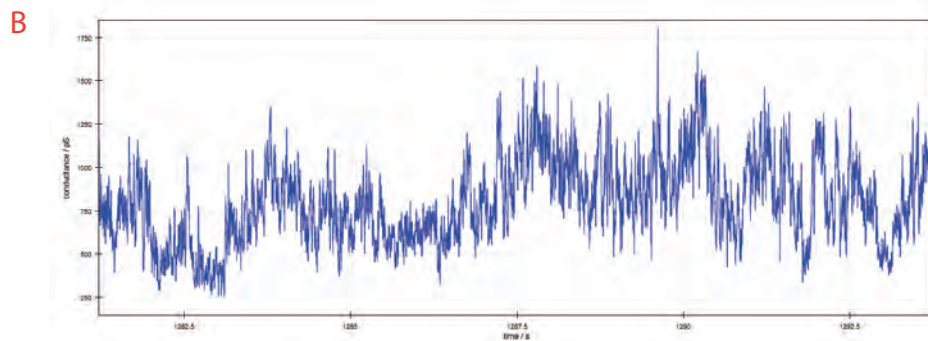
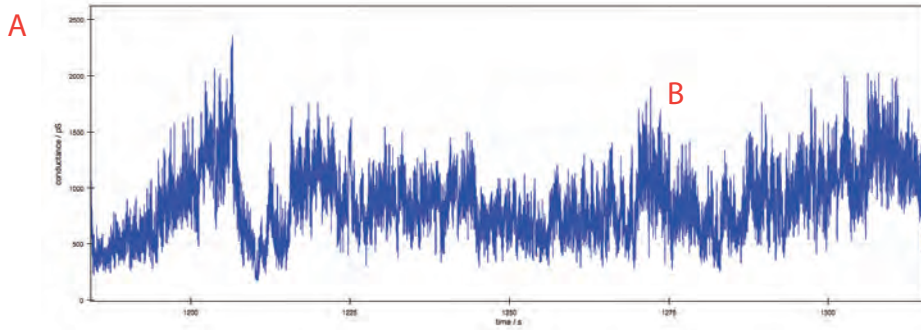
134-0002



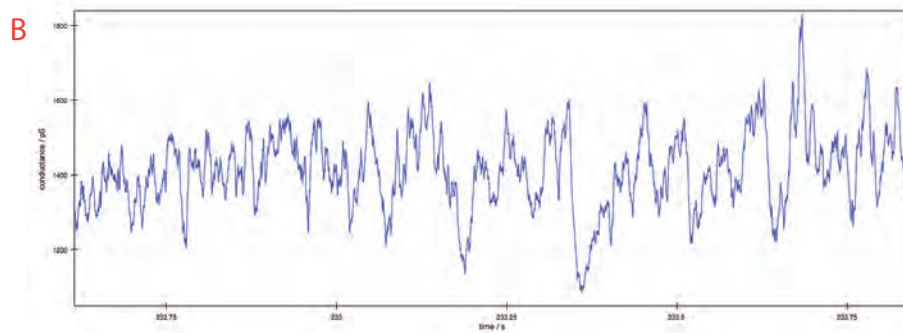
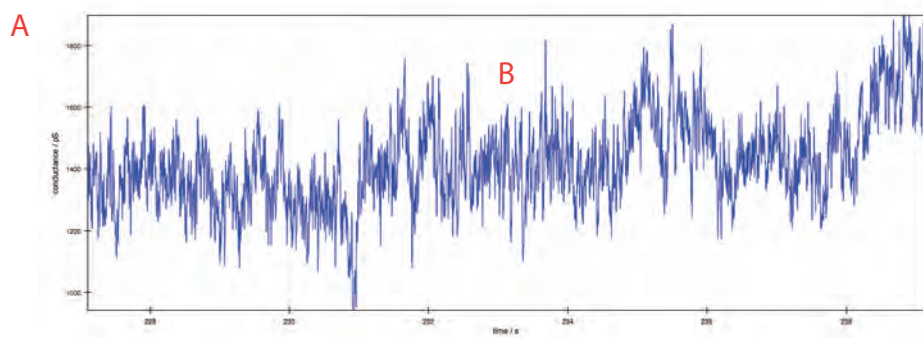
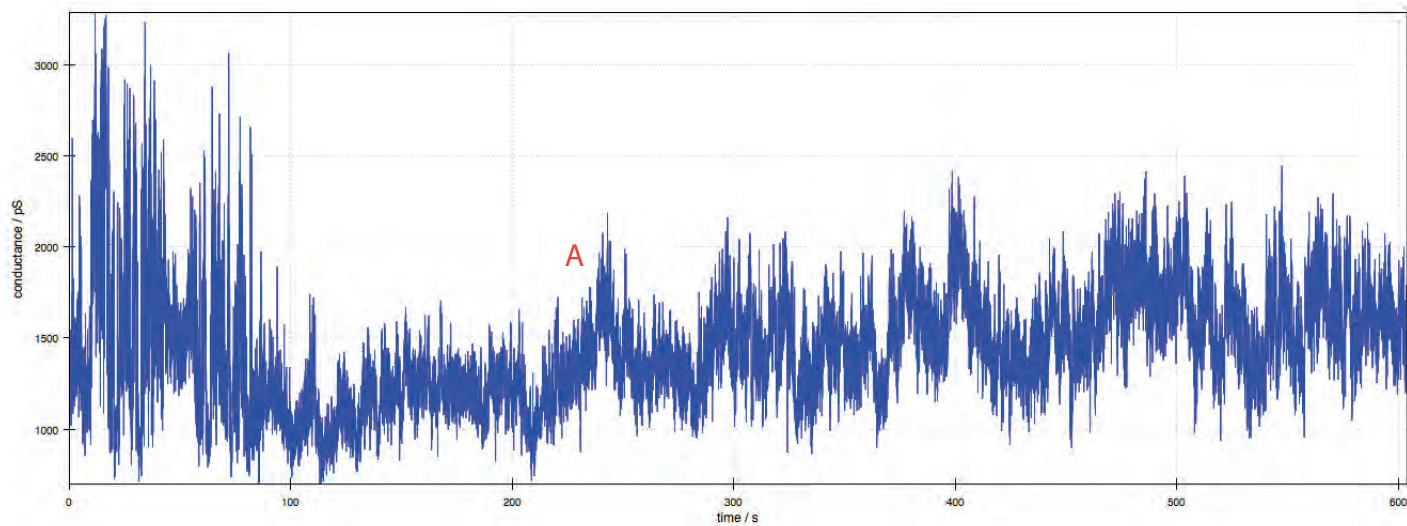
fractal?



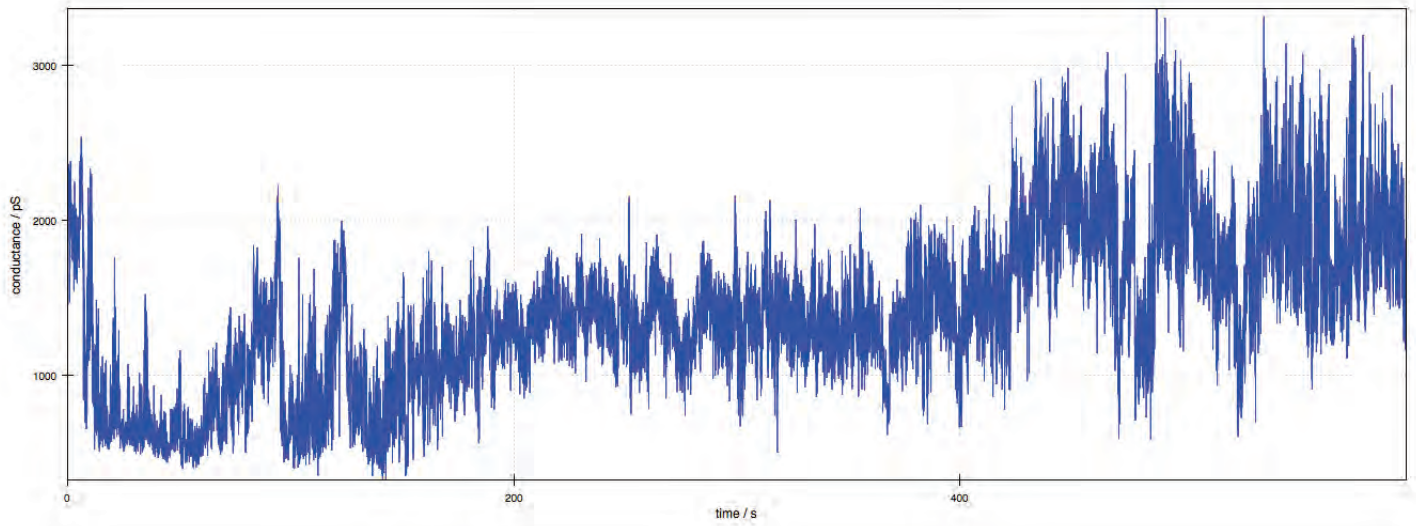
fractal



134-0004

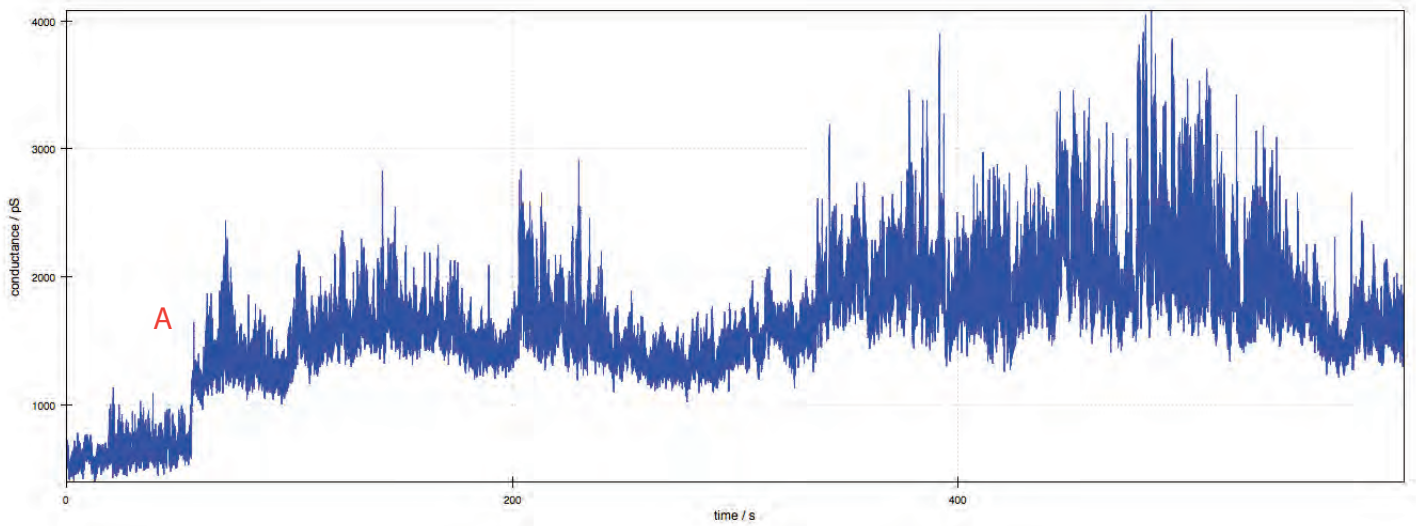


134-0005

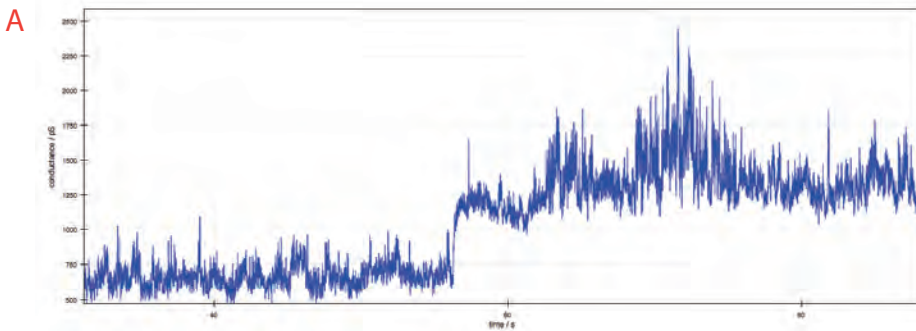


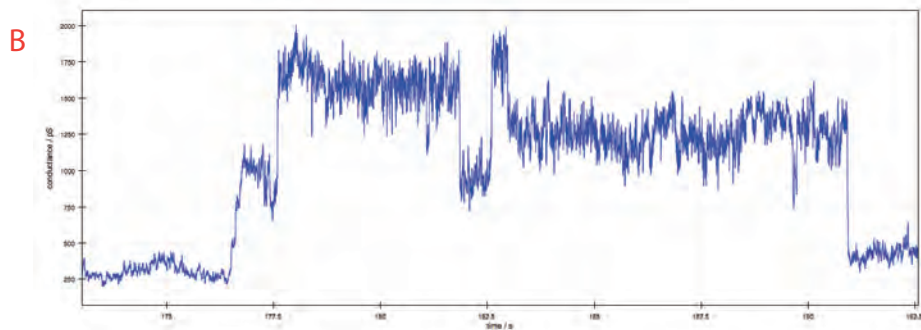
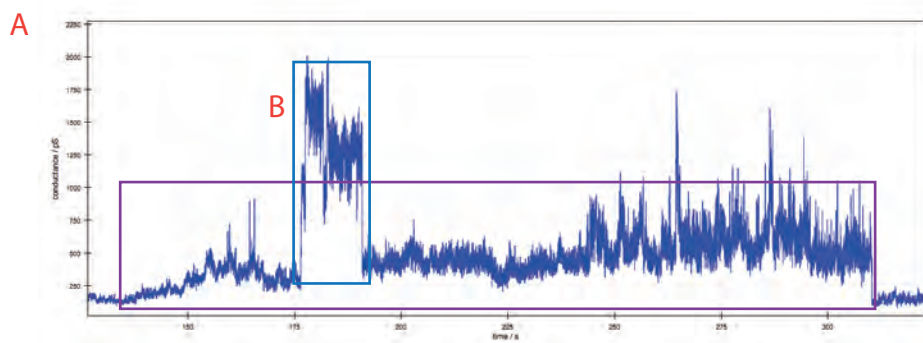
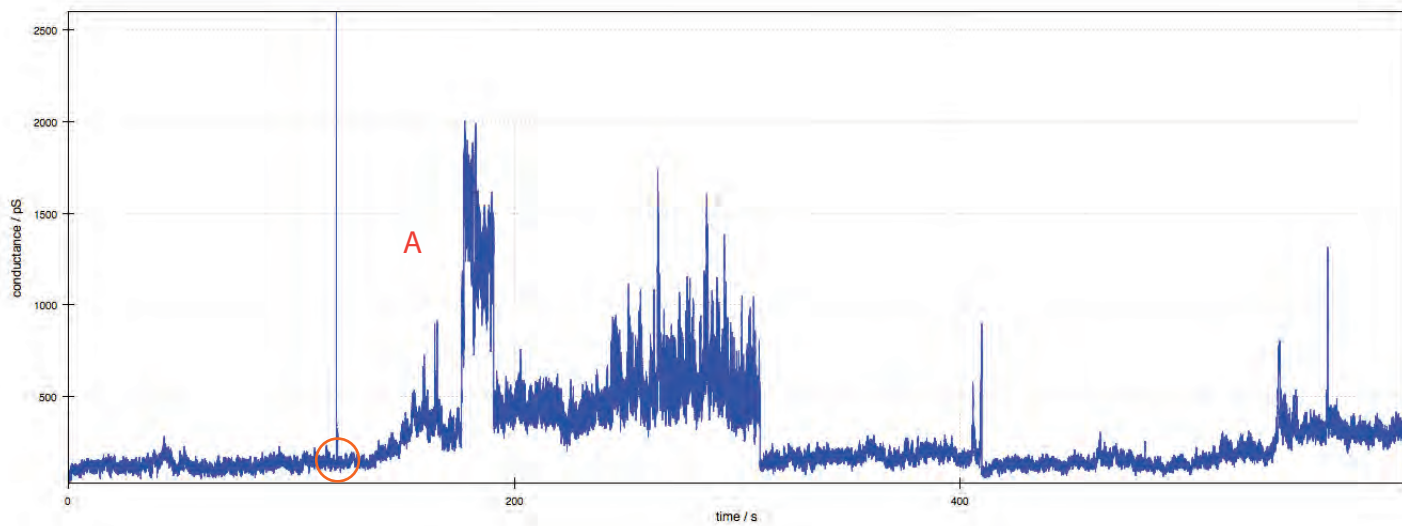
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134-0006

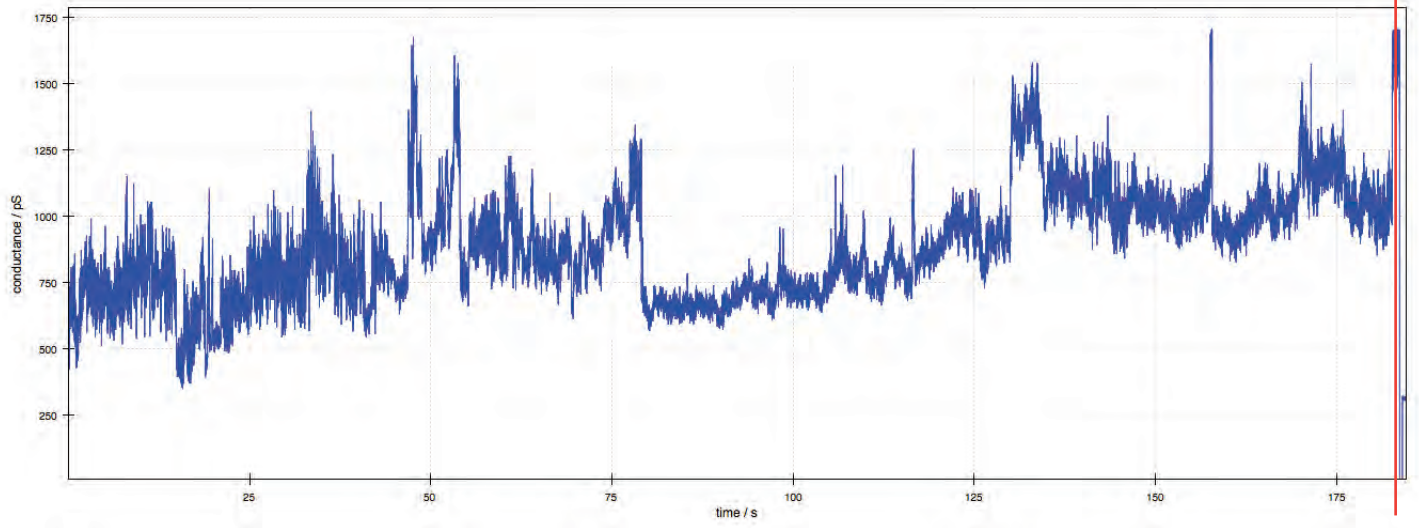


fractal

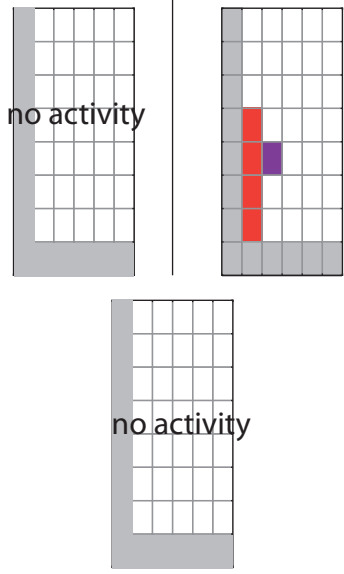
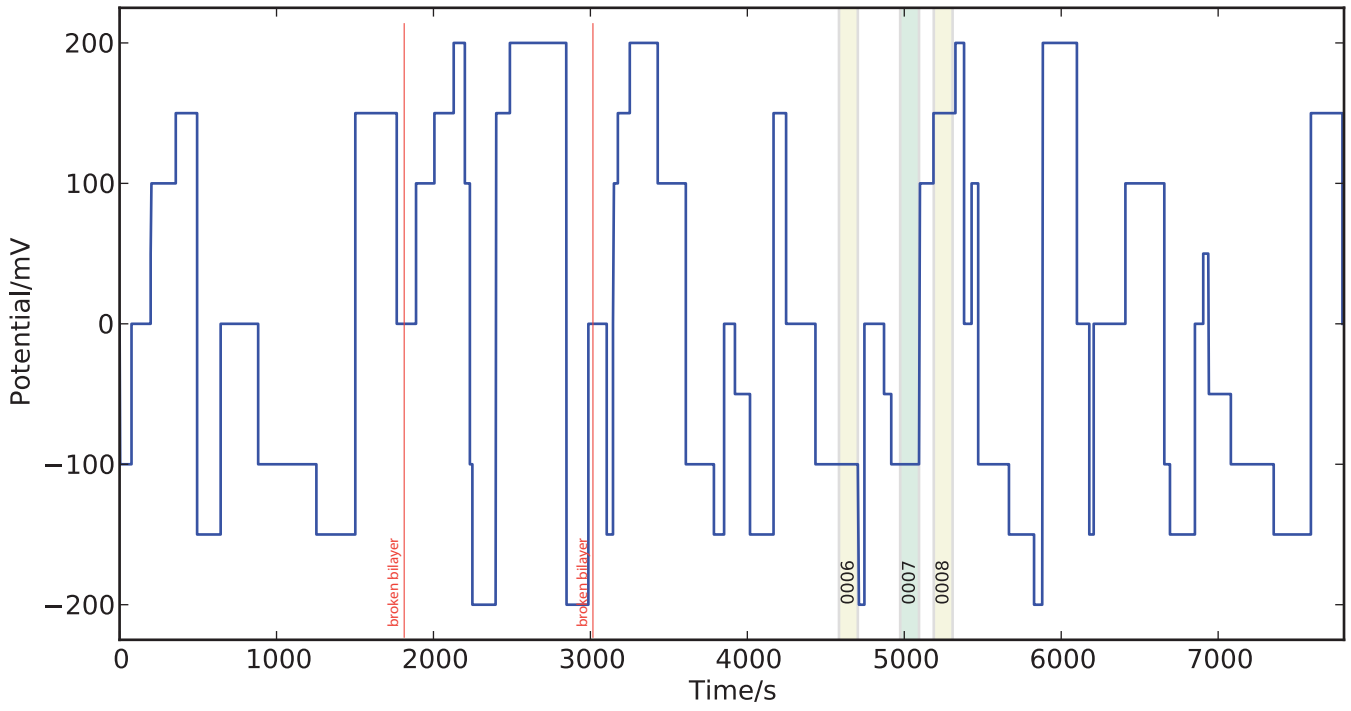




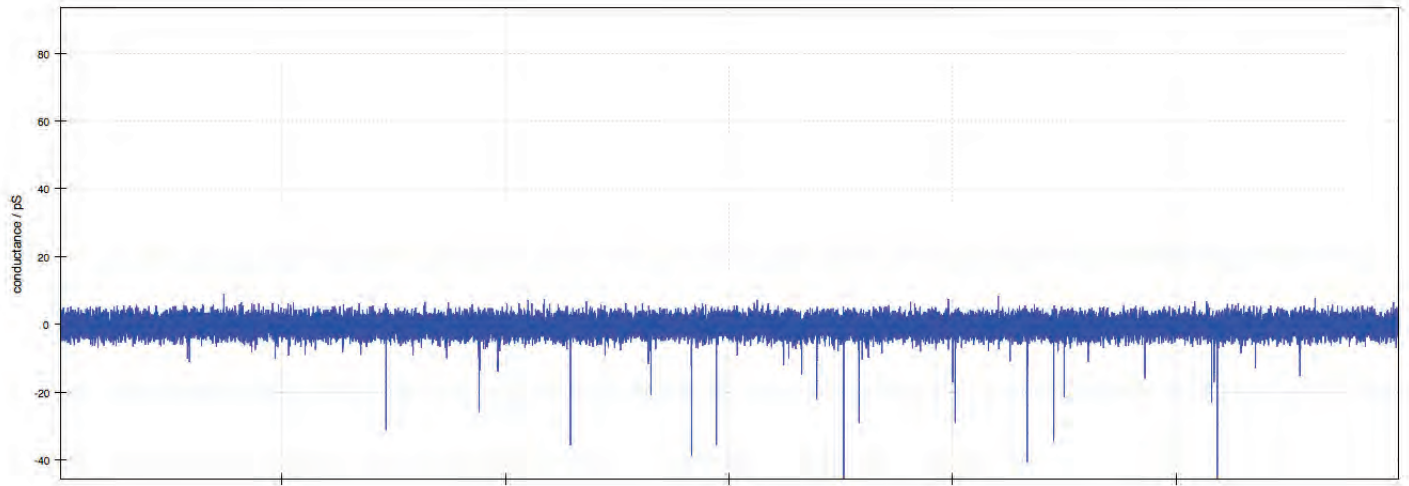
134-0008



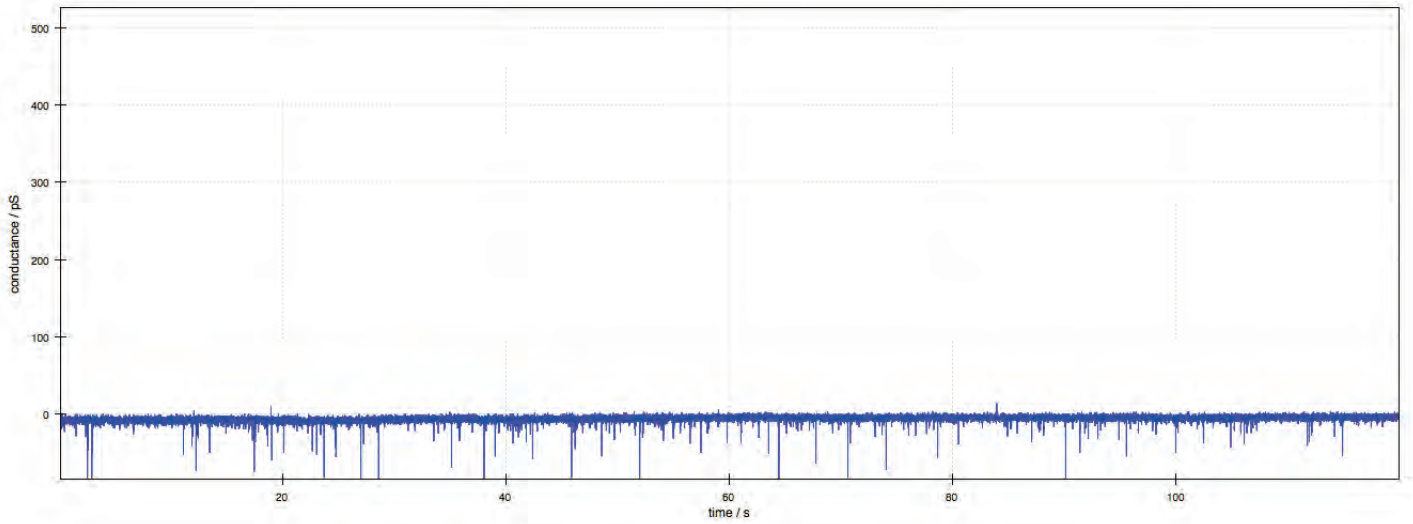
JC-138 JC-V-23 bCD-Ethis 1percent premix AdNH2 1M CsCl



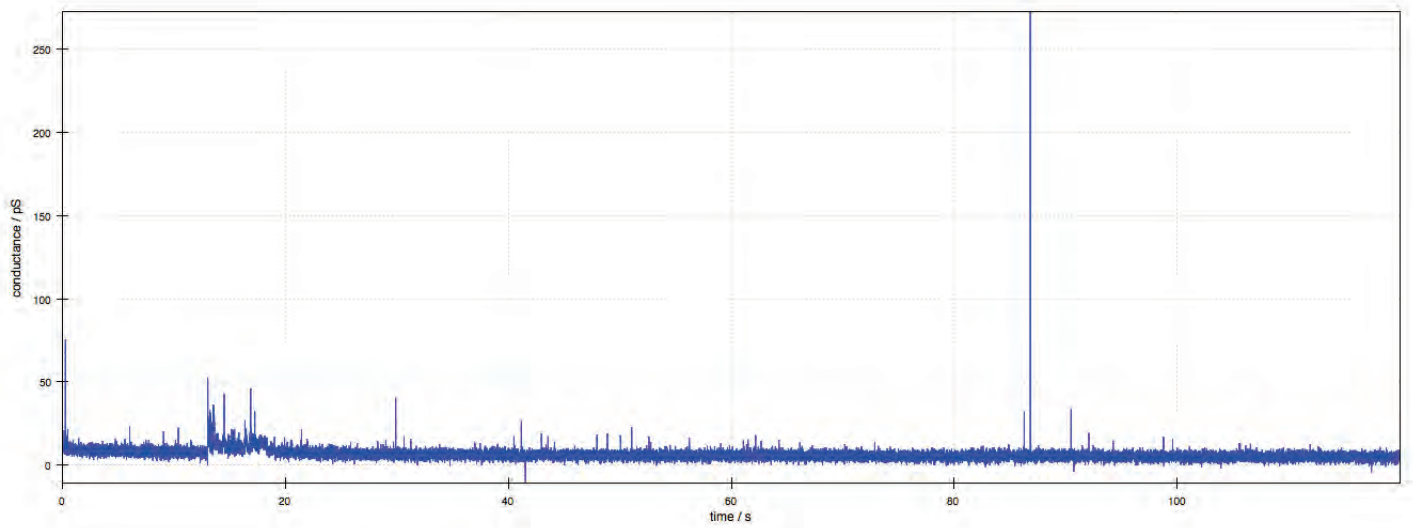
138-0006



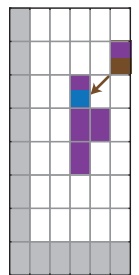
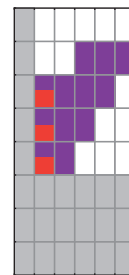
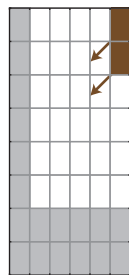
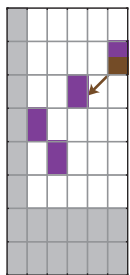
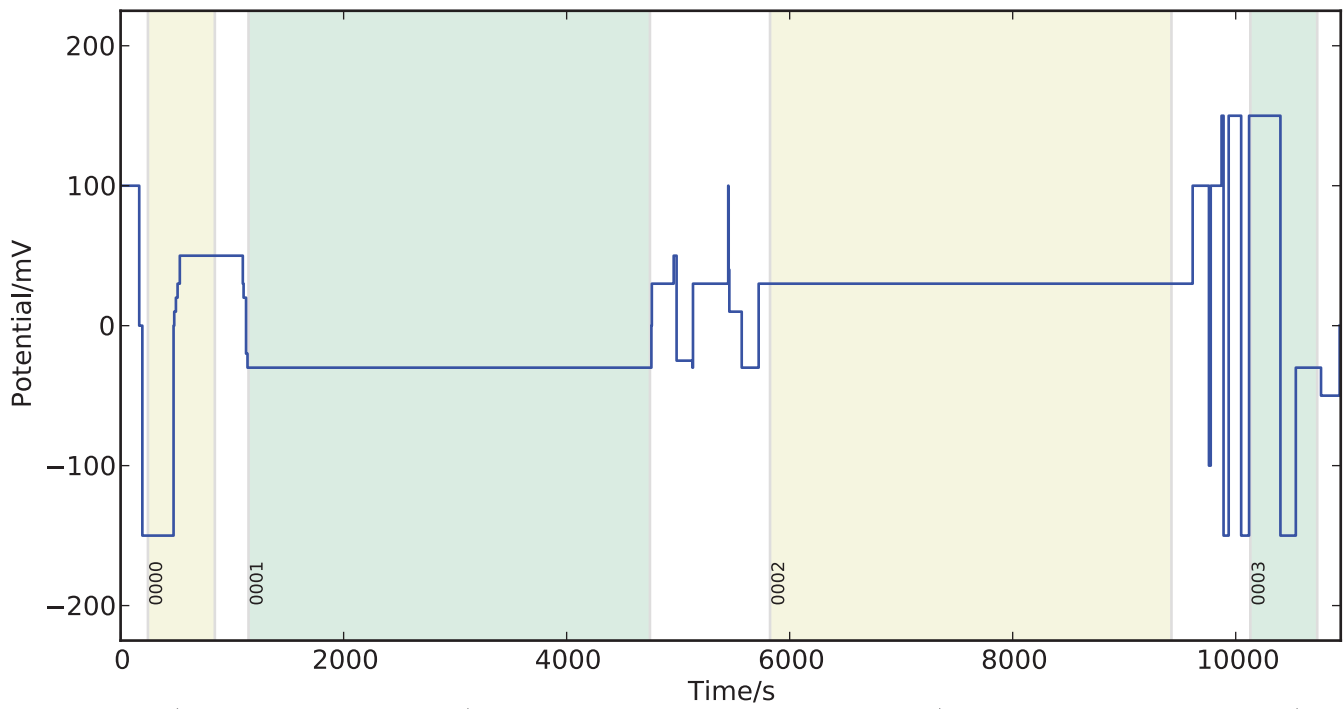
138-0007



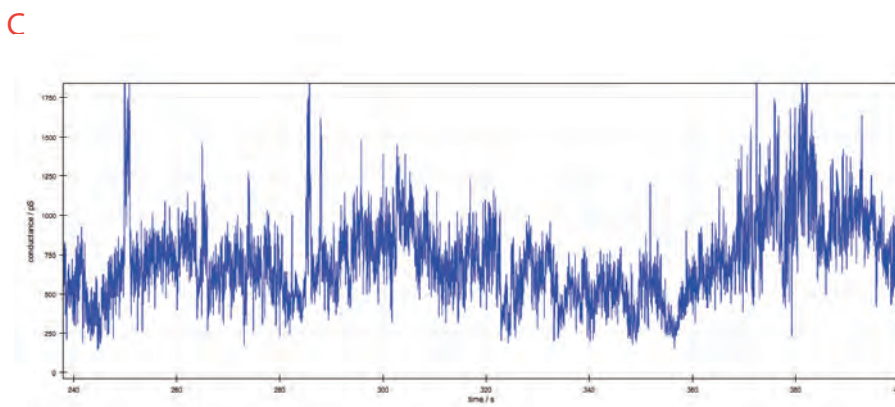
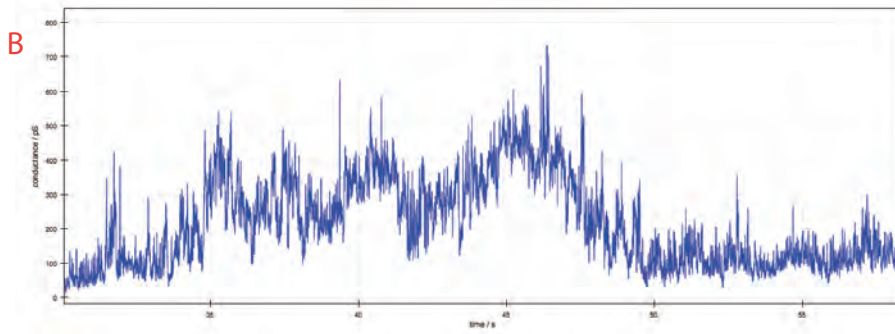
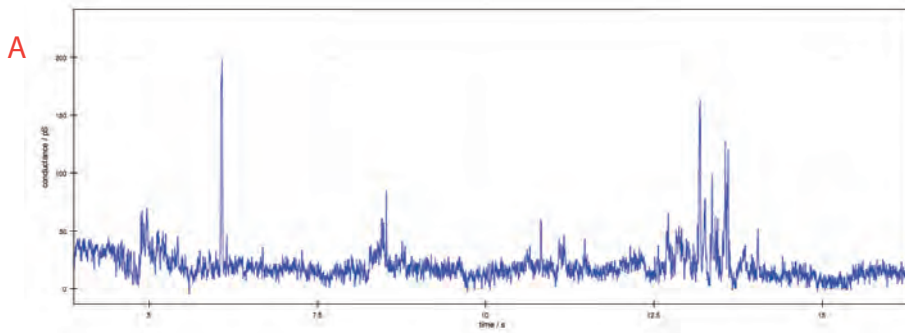
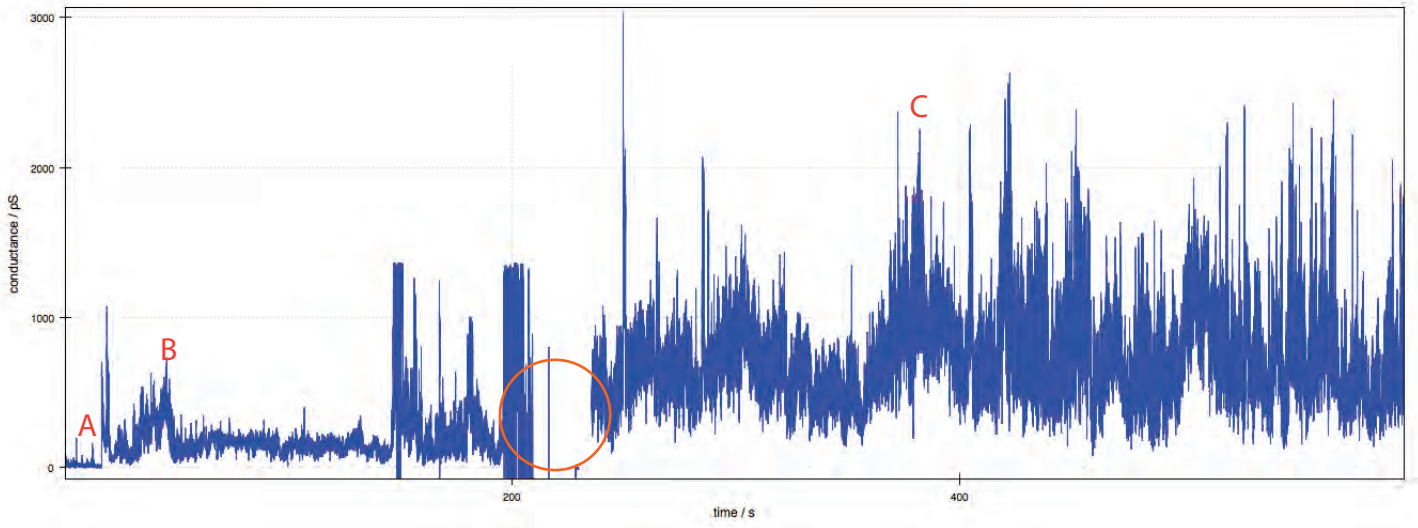
138-0008



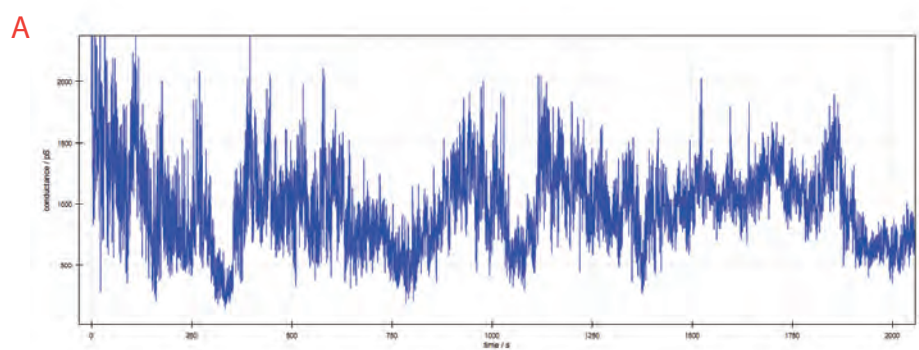
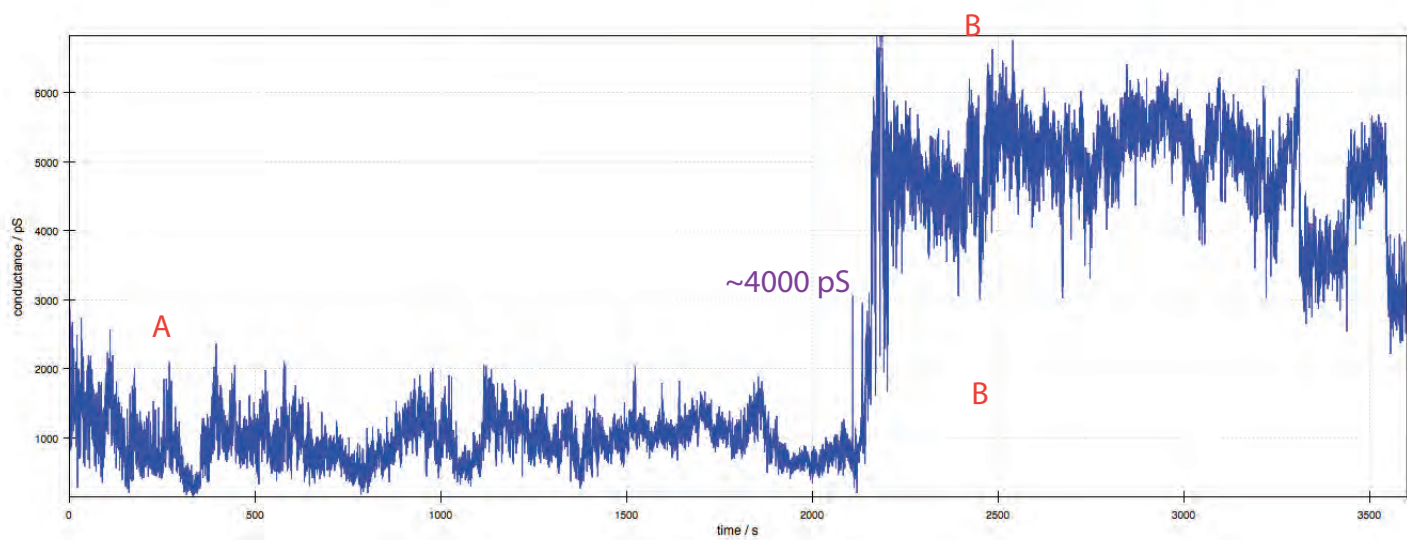
# JC-139 JC-V-23 bCD-Ethis 1percent 1M NEt4Br



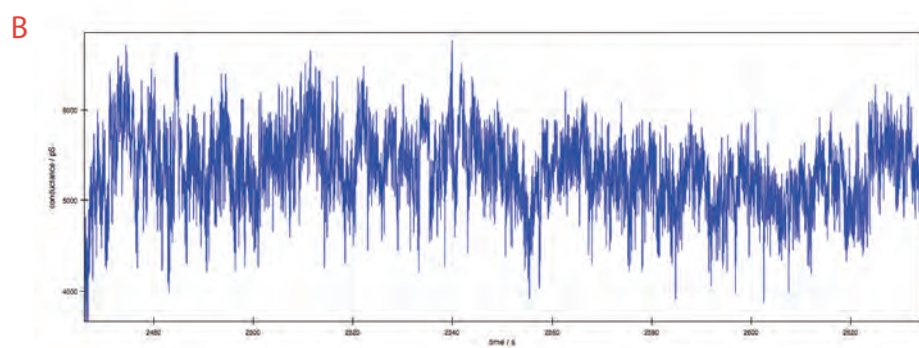
Two level fractals  
(4000 pS separation)

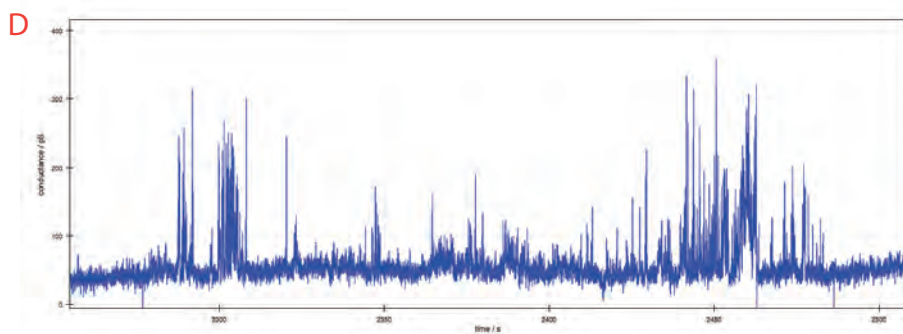
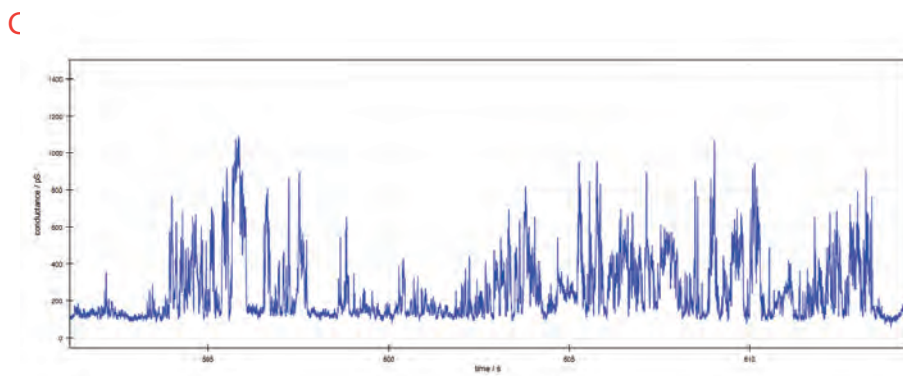
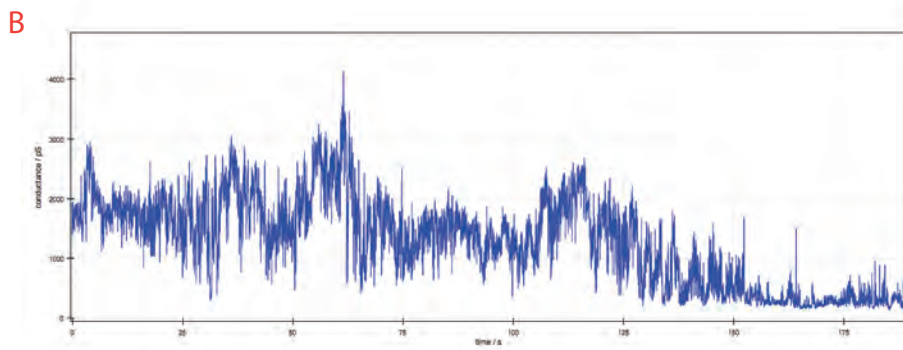
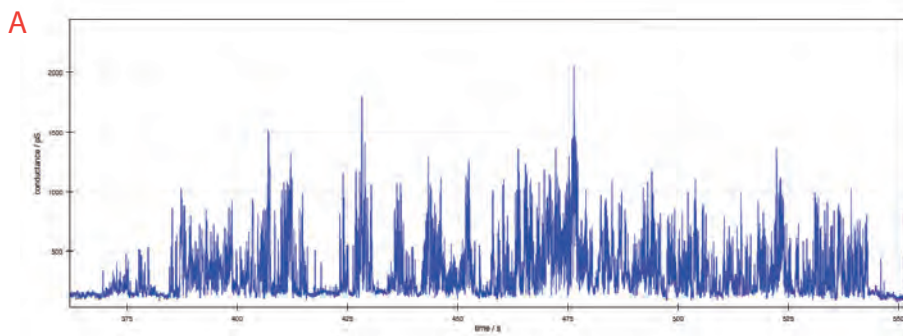
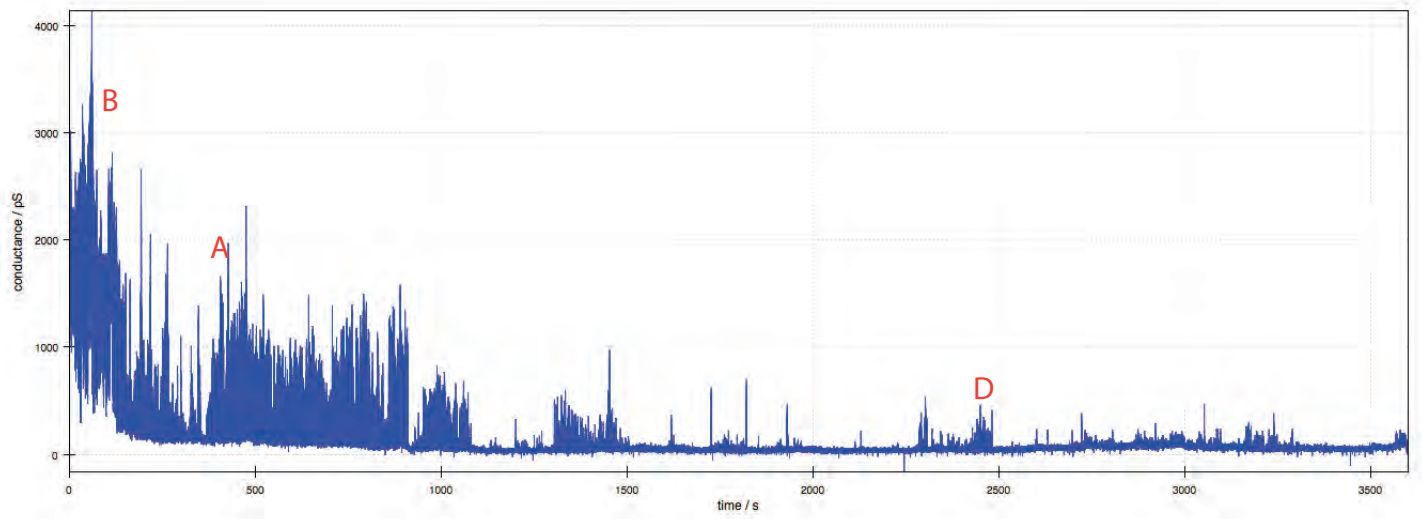


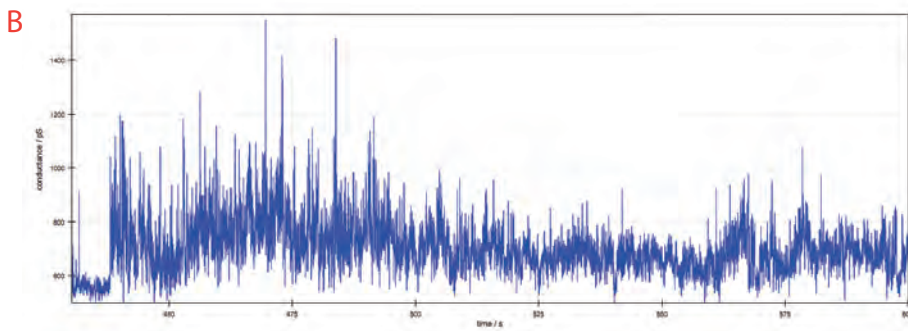
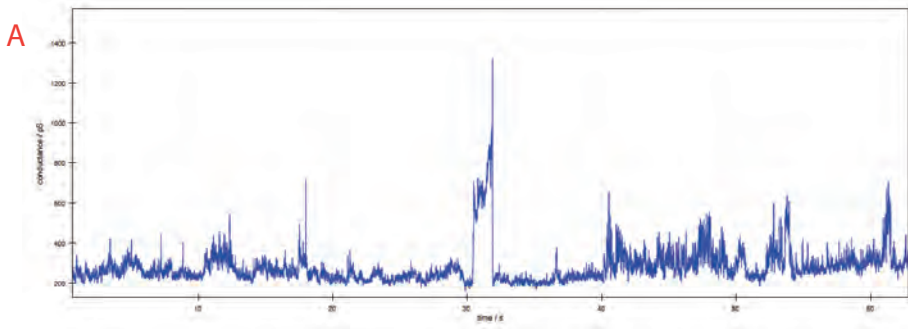
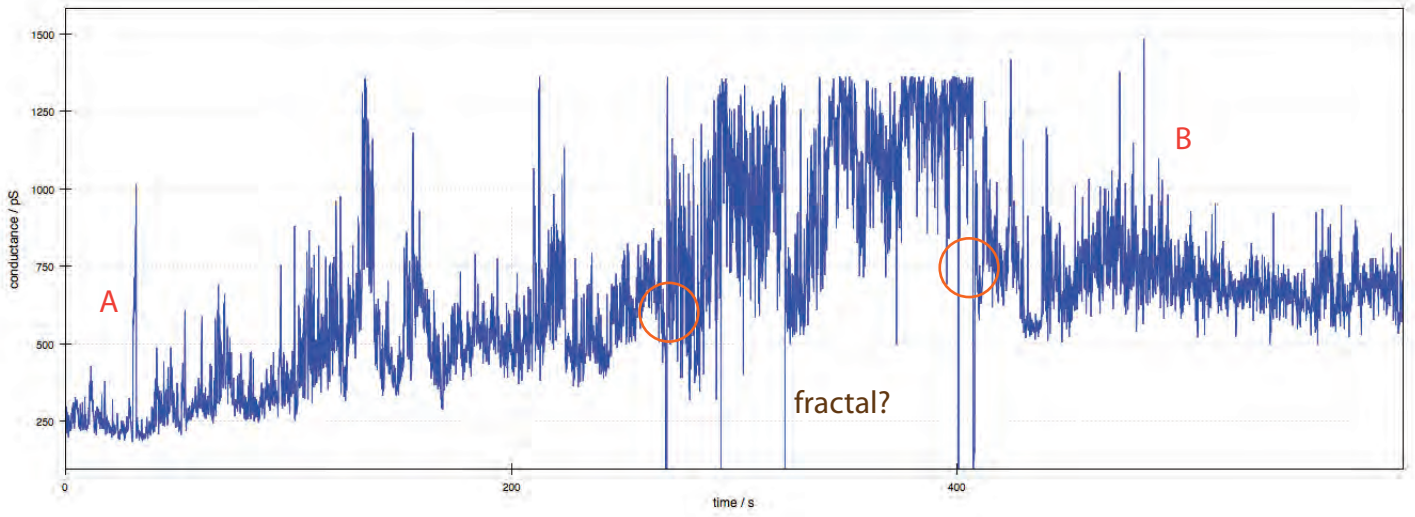
fractal?



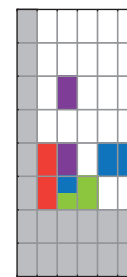
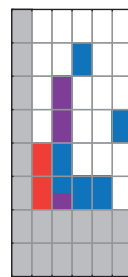
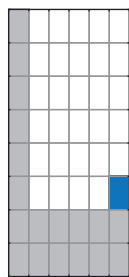
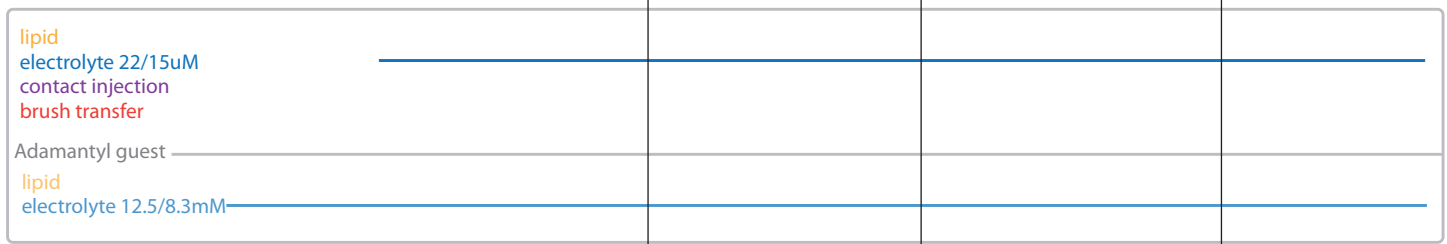
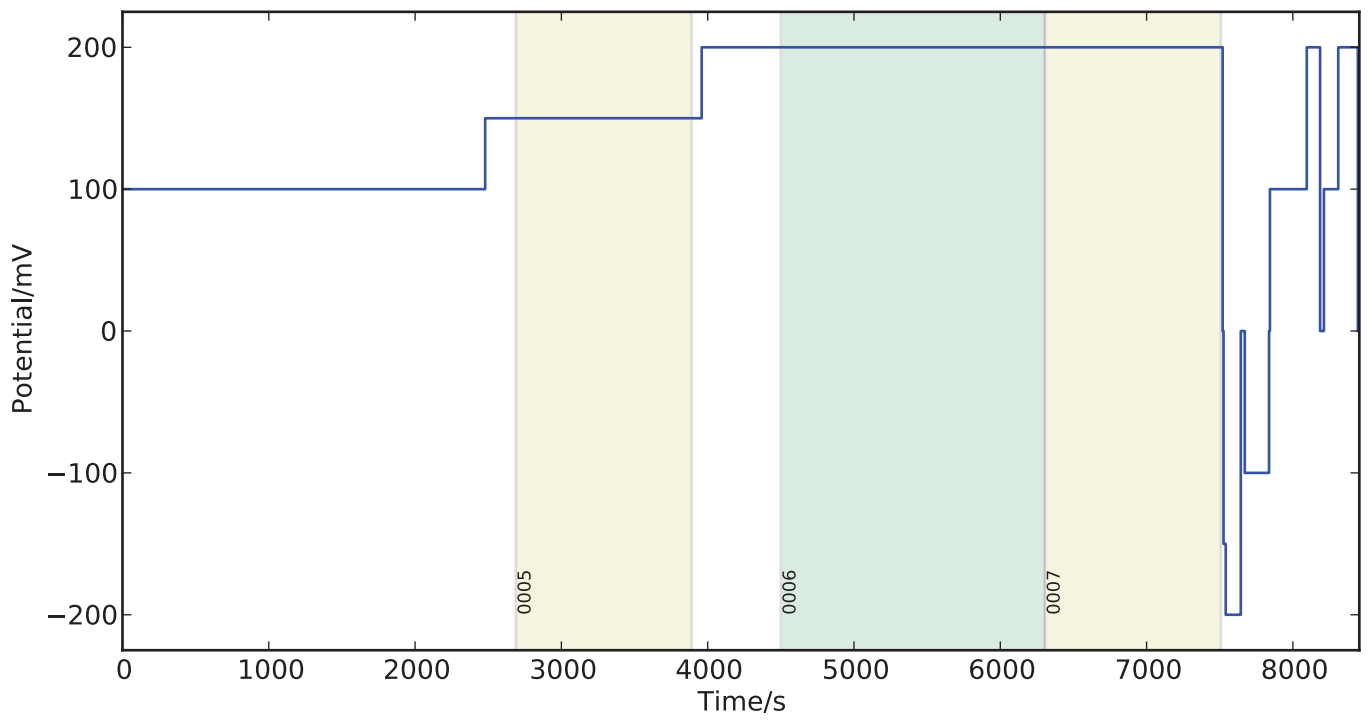
Fractal



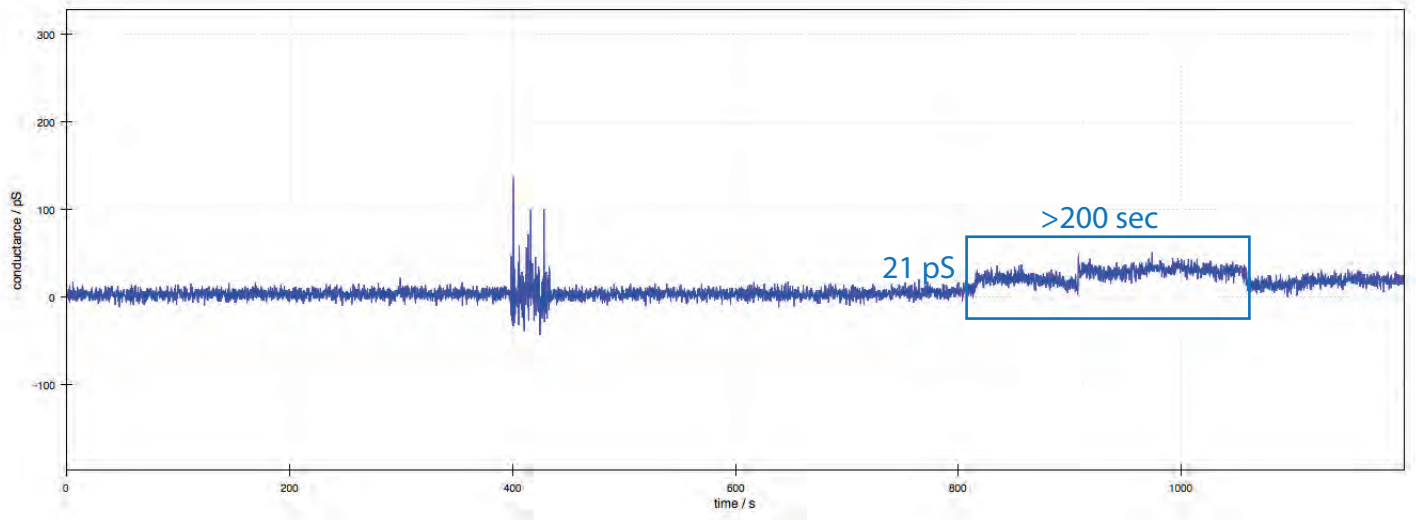


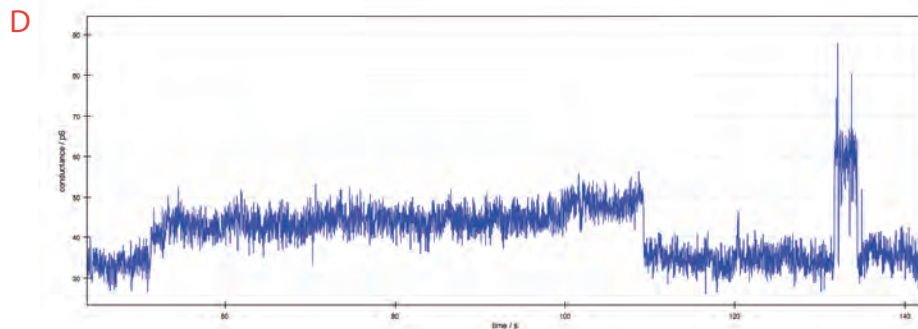
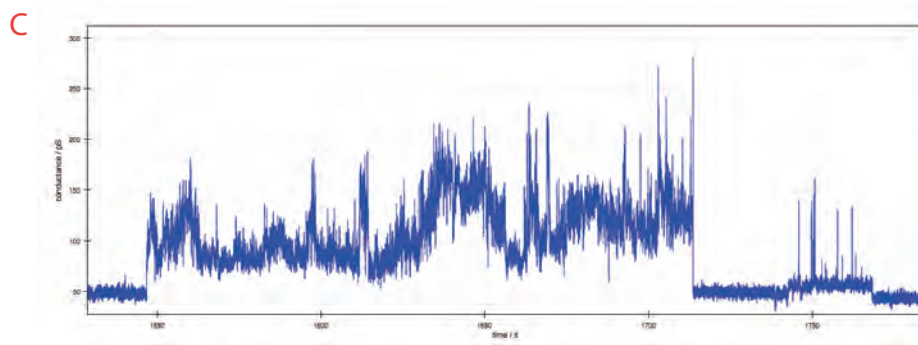
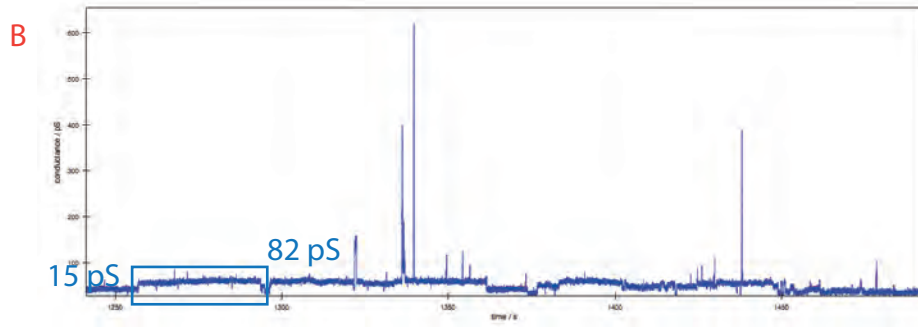
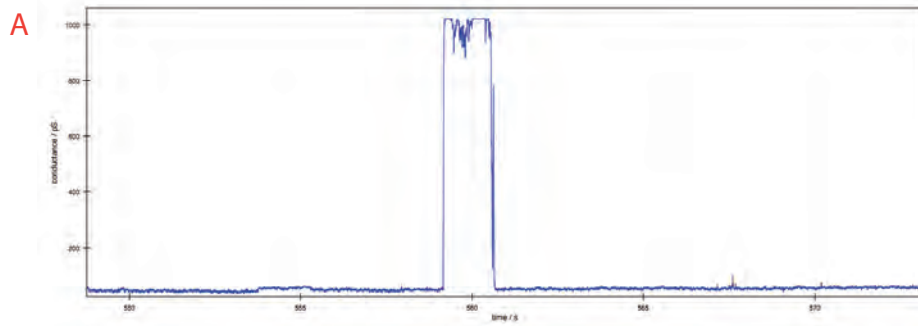
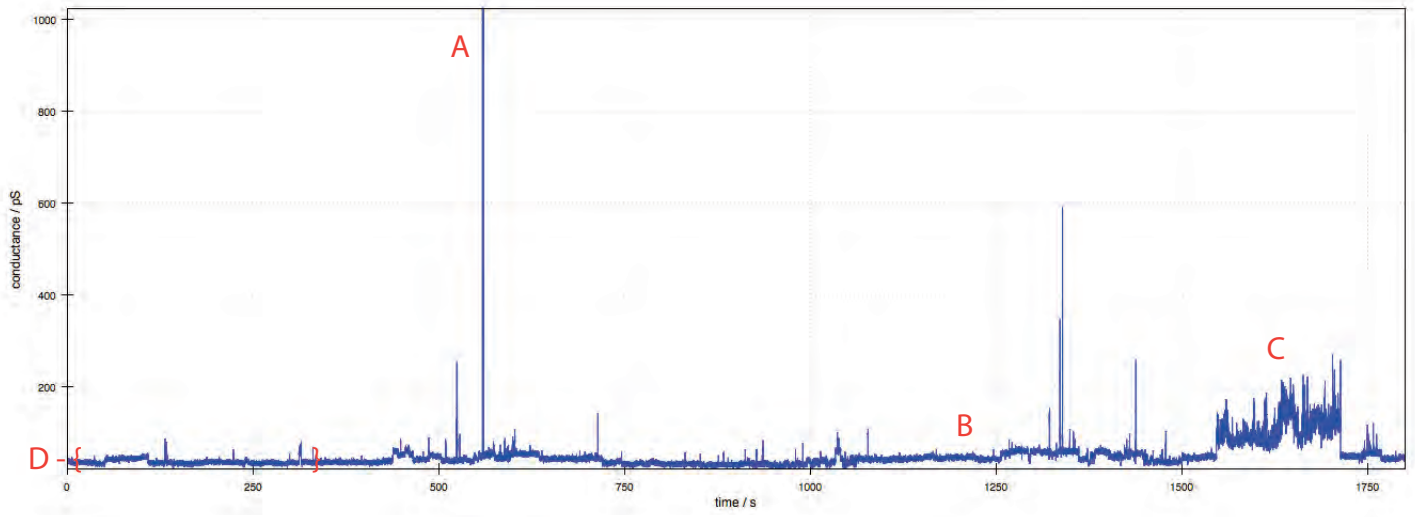


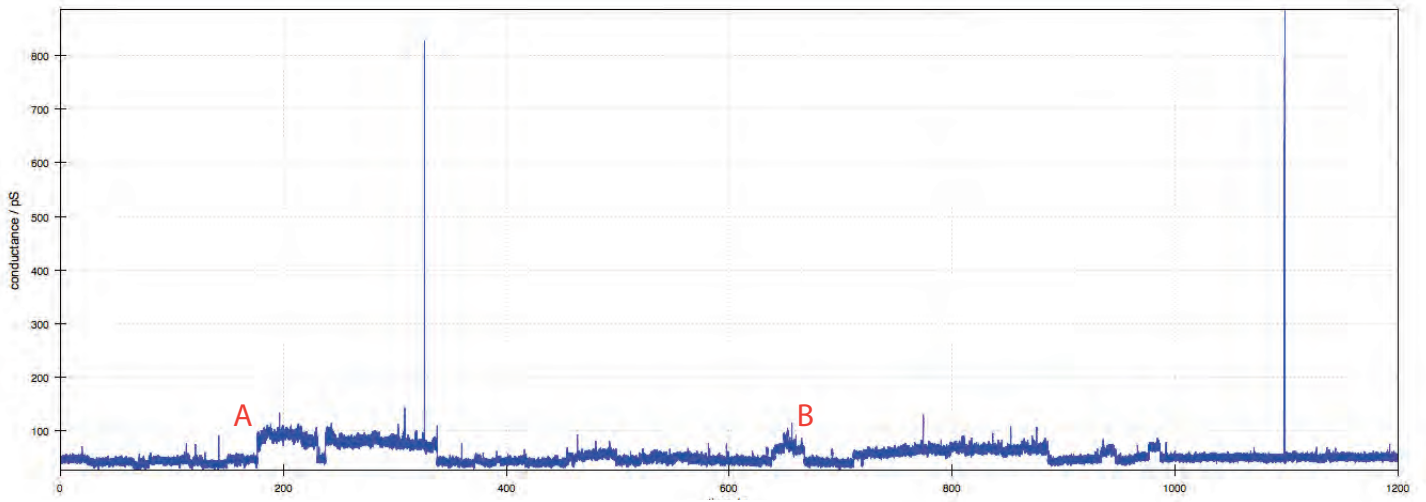
# JC-144 bCD-Ethis 1M CsCl pH 5 200mM succinate addn of AdNH2



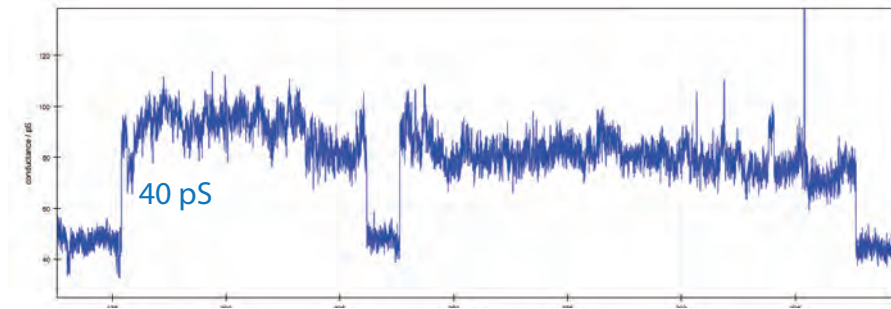
144-0005



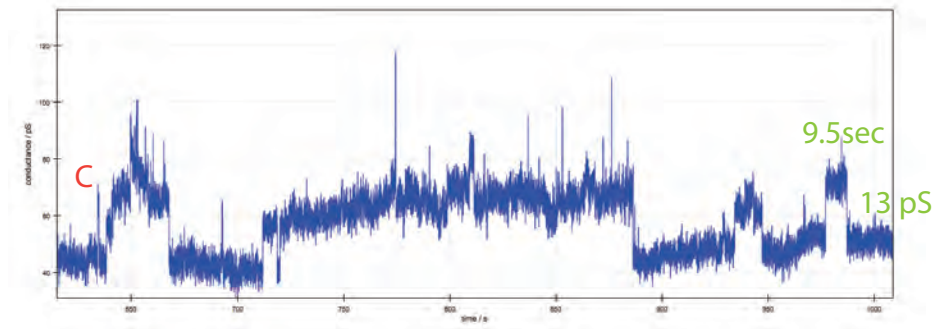




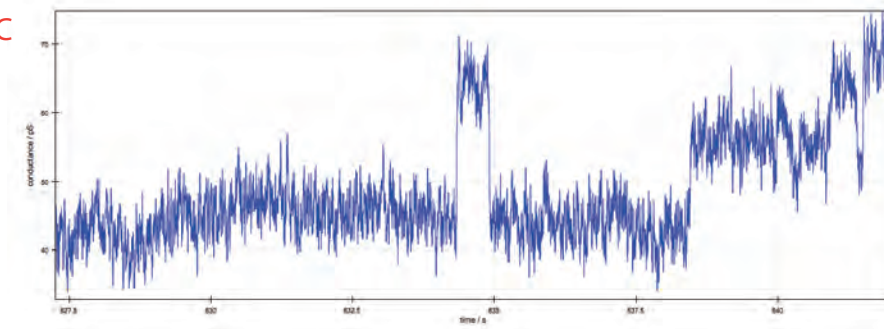
A



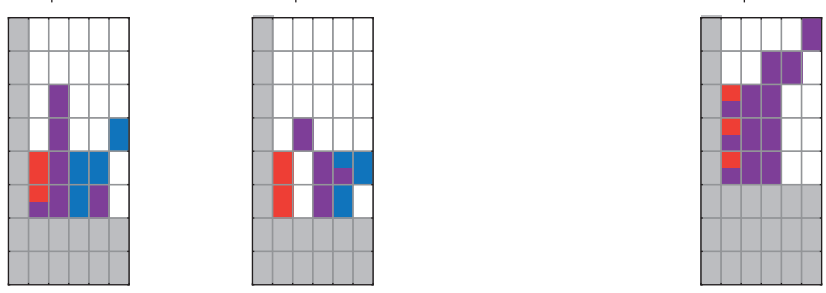
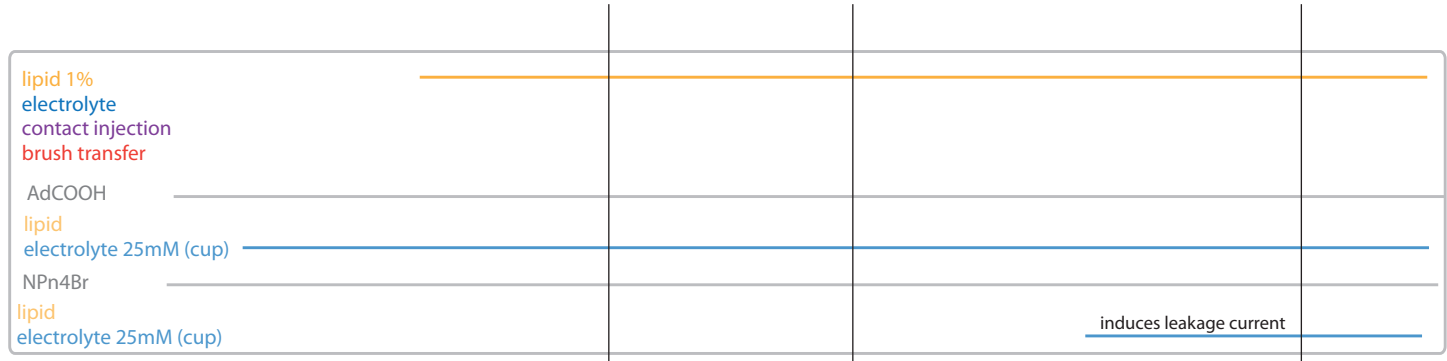
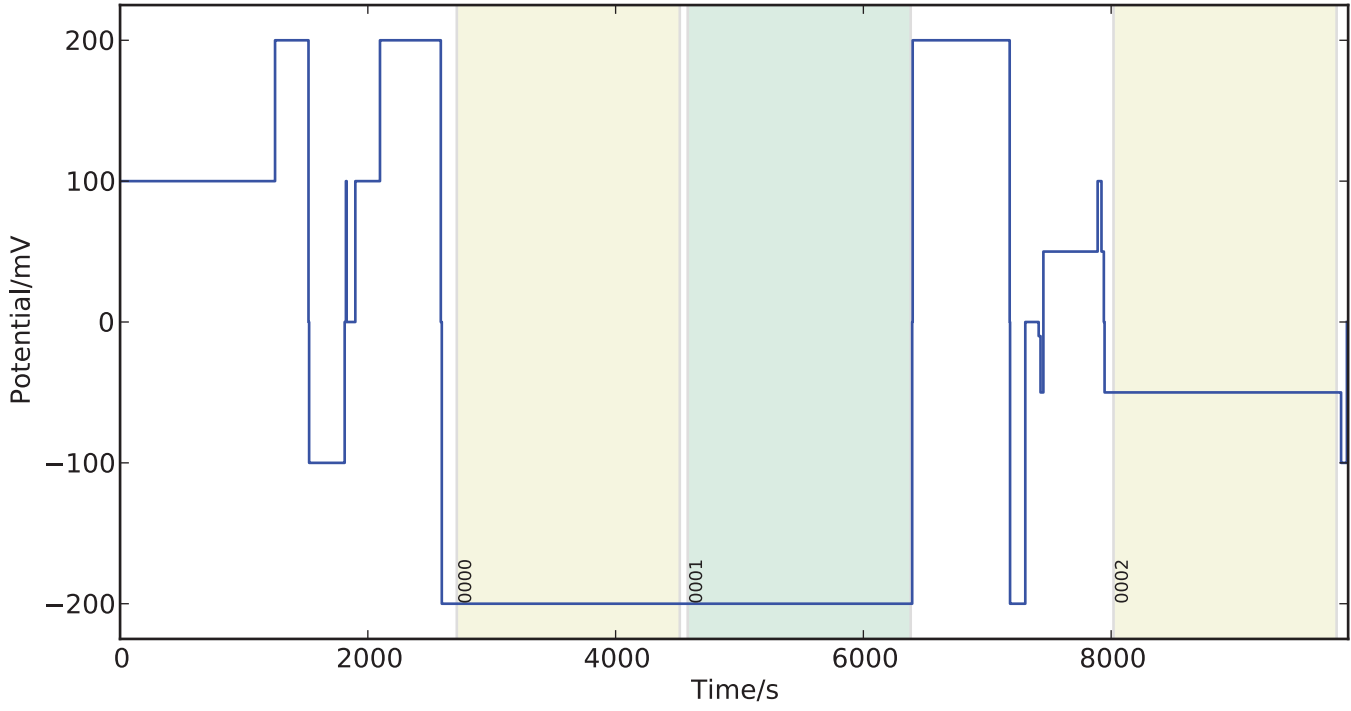
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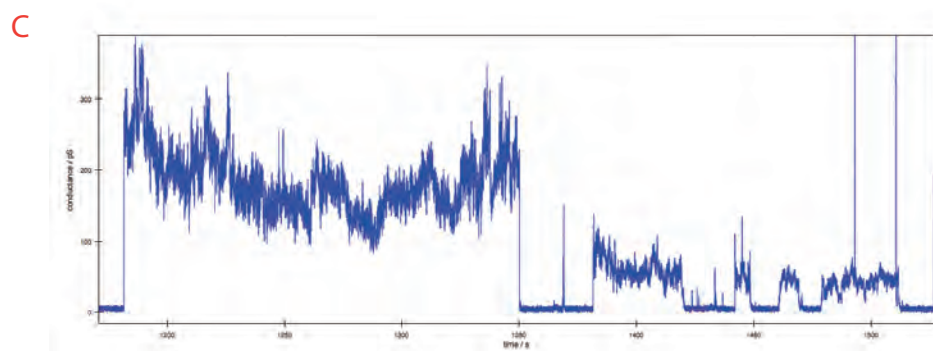
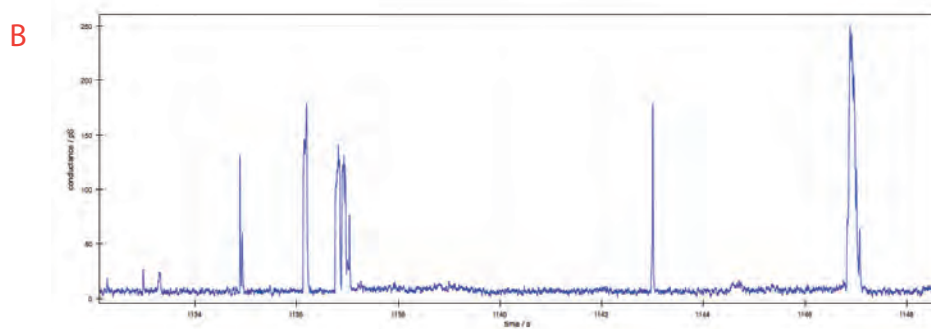
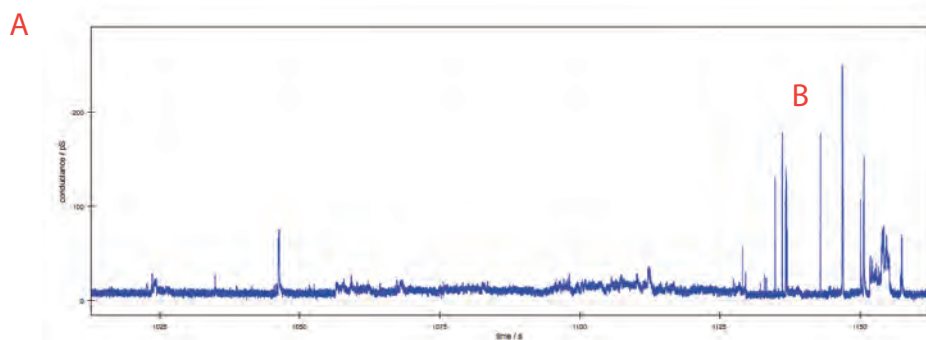
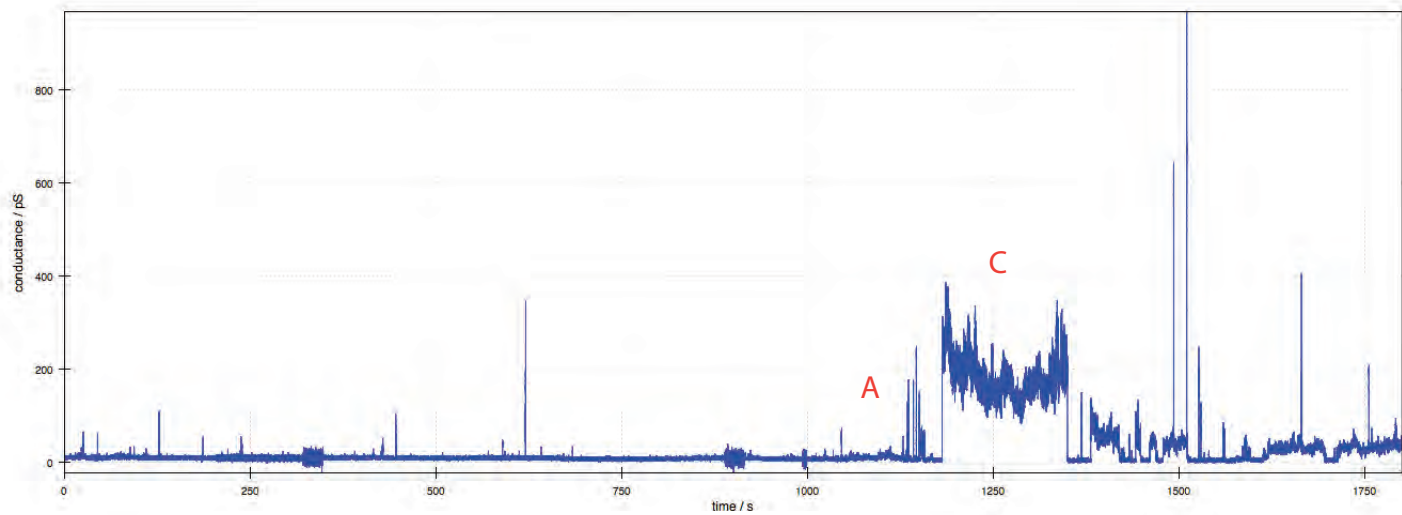


C

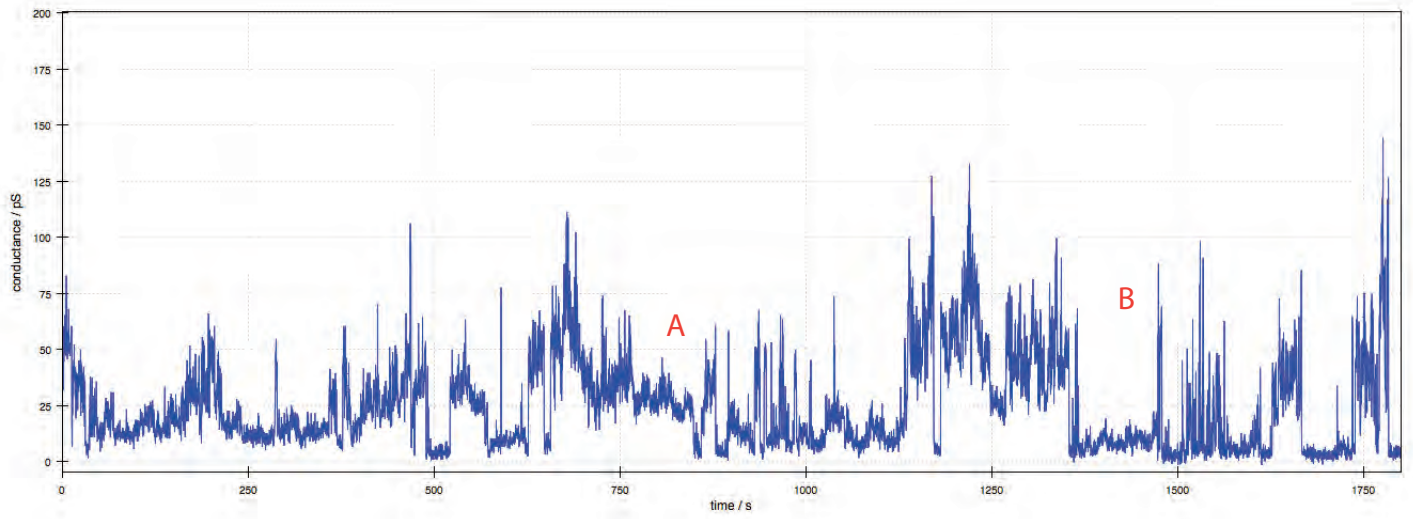


JC-145 JC-V-23 bCD-Ethis 1M CsCl pH7 addn of AdCOOH

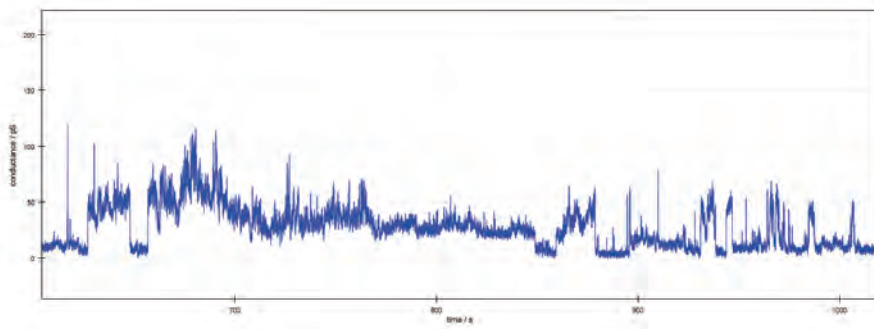




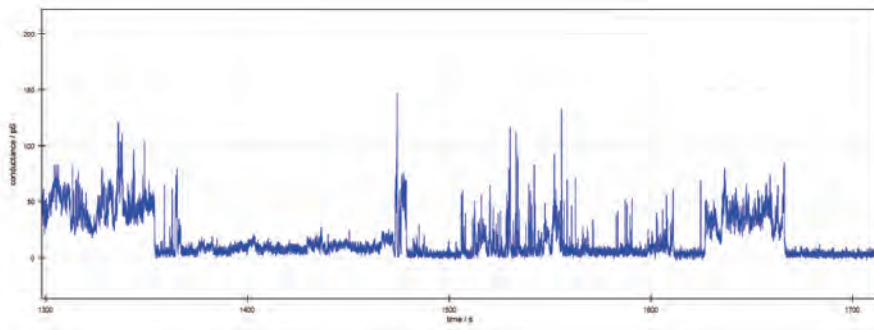
145-0001

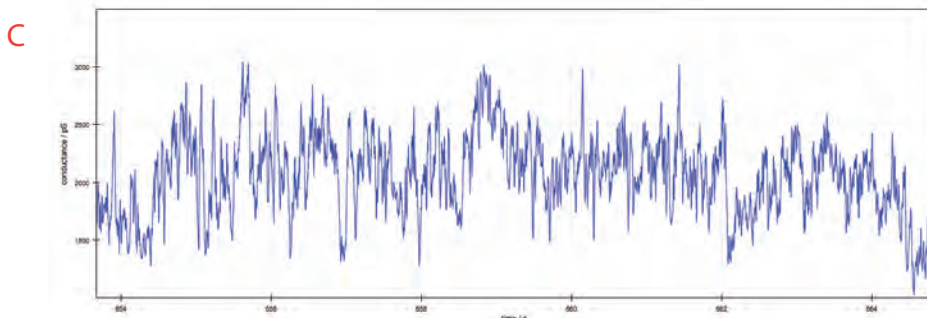
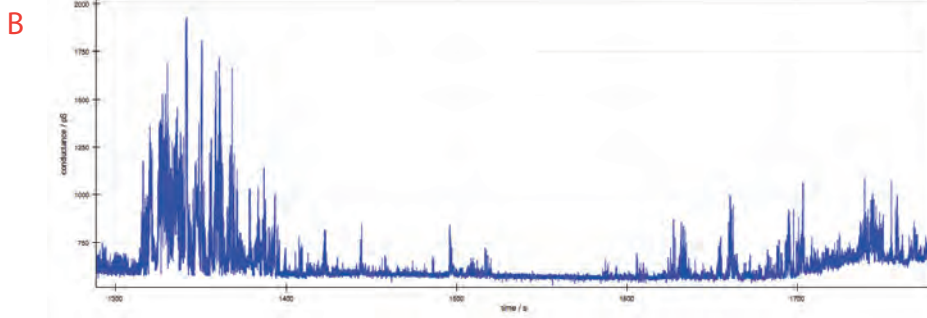
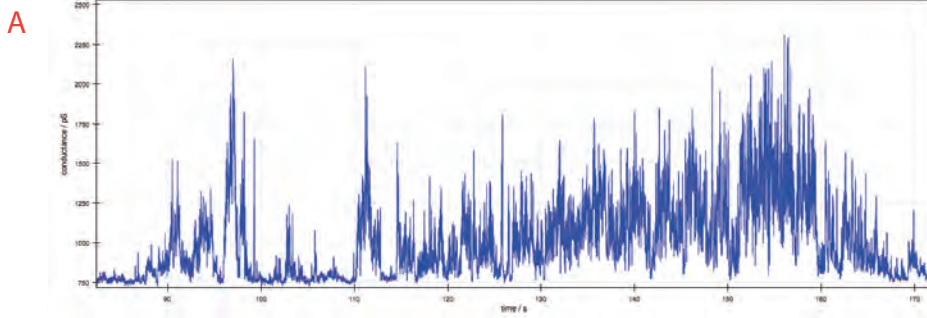
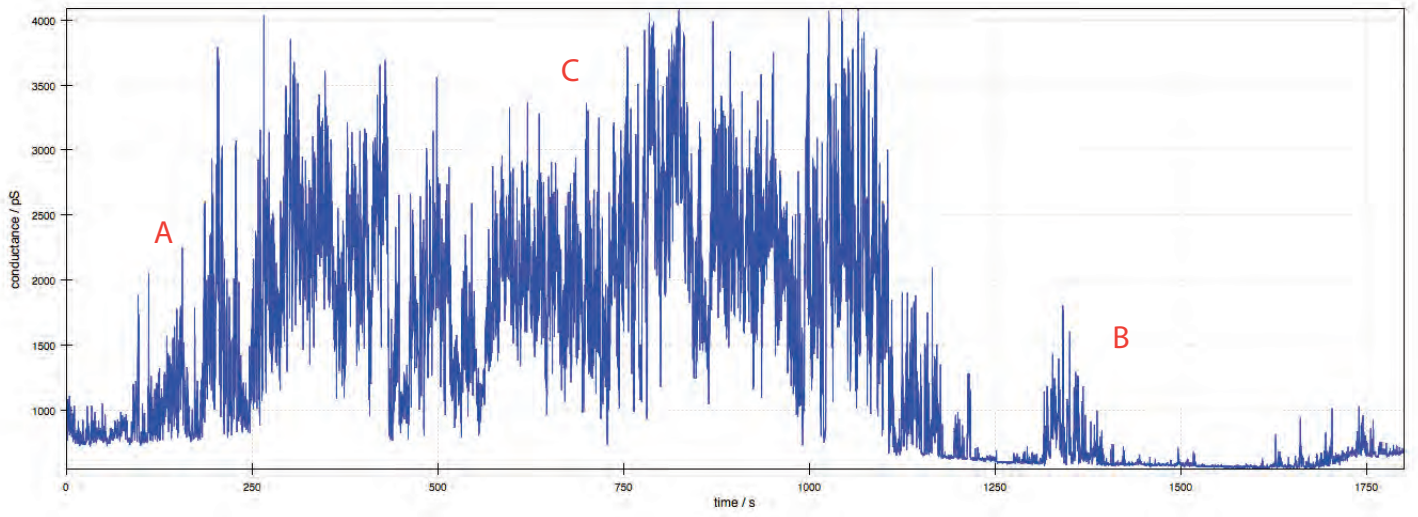


A

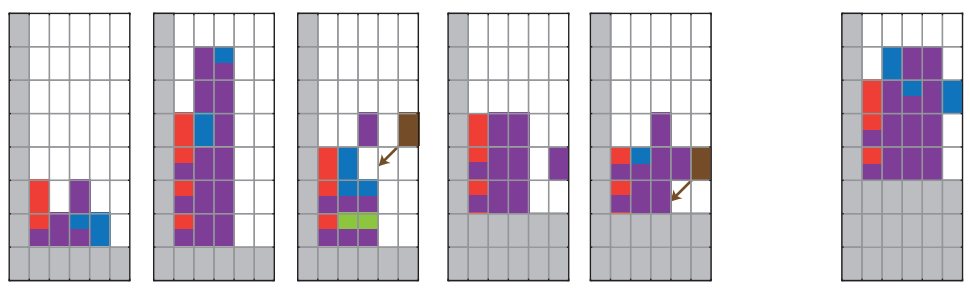
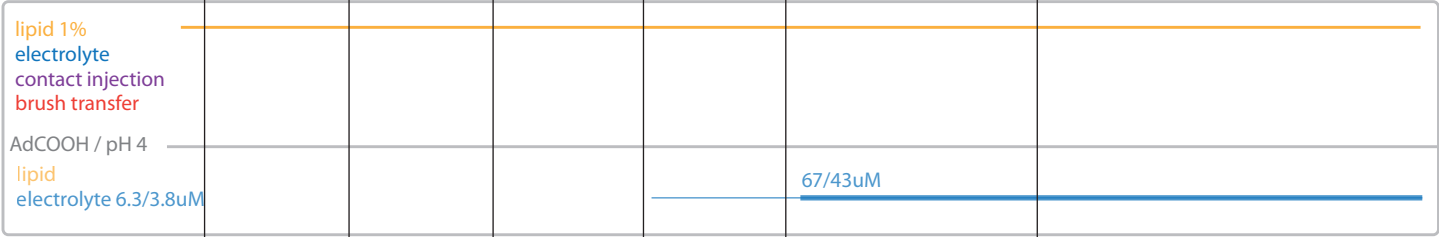
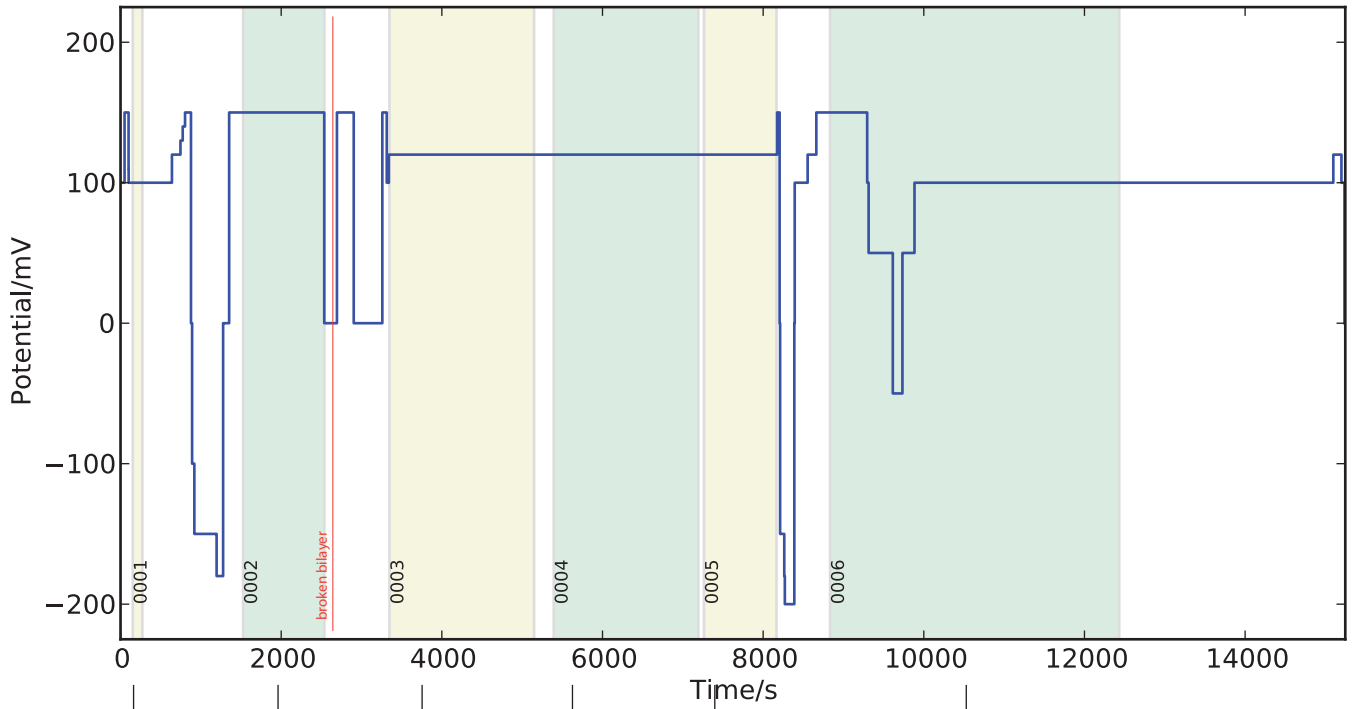


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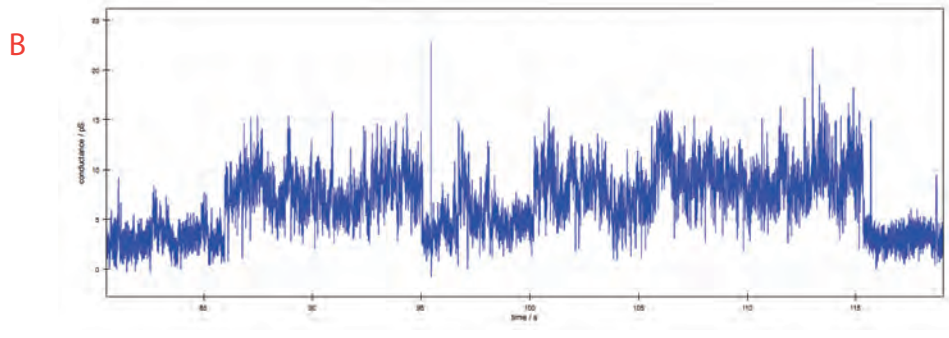
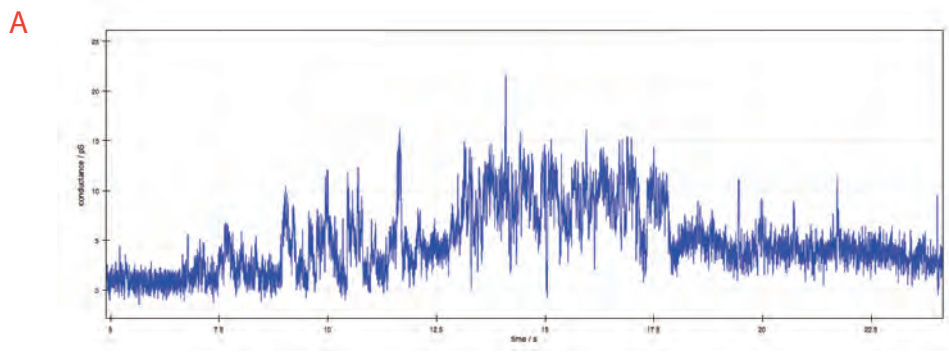
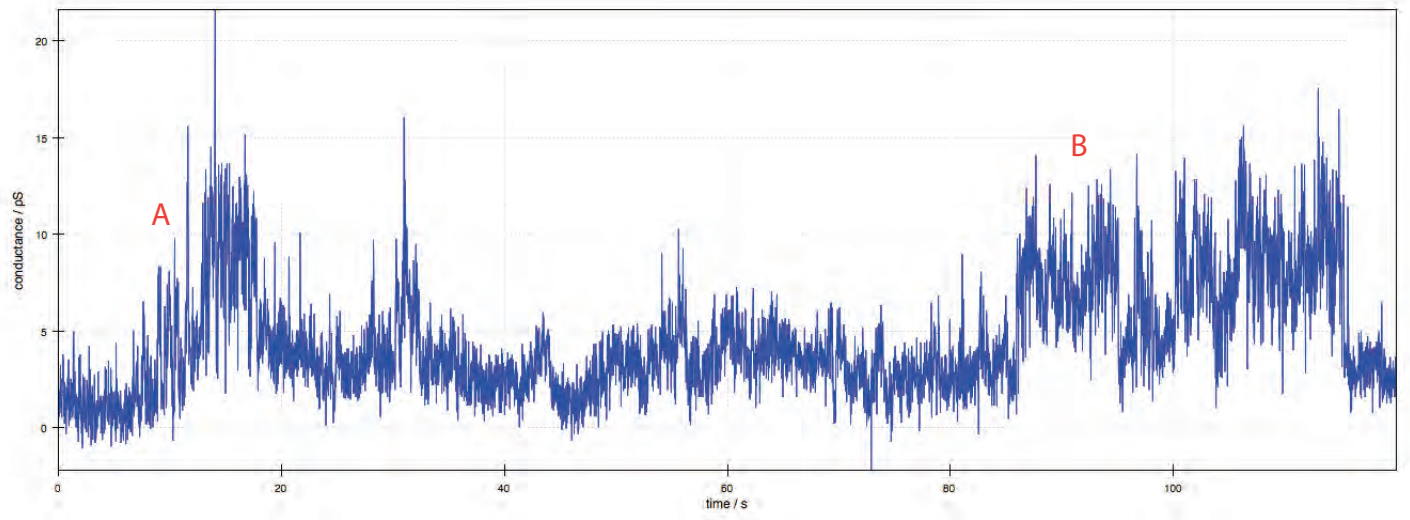


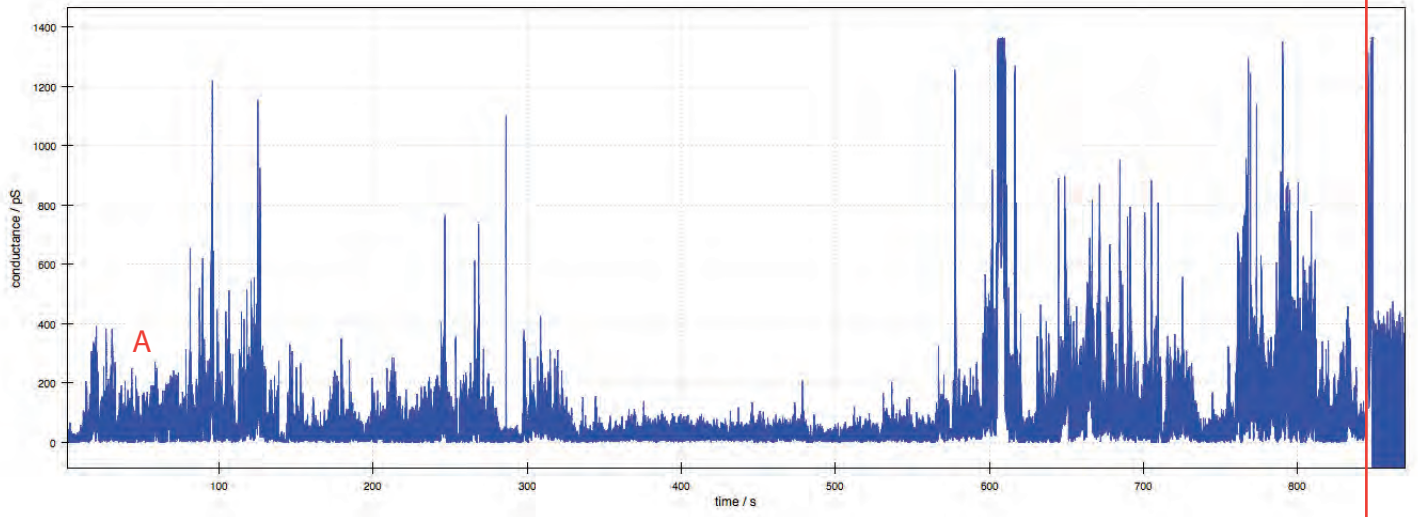


# JC-151 bCD-Ethis 1percent 1M CsCl pH 4.5

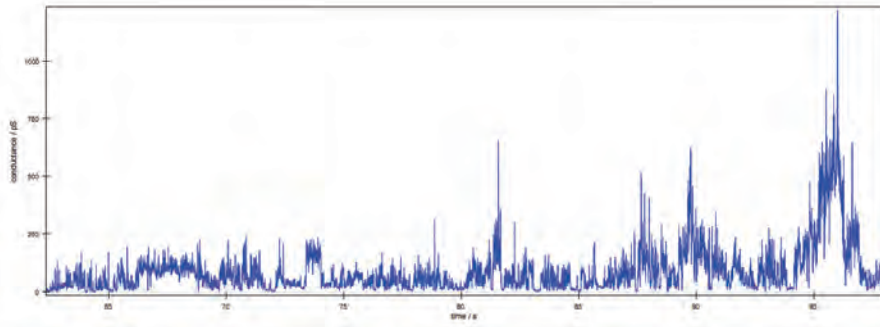


monitored addition of AdCOOH

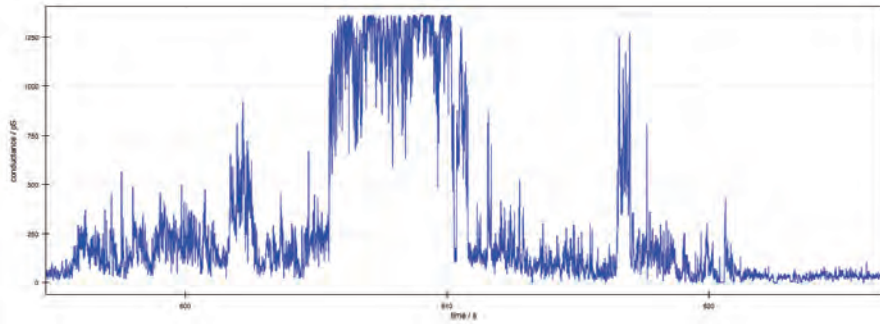


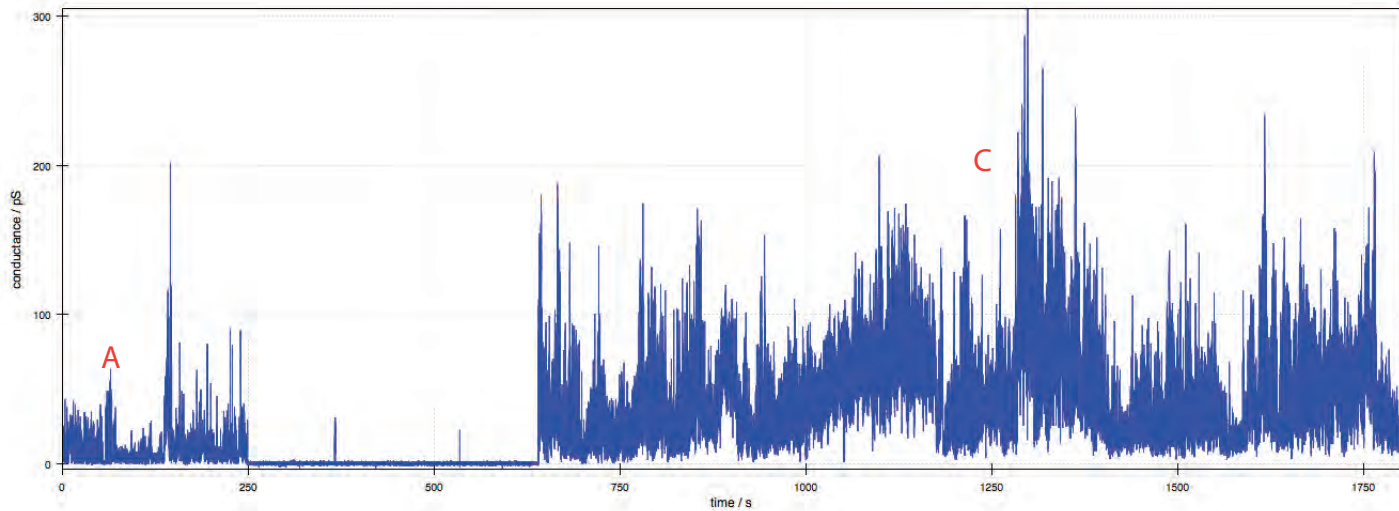


A

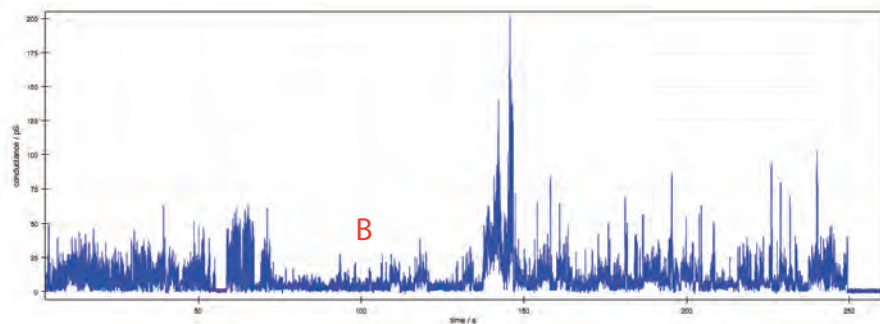


B

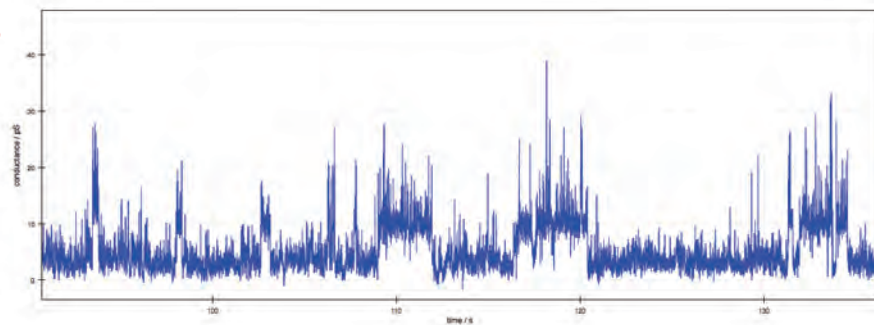




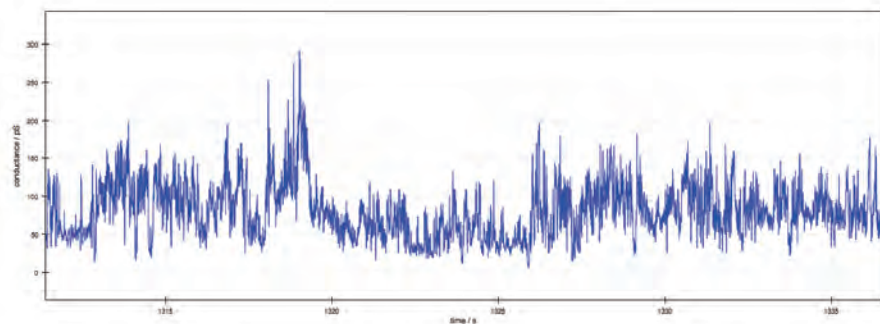
A



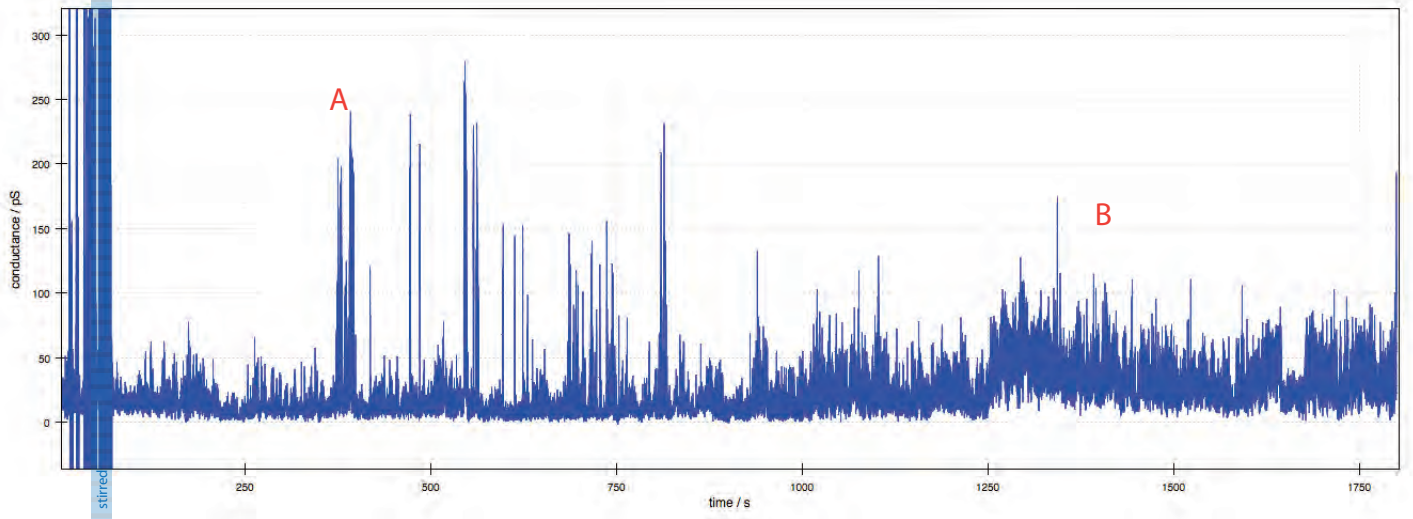
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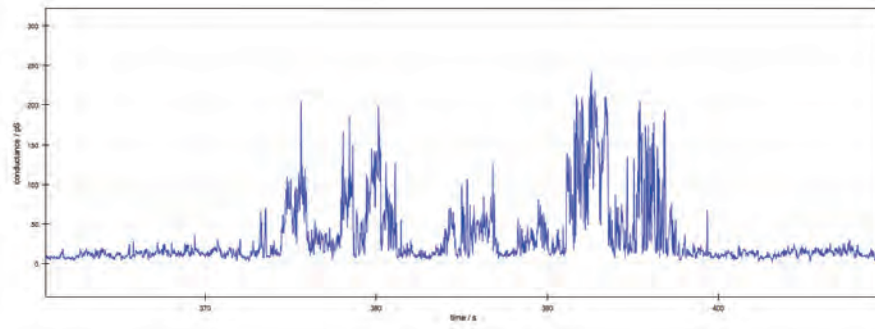
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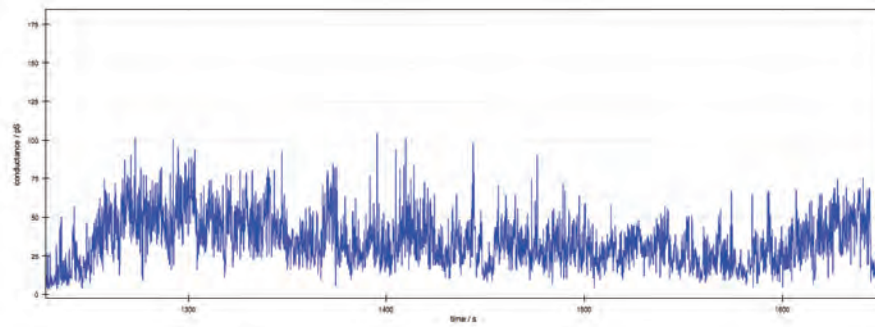
151-0004

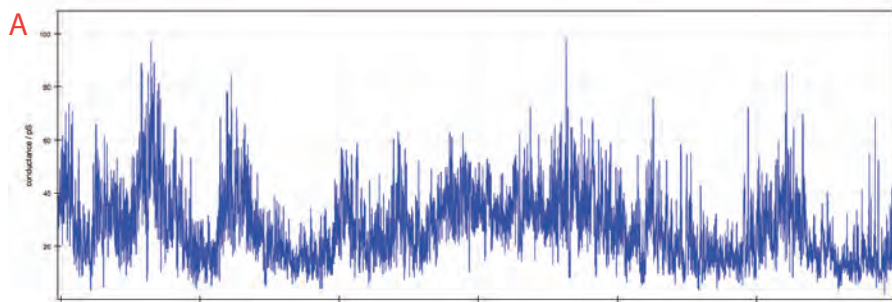
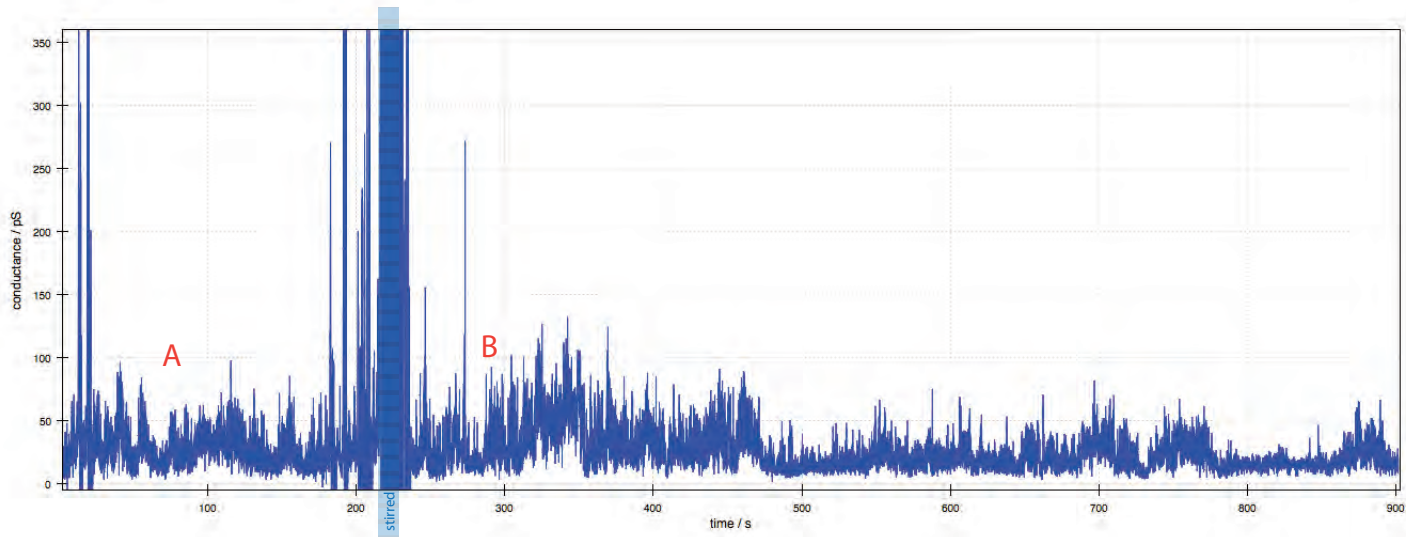


A

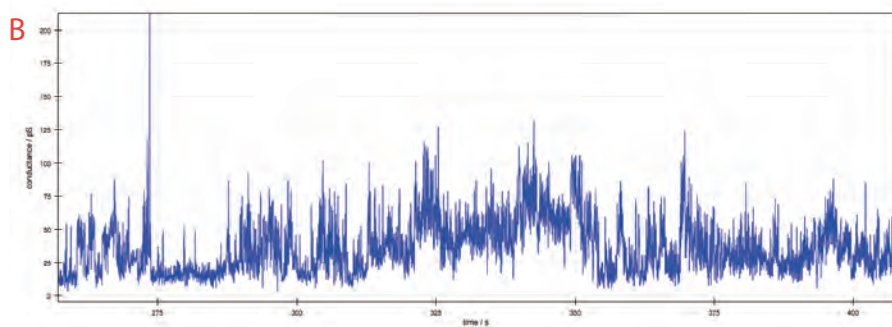


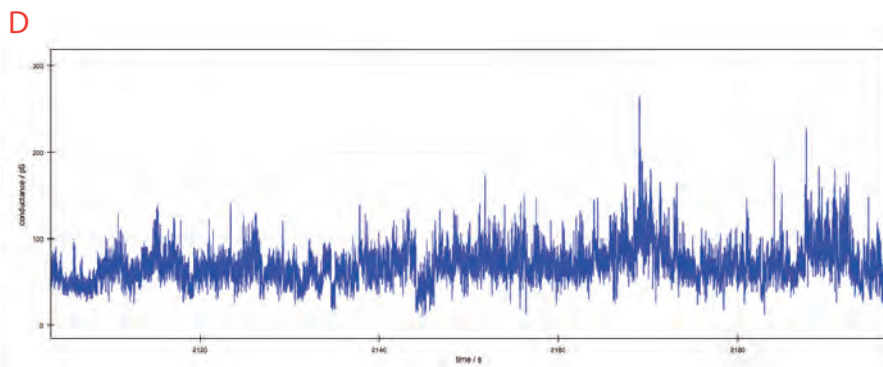
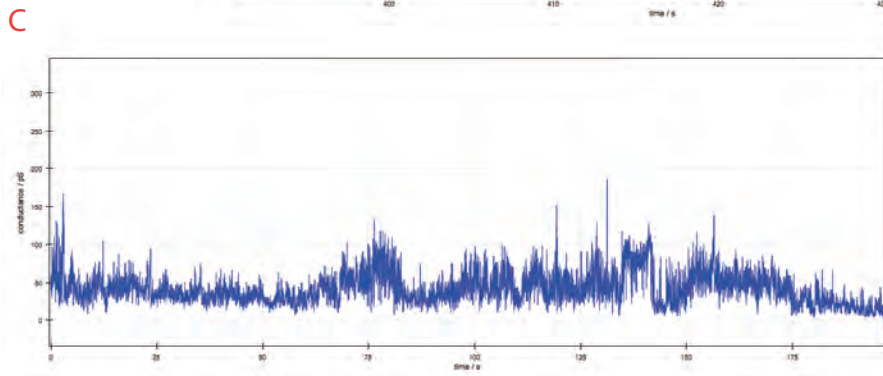
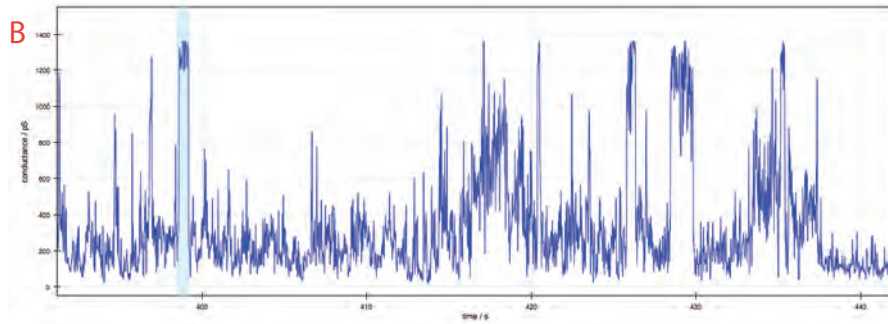
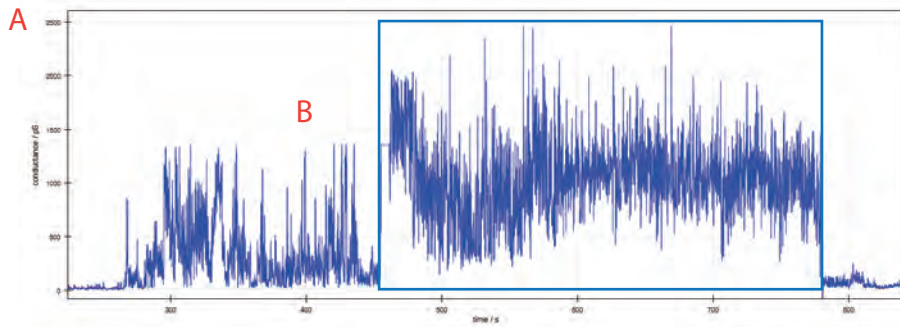
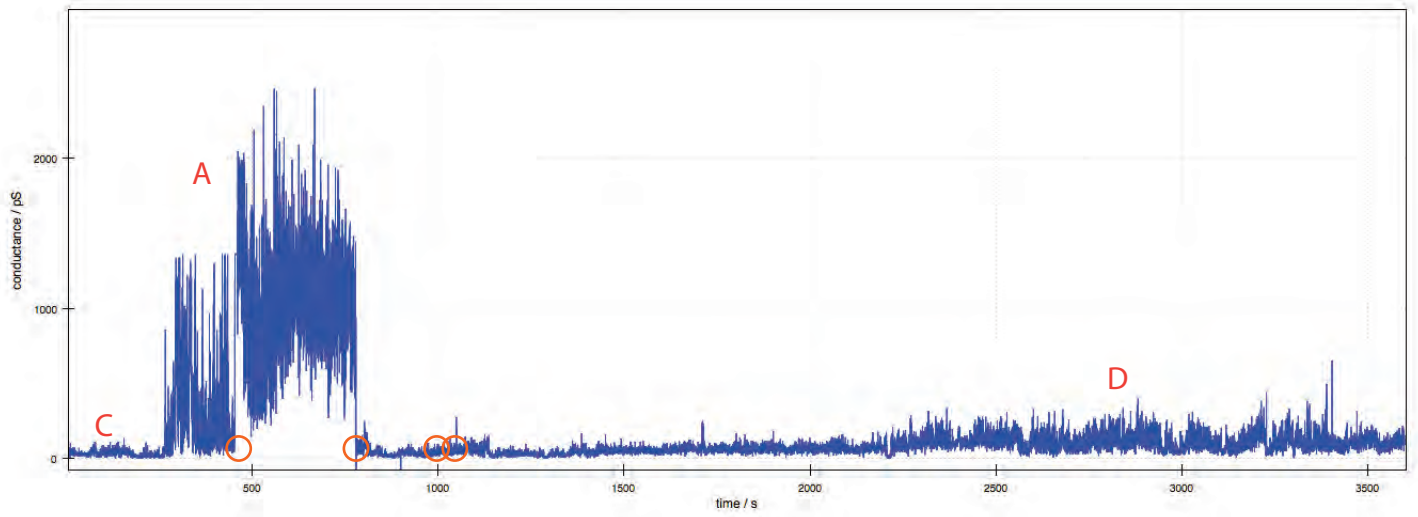
B



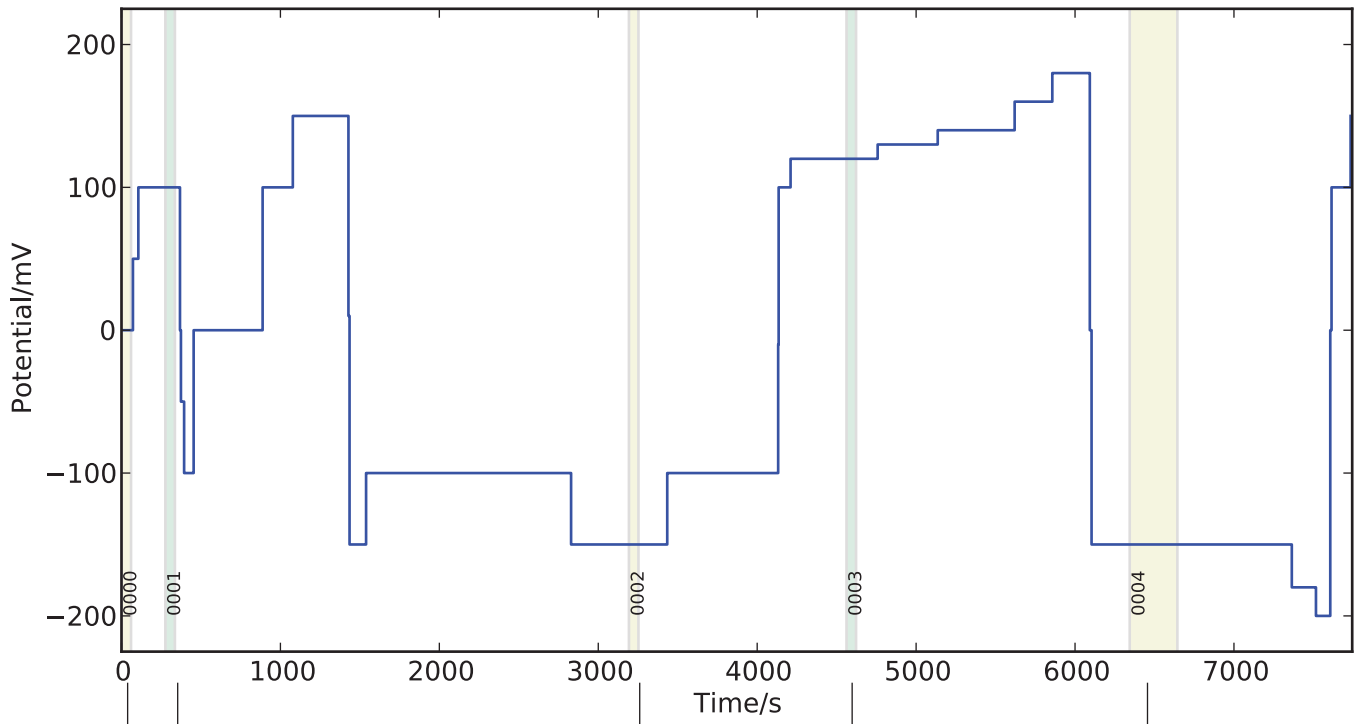


fractal-like - no clear events

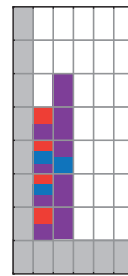
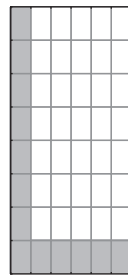
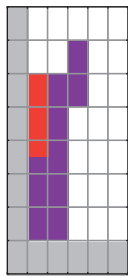
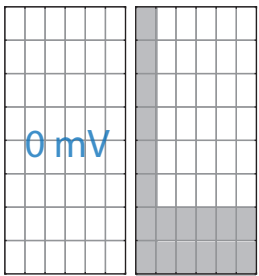




JC-128 aCD-Ethisterone JC-V-25 f31-48 1percent - 1M CsCl pH 7



lipid 1%  
electrolyte  
contact injection  
brush transfer



0001

