Characterization of Protein Aggregation by Solid State Nanopore

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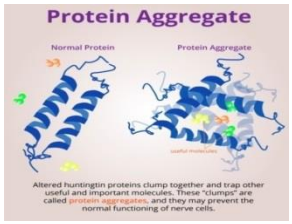
Background/Relevance

- Many neurodegenerative diseases like Alzheimer, Parkinson and Prion are found to be linked to protein aggregation. Existing protein characterization methods are:
  - Not easily available.
  - Expensive.
  - Low precision rate.



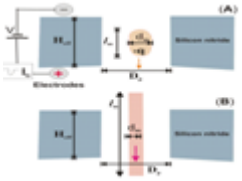
Innovation

- Build a new system that can be used to:
  1- Characterize protein aggregation.
  2- Low cost and high precision.
  3- Easily moveable/reduced size.

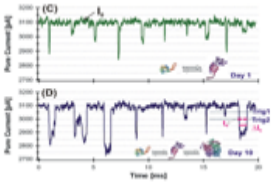
Ross, CA., Poirier, MA., *Protein aggregation and neurodegenarive disease.* Nat. Med., 2004. **10**: p. S10-S17

Approach

- Proteins translocate through a single nanopore in a Si_3N_4 membrane that separates two salt solution-filled chambers whose only connection was via the electrolyte (KCl) solution inside the nanopore.



- Protein molecules translocating through a nanopore partially block the ion flow and the current blockage pulse or event can be measured.



- By measuring the current and using nanopore geometry the translocated protein and its aggregations can be characterized.

Key Results

- Solid-state nanopore (6-30 nm) has been fabricated and imaged using TEM.
- Tetrameric and hexameric aggregations of β-lactoglobulin protein were detected using 18 nm nanopore.
- Dimeric aggregations of tau protein were detected using 10 nm nanopore as a function of salt concentration and pH.
- The dimeric aggregations of α and β tubulins were detected in 1M KCl solution at 60 – 210 mV.
- The pentameric to heptameric aggregations of tau and tubulin were detected in 1M KCl solution at 60 – 210 mV.

Conclusions

- This work supports the understanding of the theory and principle of
  - Tau and tubulin aggregations in ionic solution using solid-state nanopore device.
  - In vitro tau and tubulin aggregations manipulations using pH and salt concentration changing .
  - In vitro protein aggregation reduction using applied voltage.

Future Work

- Study on the mechanisms of protein aggregations in live cells and pH, voltage, temperature and salt effects on the aggregation.

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