ION CHANNELS AS NANOPORES - FROM PRINCIPLES TO BIOSENSORS

Oliver Beckstein (for Mark S.P. Sansom) – Feb 2005

Lecture 1
- Basic properties of channels & pores [1]
- Molecular picture of a transbilayer pore [2]
- Biological example – KcsA why ion channels may be too complex for bionanotech
- Unique effects due to nano scale size (eg [3])
- Two basic aims – understand channel biology at a single molecule level; exploit this understanding at the chemistry/biology interface
- Single channel measurements – technologies – sensitivity of electrical measurements
- Electrical measurements from ion channels – refresher
- Patch clamp recording [4]
- Planar bilayer technologies [5, 6]
- Conductance, selectivity, block, gating…
- How to interpret a single channel recording
- What is meant by conductance and by selectivity
- Block – formal analysis of kinetics (and why it is important); voltage dependency
- Model channels for bionanotechnology: (i) gramicidin [7, 8,9]; (ii) alamethicin [10]; (iii) α-haemolysin [11]
- Advantages of β-barrels – e.g. porins - stability

Lecture 2
- Two basic aims – (re)-engineering & sensing
- Making a semi-synthetic Cl- channel – Alm-K18: (i) covalent Alm dimers – more stable channels; (ii) Alm-K18 – design & reality; complexities of its selectivity; single (de)protonation events; lessons learned & therapeutic possibilities [12, 13]
- Making a channel-based biosensor – gramicidin & antibodies; basic design of the biosensor; electrical measurement; does it work? [14, 15, 16]
- α-Haemolysin I – using a protein pore as a template: (i) basic concept, using cyclodextrins; (ii) first results – v. promising; (iii) recent refinements [17, 18, 19]
- α-Haemolysin II – watching a polynucleotide moving by: (i) basic concept; (ii) first studies; (iii) recent refinements; (iv) will it be useful for sequencing? [20, 21]
- Sensing single sugar molecules [22]

References


Also….

Meller et al. (2000) Rapid nanopore discrimination between single polynucleotide molecules PNAS 97:1079-084