J-DSP for Ion Channel Signal Processing

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Introduction to Ion Channels

- Ion channels are proteins that mediate the flow of ions and molecules across membranes such as cell walls.

- The utility of ion channels for *stochastic sensing* has been pioneered by Bayley and several collaborators

- Stochastic fluctuations in the ion channel current resulting from discrete binding events between the analyte and the channel are measured.

- They can be used in analyte classification, and they also sense at molecular levels

- Naturally occurring ion channels, such as α-hemolysin can be modified to include binding sites for a variety of different analytes.

- After binding, the analyte partially 'blocks' the conduction pathway and leads to a modulation in the ion current that can be used as a unique signature for sensing purposes.

Stochastic Sensing in Ion Channels

Stochastic sensing
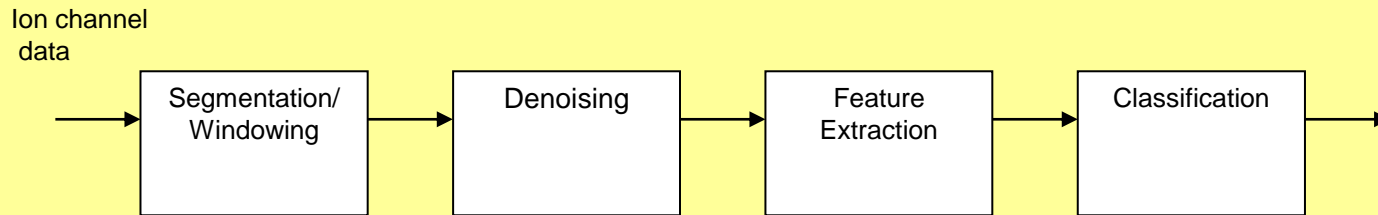- based on single molecule detection
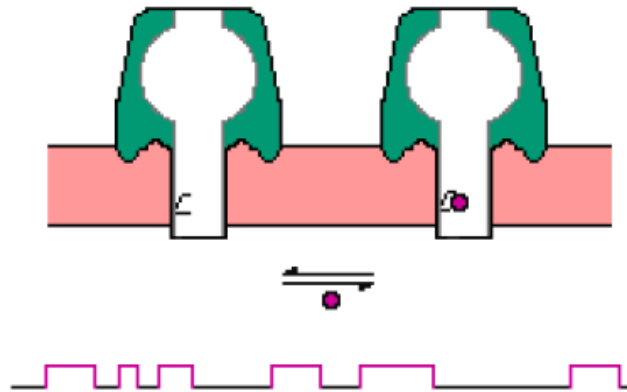
measure the ionic current flowing through a single protein pore with an engineered binding site

- frequency of occurrence of events
    - concentration of analyte
- signature: τ, Δg etc- identity of analyte

Courtesy of Dr H. Bayley
Oxford University

Bayley, H. and Cremer, P.S. **Nature** 413, 226-230 (2001).

Signal Processing of Ion Channel Currents

Ion channel data

Segmentation/ Windowing	→	Denoising	→	Feature Extraction	→	Classification	→

- J-DSP is used in teaching concepts of Ion channels to students.

- It is also used to teach signal analysis to students from different background working on ion-channel signal analysis.

- Signal and sensor processing:

  - The identification of unique stochastic current signatures

  - Spectral estimation

  - Attenuation of ion-channel noise

  - Appropriate Features for ion-channel currents

  - Classification algorithms

J-DSP for Ion Channels Signal Denoising

- The signal generator block in J-DSP can be used to generate ion channel signals both in presence and absence of analyte.

- Filter blocks are used to filter the noise from the generated signals.

- Figure below shows denoising of the ion channel signals using J-DSP block models
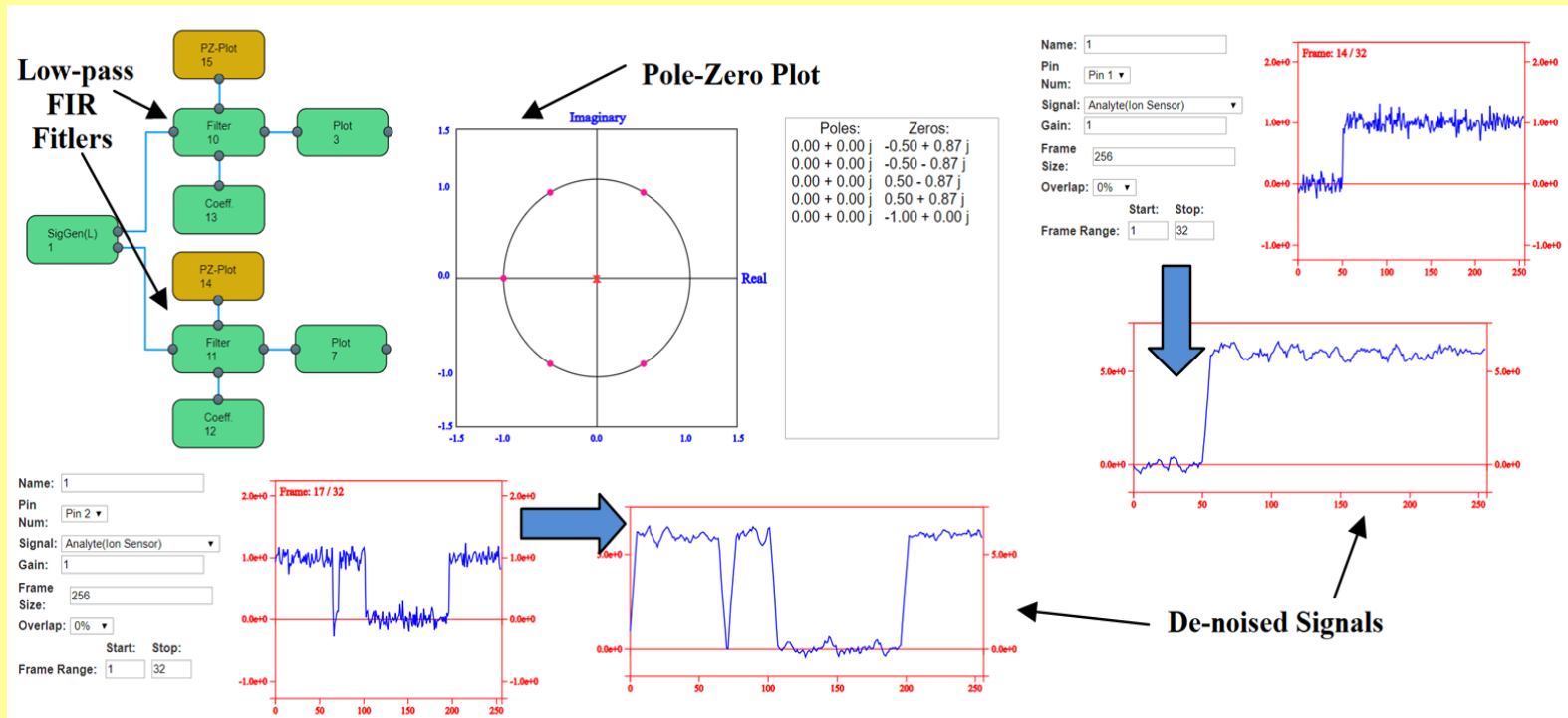
J-DSP for Ion Channels Signal Processing

- Using J-DSP we can also compute the WHT of the ion channel signals.
- Figure below shows the WHT coefficients of frames of two ion-channel signals.
- An ion-channel signal can be well characterized by the K largest peaks among the WHT coefficients referred to as WHT features.
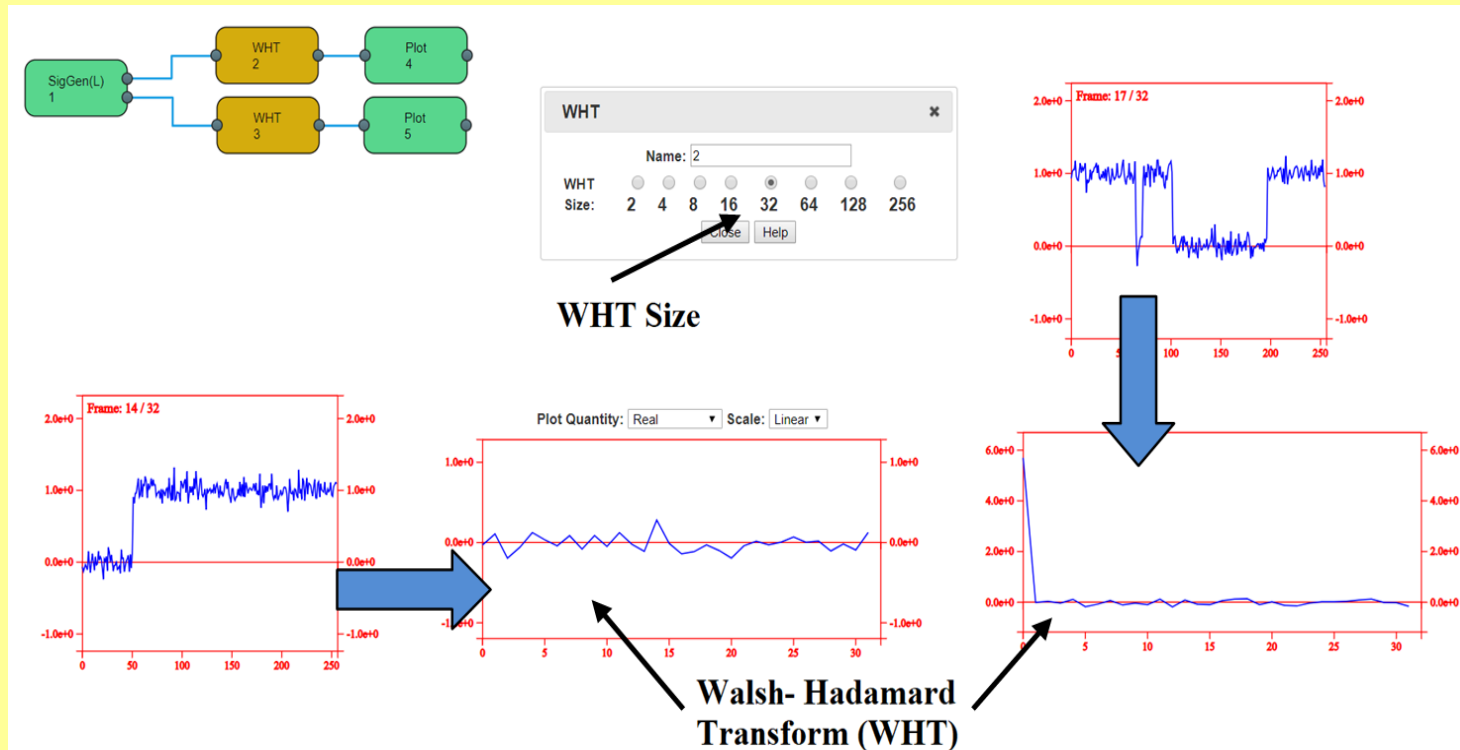
J-DSP for Machine Learning on Ion Channel data

- Using J-DSP K-means clustering is applied on the 2-dimensional feature vector of ion channels consisting of WHT and PSD features.

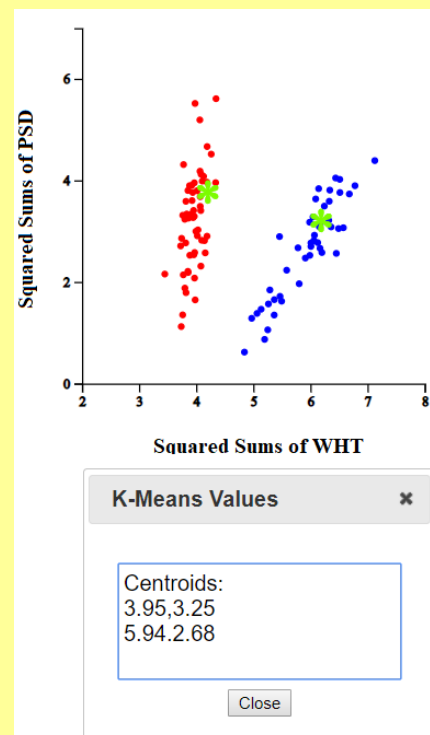- Figure below shows K-means performed in the J-DSP

Figure: K-means clustering. The two clusters correspond
to two classes of simulated ion-channel signals.

J-DSP for Machine Learning on Ion Channel data

- K-means clustering was also applied on the dwell time analyzed data of ion channels.

- The Dwell time analyzed data contains the step size and dwell time of the channel in a specific state.

- Using the cluster centers we can compute the approximate rate constants which characterize different analytes.

- Figure below shows K-means performed in the J-DSP
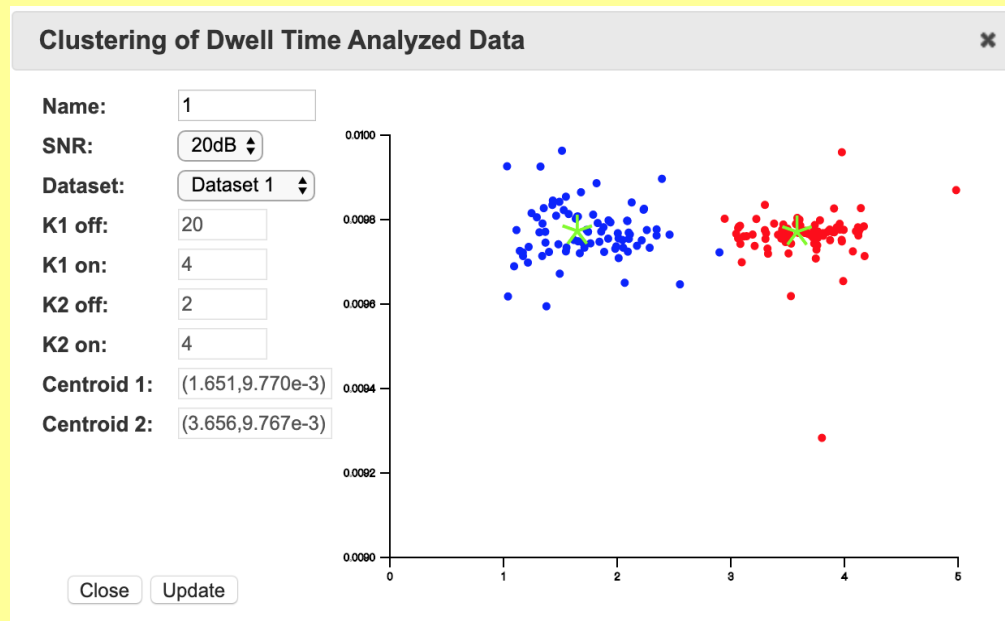
J-DSP for Teaching

- Students in the EEE598-Biosensor course performing J-DSP ion-channel experiments.

CONCLUSION

- **Several J-DSP functions were created specifically for ion-channel signal analysis and classification.**

- **The general opinion of the students was that the exercises helped them better understand the properties of the ion-channel signals.**

- **The exercise had five components: time-domain analysis, pre-processing, parametric modeling, transform domain feature extraction, and inference using clustering.**

- **Students agreed that the ease of use of the tools facilitated effective learning.**