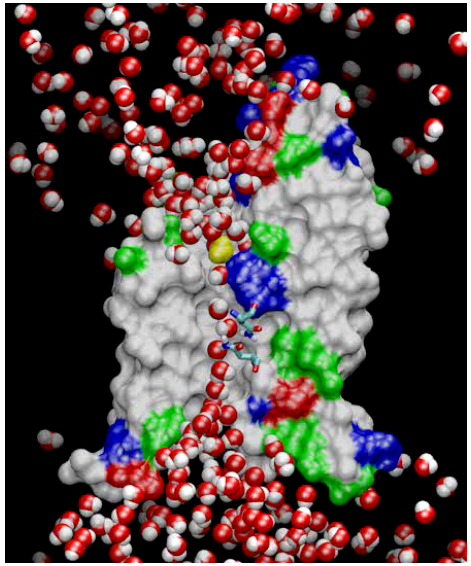
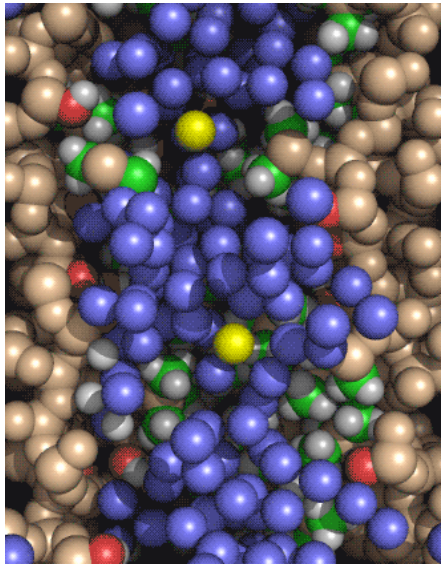
SAND2014-18517C

Biomimetic Membranes for Water Purification



protein



synthetic

Susan Rempe
Sandia National Laboratories
Albuquerque, NM

Sandia National Laboratories is a multi-program laboratory operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000.

Sandia Mountain, Albuquerque, NM

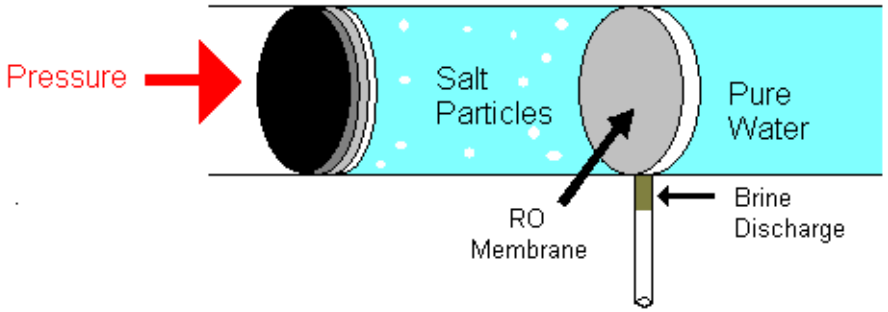
Clean Water: *A Global Crisis*

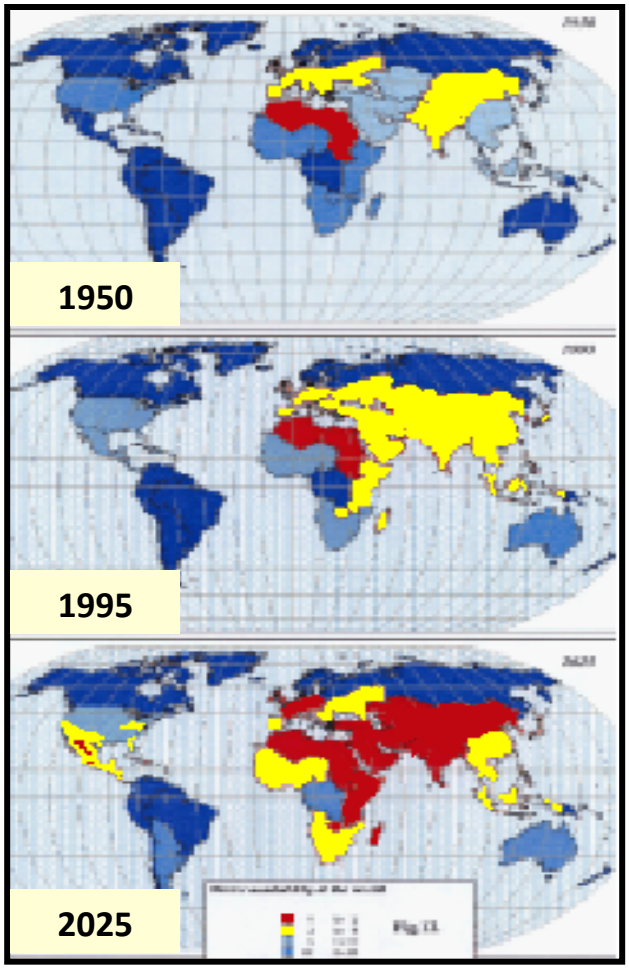
- Half of world's population lacks clean water:

  - public health crises
  - Water / energy link
  - RO membranes: expensive & overly sterile H_2O
  - R. Electrodialysis: high resistance to ion permeation

- Membrane needs new design for efficiency:

  - fast (barrier-less) water (or ion) transport
  - select ion exclusion (mineral water)

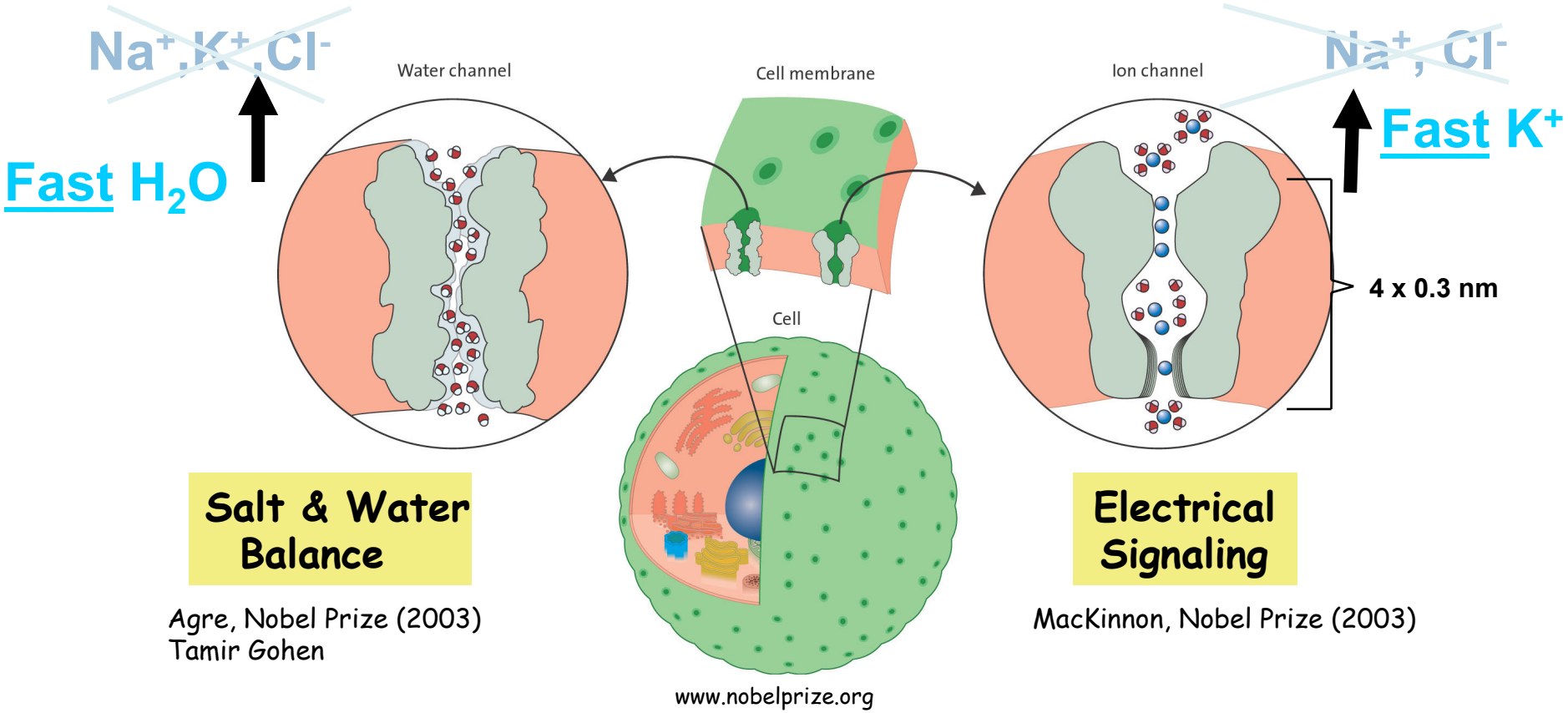




"Water promises to be to the 21st century what oil was to the 20th century: the precious commodity that determines the wealth of nations."

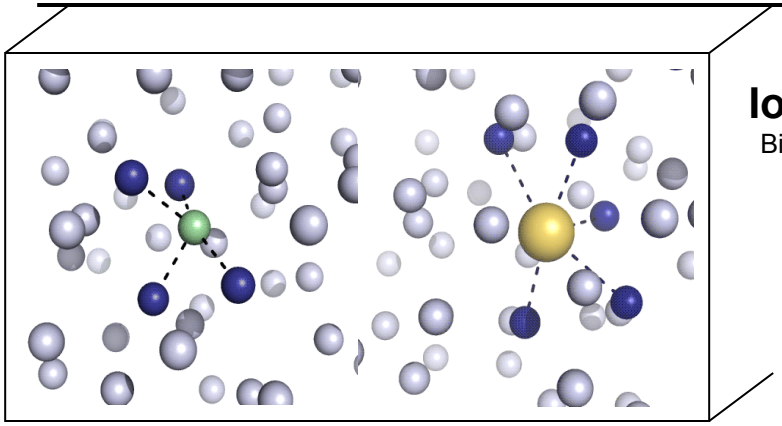
Fortune Magazine, May 15, 2000

Biological Channels Inspire:
Catalyze fast, selective permeation



- **Structurally Similar / Diverse Functions:**
  - **General: narrow + thin + uniform/robust**
  - **Specific: polar**

Natural protein channels: Not just simple holes!



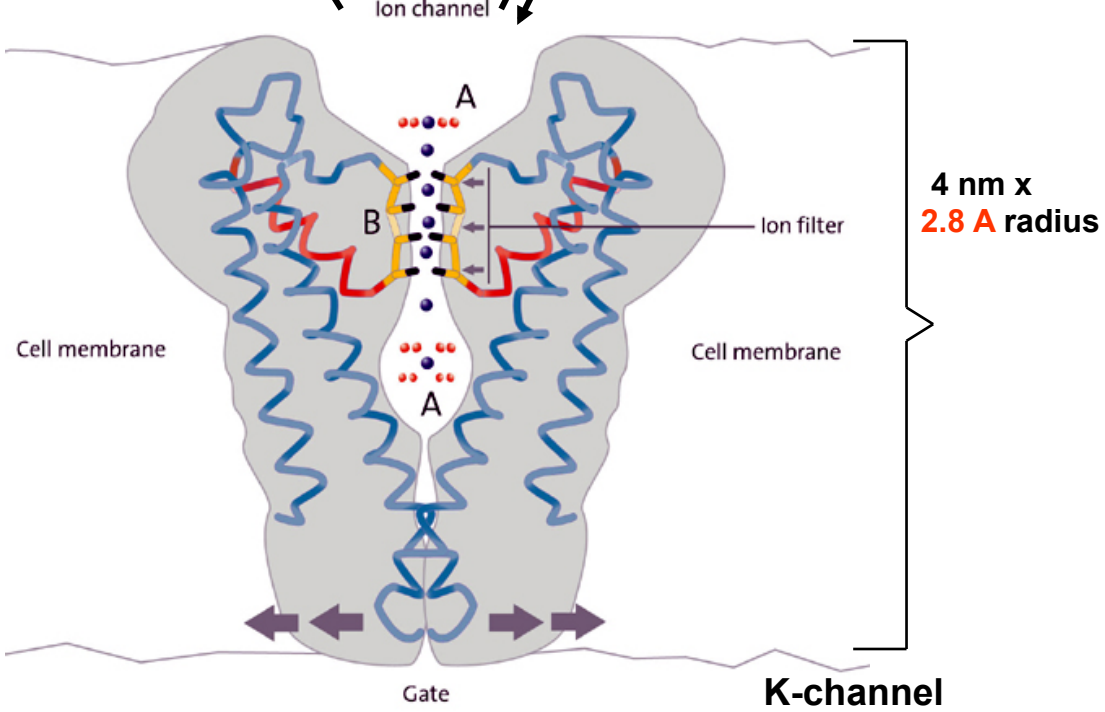
Ions in water
Biophys Chem 2006

- Ions 'happy' in liquid water

How do channels work?
- K^+ equa-energy?
- Na^+ barrier?
- same structure – varied function?

Smaller Na^+ rejected

Larger K^+ permeate fast



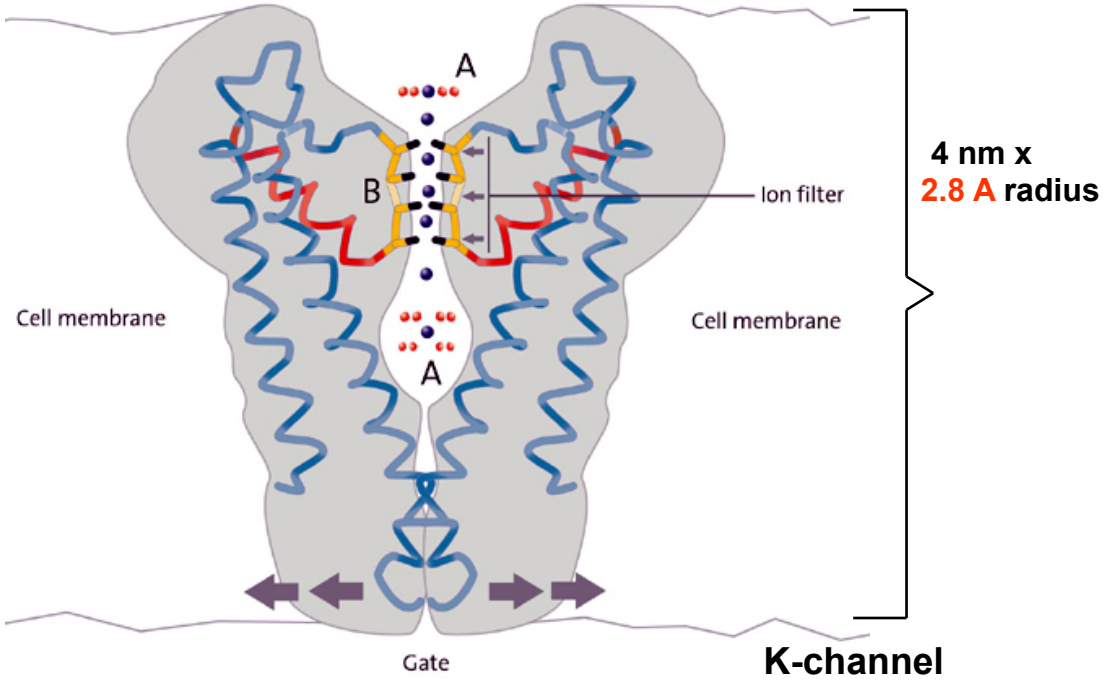
4 nm x 2.8 A radius

K-channel
www.nobelprize.org

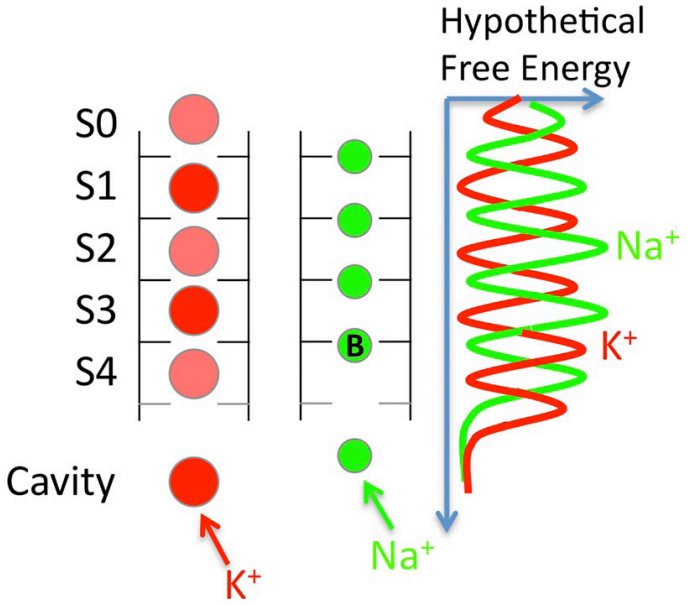
Natural protein channels: Not just simple holes!

- Ions 'happy' in liquid water

How do channels work?
- K^+ equa-energy?
- Na^+ barrier?
- same structure – varied function?



K-channel
www.nobelprize.org

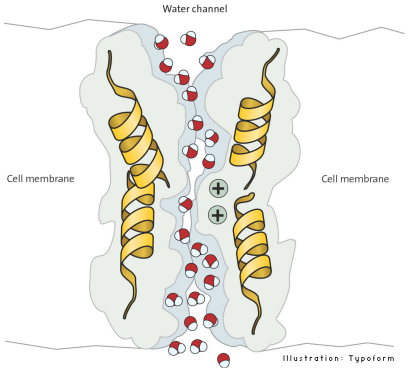


Nimigean & Allen *JGP* 2011

Efficient Membranes: Biomimetic

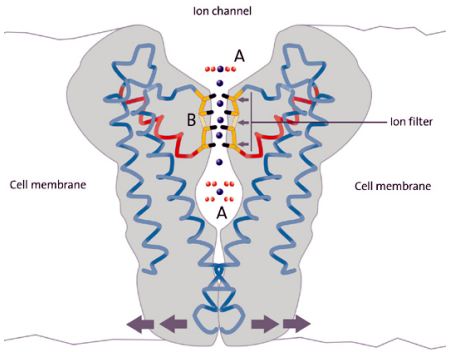
Understand, design, engineer nano-channels for desalination

Water channels



• transport H_2O fast

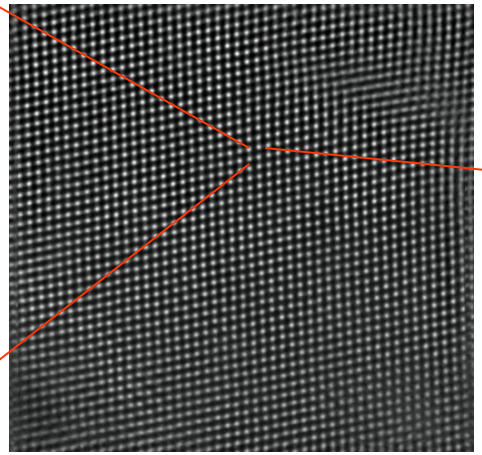
Ion channels



• select minerals fast

• Bio-inspired design

• Theory to reveal mechanism



• Inorganic membrane synthesis

Brinker Lab

J Membr Sci (2007)

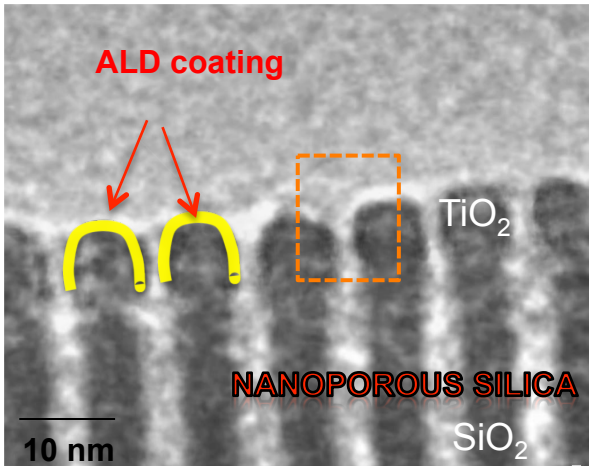
JACS (2007)

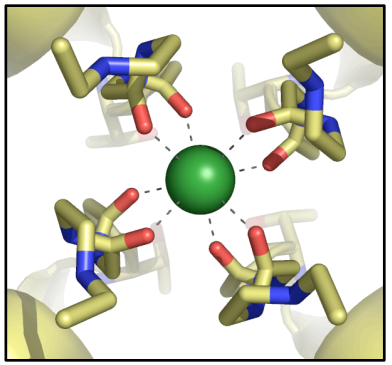
Solution: Harness molecular biomechanisms.
Gain 100x in water flux + minerals.

Models to study ion discrimination

- **Link pore structure –- solvation -- & water/ion mobility**

(ΔG) **(D)**

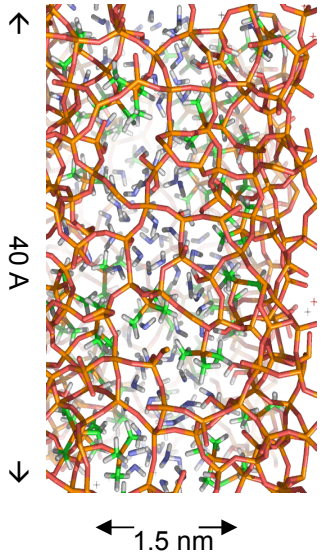


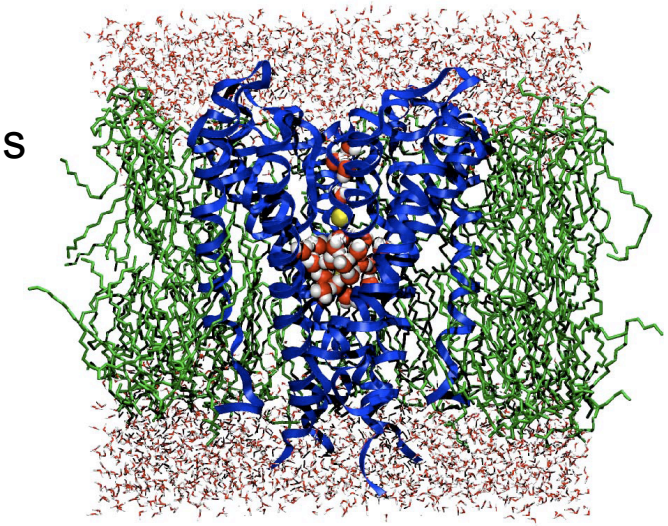


Binding Sites

Synthetic ↔ Biological

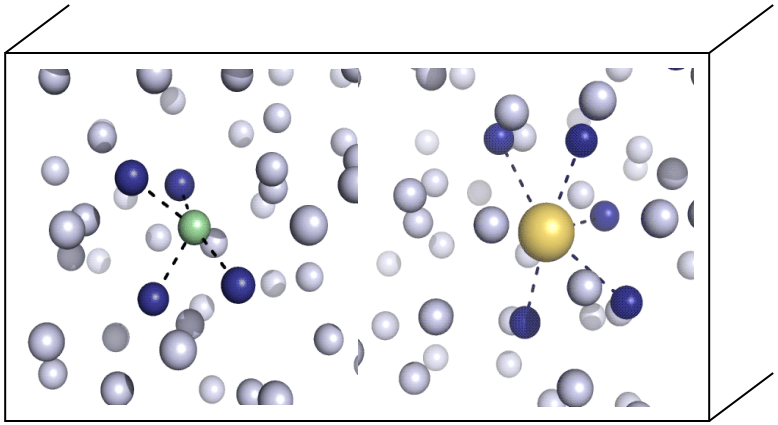
Whole Channels





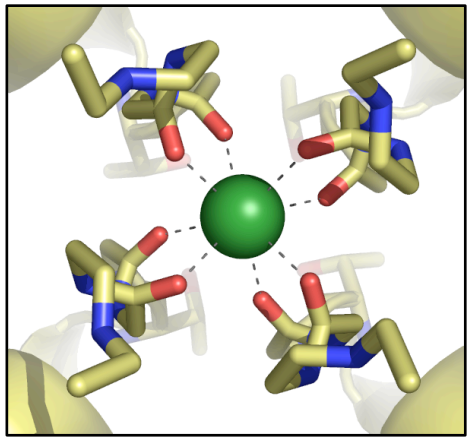
Modeling to study ion discrimination

- **Link pore structure –- solvation -- & water/ion mobility**
  (ΔG) (D)



Dynamic structures

$F = ma$



Static structures

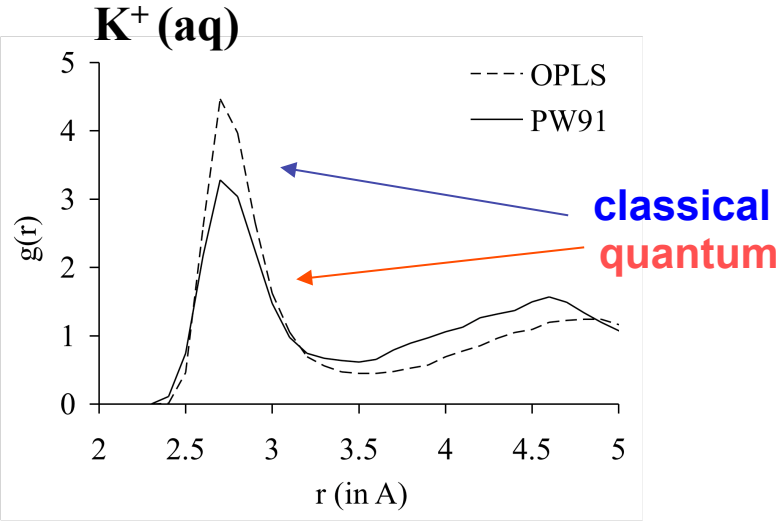
$F = 0$

Forces?
capture discriminating interactions

- **Quantum (*ab initio*) interactions:**
  - expensive; describe multi-body interactions
- **Classical atomic interactions:**
  - inexpensive; parameterized

- **Example 1**

Classical ions bind more ligands??



Whitfield, Varma, Rempe, Roux et al. *JCTC* (2007)
Leung & Rempe, *PCCP* (2006) Ab initio rigid water
Klein & co, *JCP* (2013) Dispersion over-structures

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• Example 1

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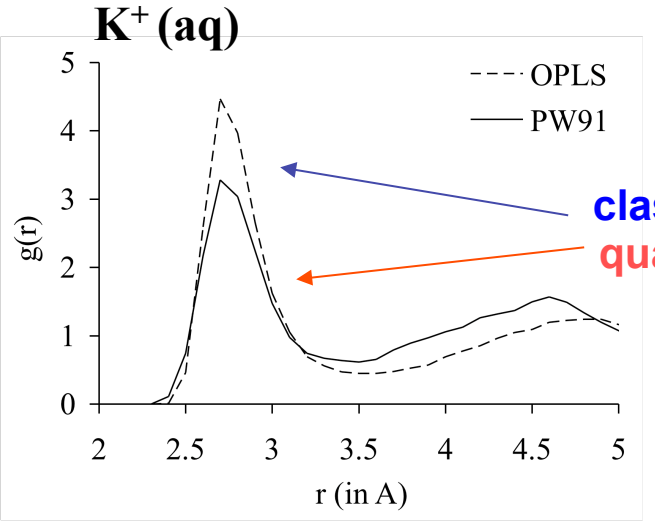
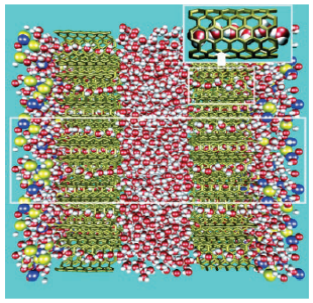


Whitfield, Varma, Rempe, Roux et al. *JCTC (2007)*
Leung & Rempe, *PCCP (*2006) Ab initio rigid water
Klein & co, *JCP* (2013) Dispersion over-structures

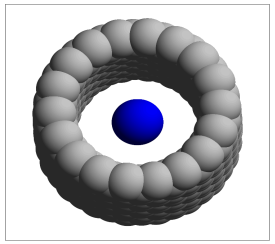
• Example 2

Classical nanotubes Exclude ions??



Hummer & co *PNAS* (2003)

Quantum tubes Admit ions!!



Na+ : -210 kJ/mol

Leung, Marsman *JCP* (2007)

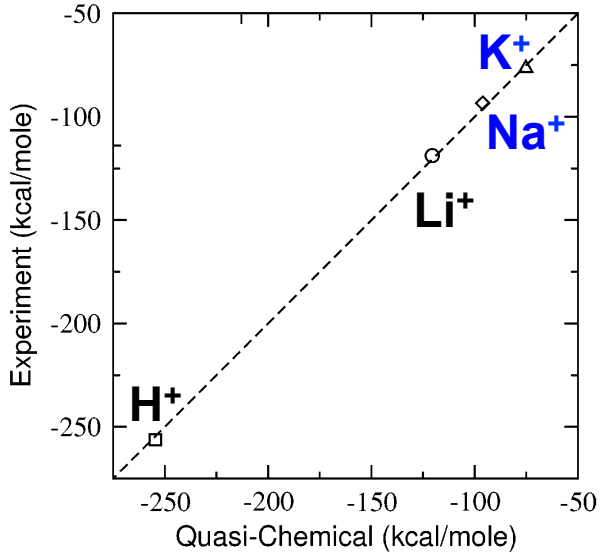
"When in doubt,
solve the Schroedinger equation"

- courtesy P. Jeff Hay, LANL

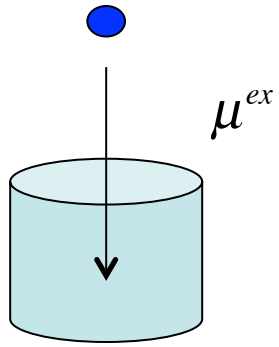
… locally!

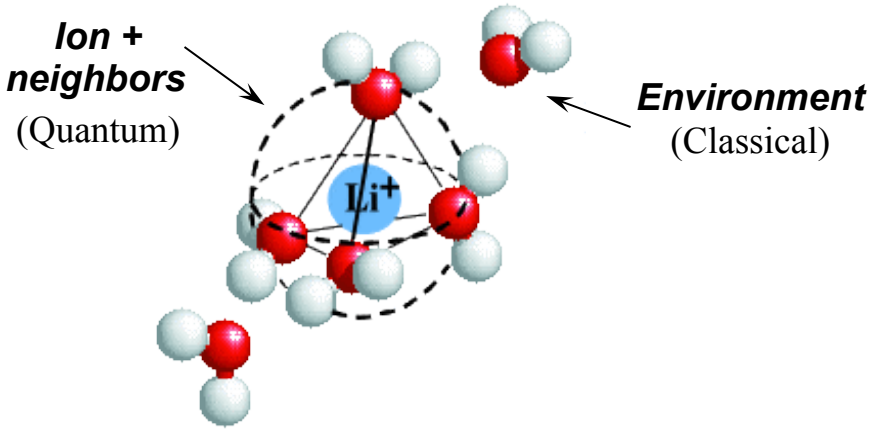
Apply QM locally via Quasi-Chemical Theory:

- Theory well-tested for ion hydration:



JACS (2004)



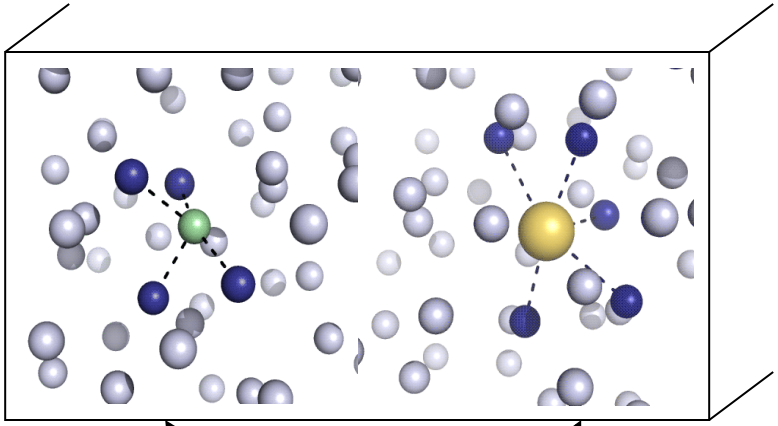


- Adaptable to ion solvation in binding sites??

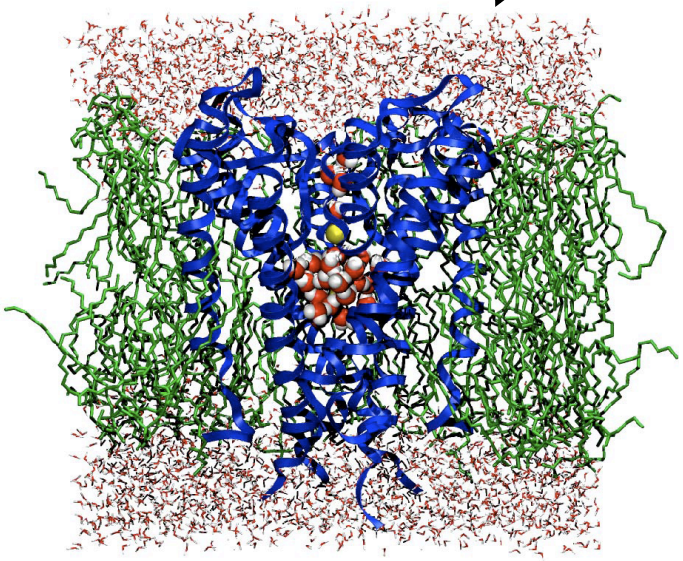
State-of-the-art all-QM for Na^+(aq) agrees with QCT:
Leung, Rempe, von Lilienfeld *JCP* (2009)

QCT (Pratt & co):
Pratt & Rempe '*Red Book*' (1999),
Chem Phys Lett (2010), *Ann Rev Comp Chem* (2012)

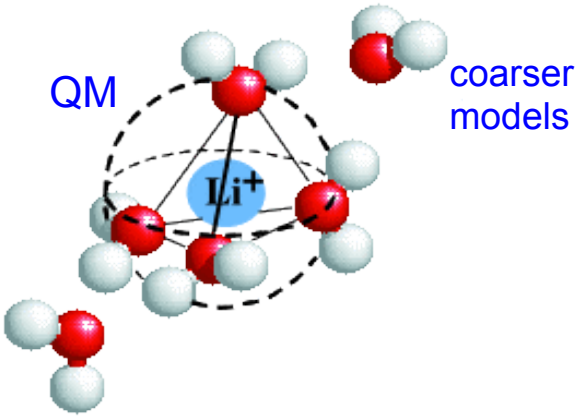
Same theory for ion solvation in channels:



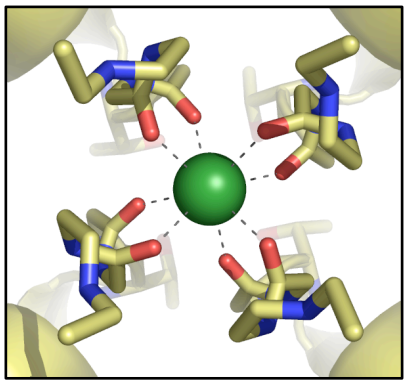
ΔΔG



Ions in water



Ions in channels



JPCB (2011)
Ann Rep Comp Chem (2012)

Ion Selectivity = free energy differences

- **Ion solvation: local + environment**

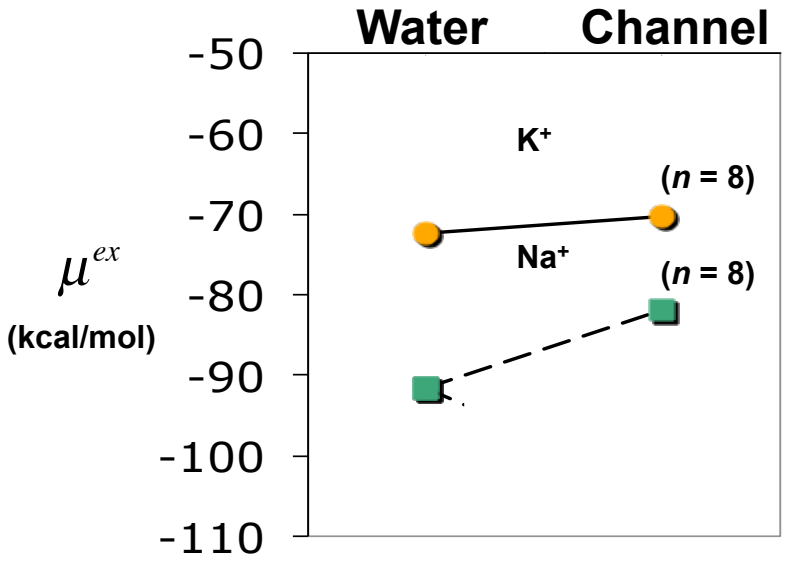
$$\mu^{(\mathrm{ex})}_{\mathrm{Ba}^{2+}} = -kT\ln K^{(0)}_n \rho^n_{\mathrm{H_2O}} + kT\ln p_{\mathrm{Ba}^{2+}}(n) + \mu^{(\mathrm{ex})}_{\mathrm{Ba(H_2O)}^{2+}_n} - n\mu^{(\mathrm{ex})}_{\mathrm{H_2O}}$$

absolute value

chemistry + ligand density

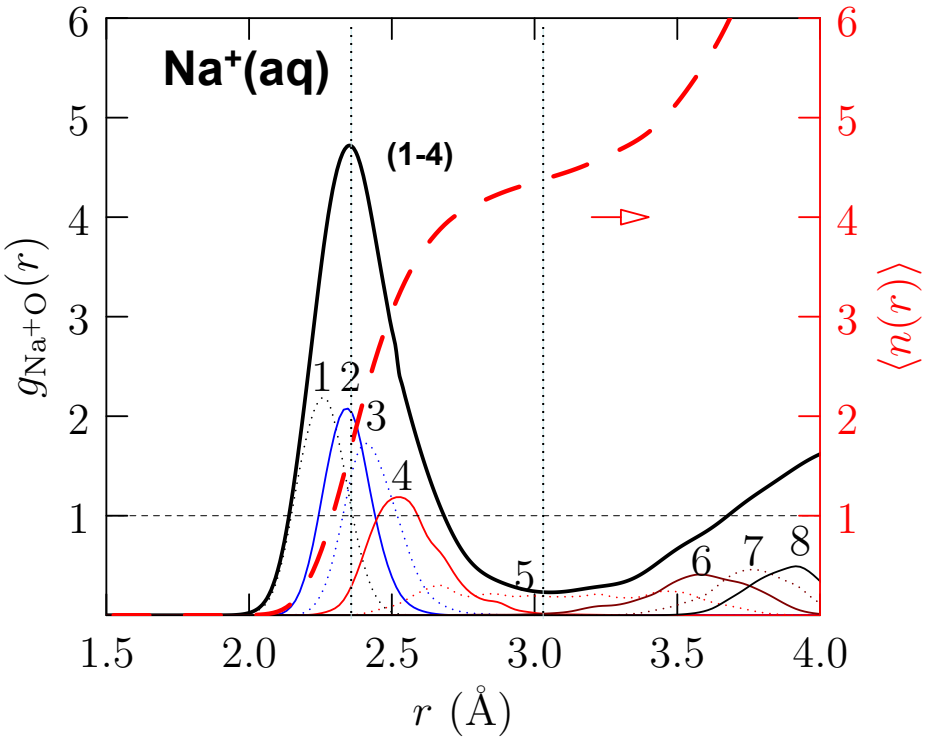
environment

- **Selectivity: subtle balance between hydration vs solvation by channel**



Ab initio structures tested against experiment

- **Peaks & wells match scattering experiments:**

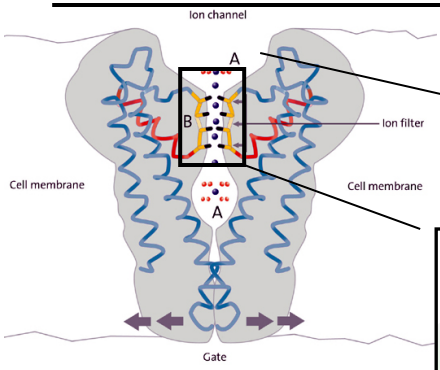


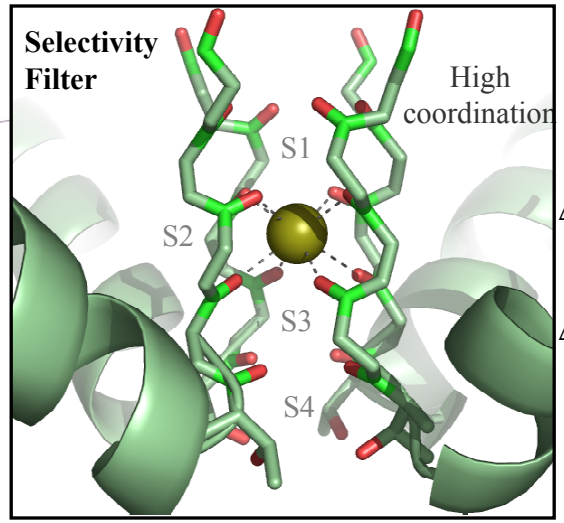
- **Additional info obtained by AIMD:**
  - individual water distributions
  - *n (r)*

Ann Rep Comput Chem (2012)

K^+/Na^+ Ion Discrimination Problem:

Prominent Views

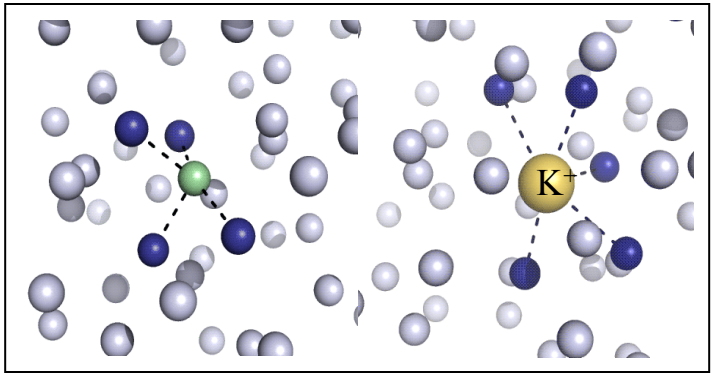




n = 8, r = 2.8 A

$\Delta G_{K+} \sim 0$

$\Delta G_{Na+} > 0$



Directly coordinating waters highlighted

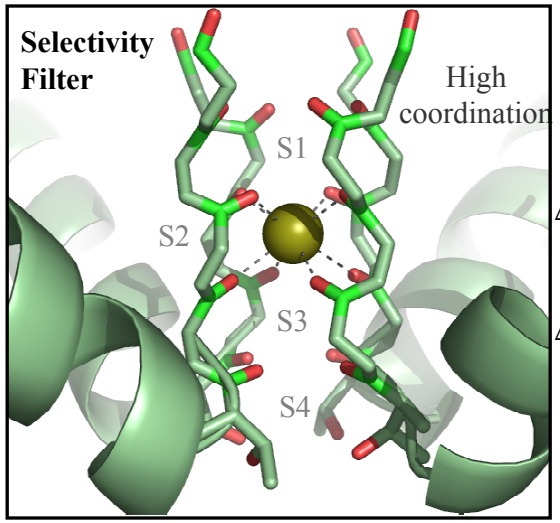
1. K^+ equa-energy? Mimic K^+ ion hydration structures
2. Na^+ rejection? Specific cavity size fits K^+ [1,2] vs Liquid flexibility & specific chemistry[3,4]
3. Same filter structure vs varied selectivity? X

[1]Bezanilla & Armstrong *JGP* (1972), [2]Zhou *et al.* Nature (2001), [3]Eisenman & Horn *JMB* (1983) [4]Noskov *et al* Nature (2004)
Perspectives on Ion Selectivity *JGP* (2011)

K^+/Na^+ Ion Discrimination Problem:

1. Ion hydration not mimicked!

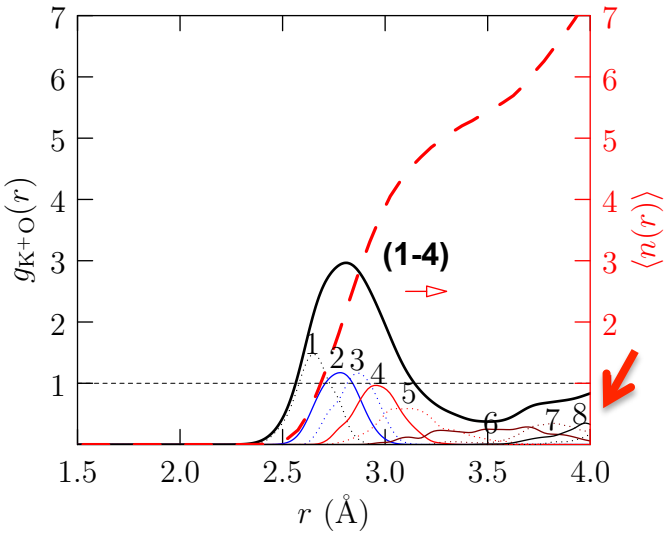
C=O density around K^+
n = 8 at r = 2.8 A



$\Delta G_{K+} \sim 0$

$\Delta G_{Na+} > 0$

Water density around K^+
n = 4 at r_{max} = 2.8 A



Ann Rep Comp Chem (2012)

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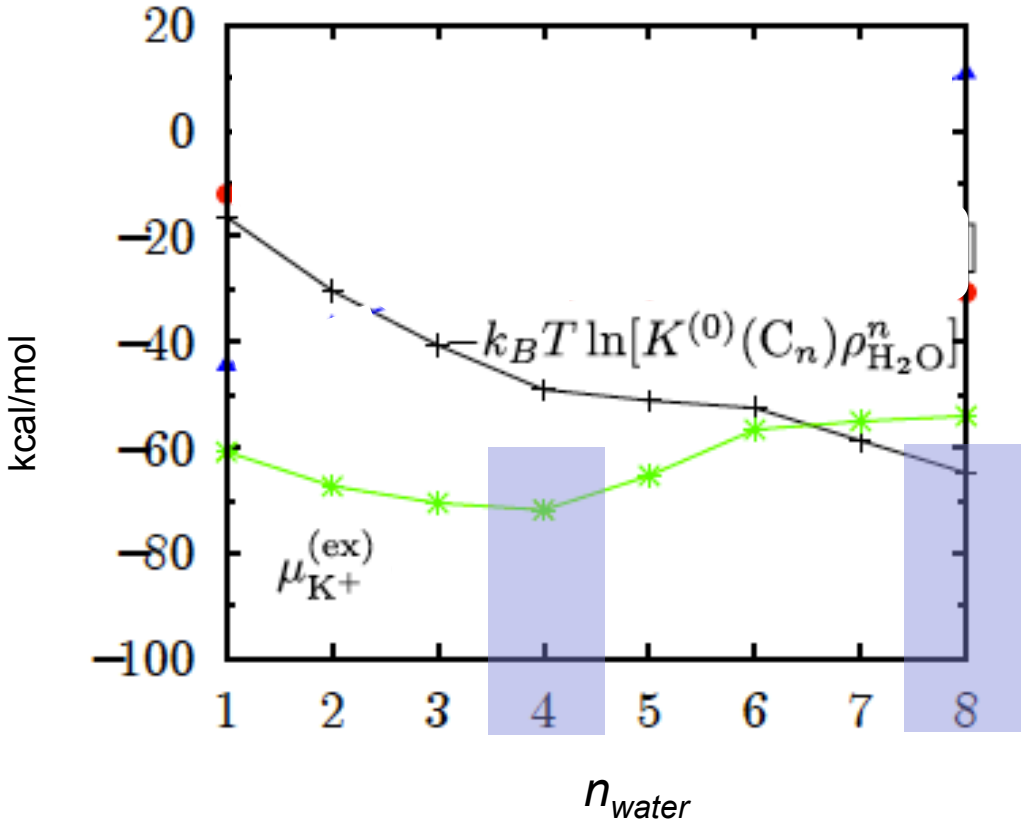
Perspectives on Ion Selectivity *JGP* (2011)

How can K^+ be stable with n = 8 in channels?

- K^+ hydration free energy vs coordinating waters

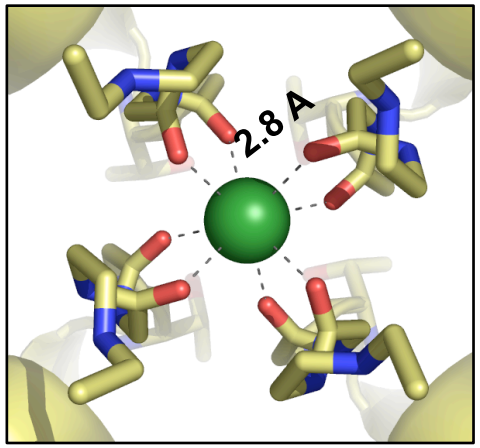


- **Solvation (chem + density)**
  - ***n* = 8**
- **Solvation (aq)**
  - ***n* = 4**
  - ligand desolvation penalty $\mu^{(ex)}_{H_2O}$

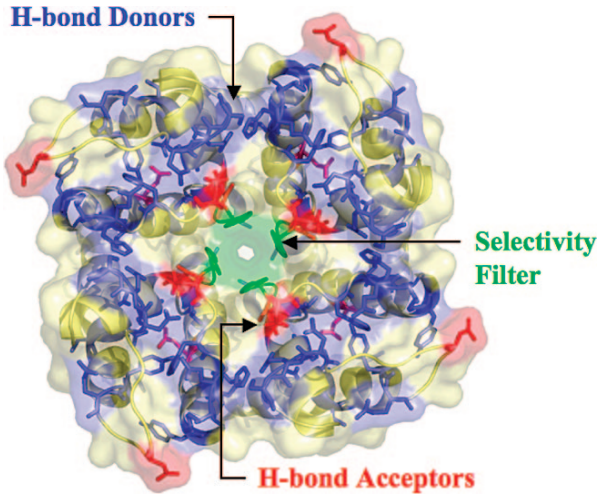
Does high ligand availability + poor ligand solvation environment account for high *n* in proteins?

Highly Selective K Channels:

High ligand availability + poor ligand solvation environ → *n* = 8



K^+ binding site



Highly selective K channels:
-- high CO density
-- few CO solvators

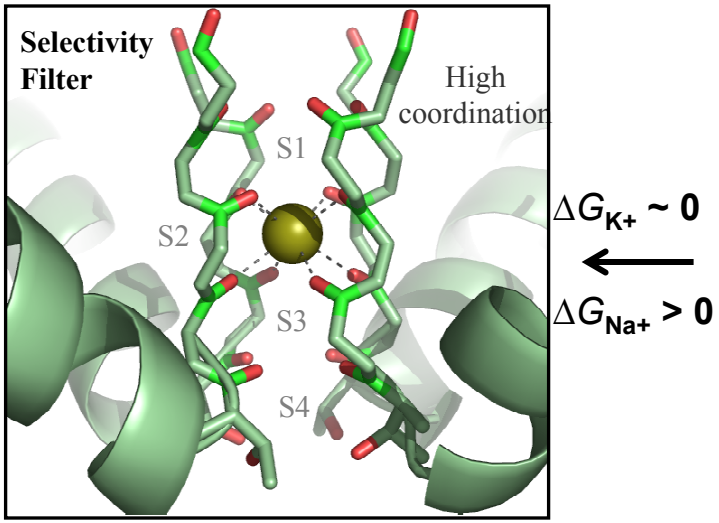
- To solvate K^+ without barrier or well,
  binding site + surrounds must 'mimic' $\mu^{ex}(aq)$

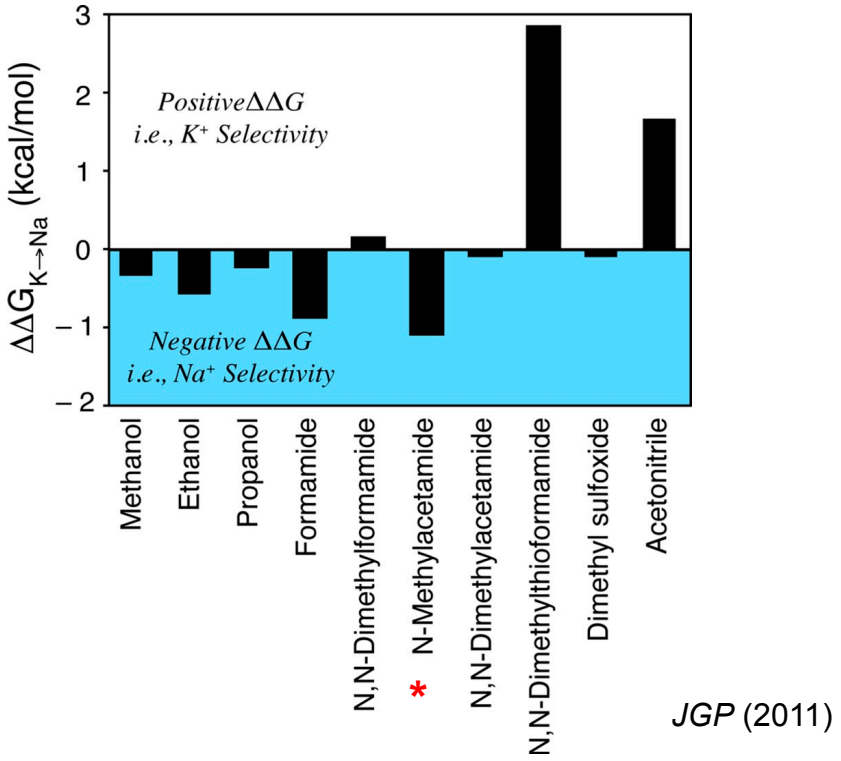
→ not necessary to mimic K^+(aq) local structure

JACS 2008

K^+/Na^+ Ion Discrimination Problem:

2a. C=O does not preferentially solvate K^+!





JGP (2011)

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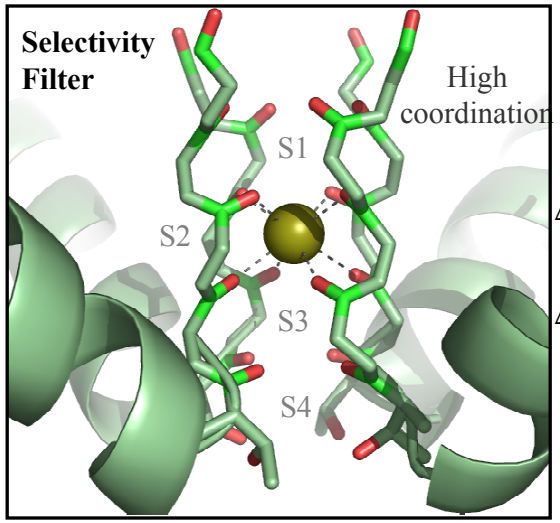
[5]Perspectives on Ion Selectivity *JGP* (2011)

K^+/Na^+ Ion Discrimination Problem:

Prevailing Views



$\Delta G_{K+} \sim 0$ ←

$\Delta G_{Na+} > 0$

n = 8, *r* = 2.7 – 3.1 A

Ion-water distances (A)
(r_{max} in AIMD)

- **K^+ 2.8**
- **Rb^+ 3.0**
- **Ba^{2+} 2.8**
- **Sr^{2+} 2.7**

- **Na^+ 2.4**

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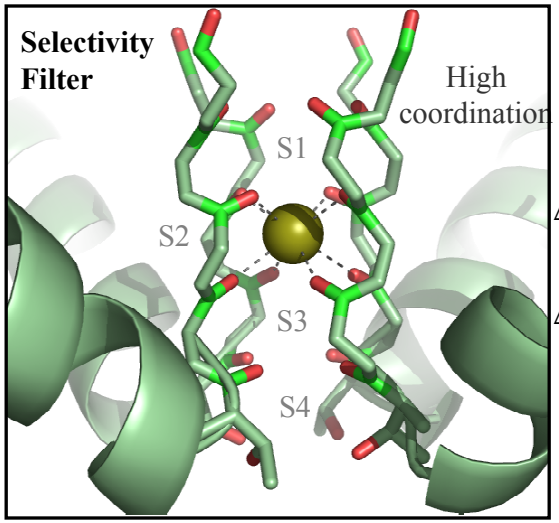
K^+/Na^+ Ion Discrimination Problem:

More complexity than just cavity size



$\Delta G_{K+} \sim 0$

$\Delta G_{Na+} > 0$

n = 8, r = 2.7 – 3.1 A

B-factors: **rmsf = +/- 0.8 A**
Static vs dynamic disorder?

Ion-water distances (A)
(r_{max} in AIMD)

•	**K^+**	**2.8**	**permeates**
•	**Rb^+**	**3.0**	**permeates**
•	**Ba^{2+}**	**2.8**	**blocks***
	Sr^{2+}	**2.7**	**excluded**
•	**Na^+**	**2.4**	**excluded**

*PNAS, 2013

1. K^+ equa-energy? Mimic K^+ ion hydration structures
2. Na^+ rejection? Specific cavity size fits K^+ [1,2] vs Liquid flexibility & specific chemistry [3,4]
3. Same filter structure vs varied selectivity? X

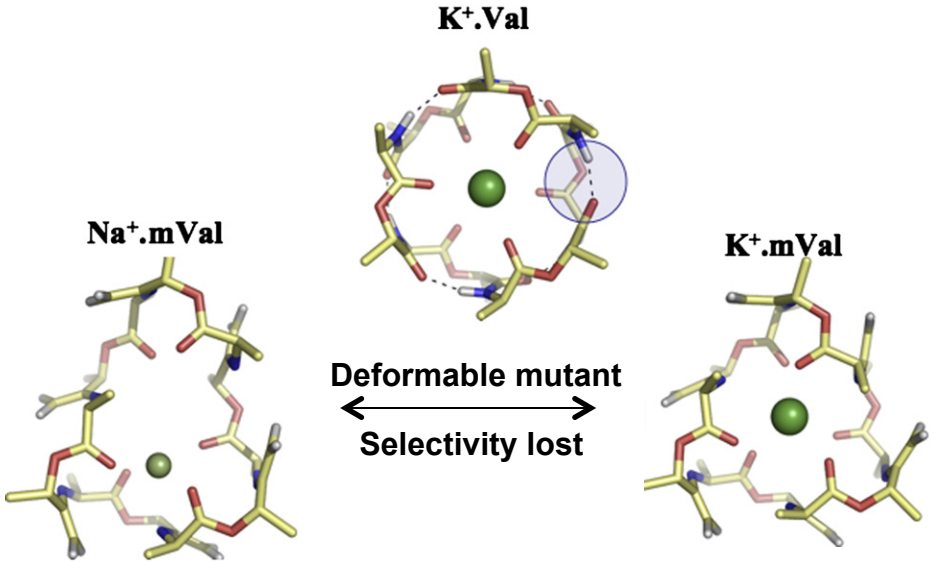
[1]Bezanilla & Armstrong *JGP* (1972), [2]Zhou *et al.* Nature (2001), [3]Eisenman & Horn *JMB* (1983) [4]Noskov *et al* Nature (2004)
[5]Perspectives on Ion Selectivity *JGP* (2011)

K^+/Na^+ Ion Discrimination Problem:

2b. Specific cavity size works – but not required!

- **Valinomycin (*n* = 6):**

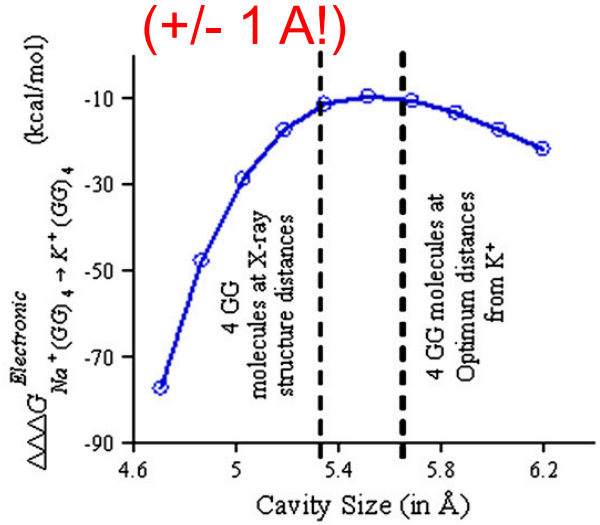
Selective by specific cavity size



J Molec Bio (2008)

- **K channel (*n* = 8):**

Selective with varied cavity size



Biophys J (2007)

1. K^+ equa-energy? Mimic K^+ ion hydration structures
2. Na^+ rejection? Specific cavity size fits K^+ [1,2] vs Liquid flexibility & specific chemistry [3,4]
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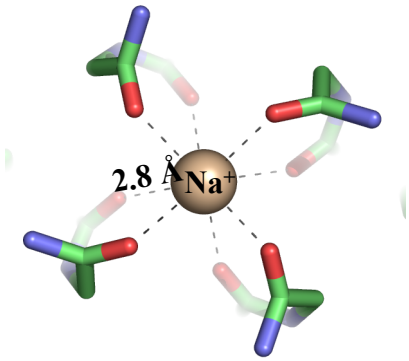
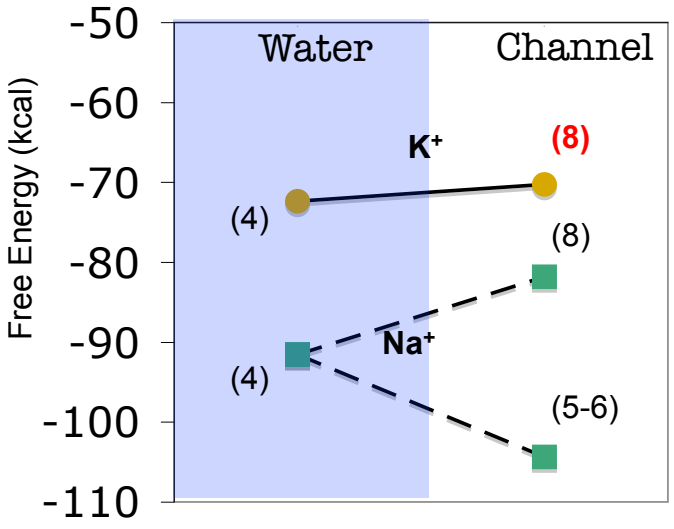
[5]Perspectives on Ion Selectivity *JGP* (2011)

K^+/Na^+ Ion Discrimination Problem:

1-3. Environment → maintain crowded (> 6) ligands → K^+/Na^+ discrimination

K^+ Channels





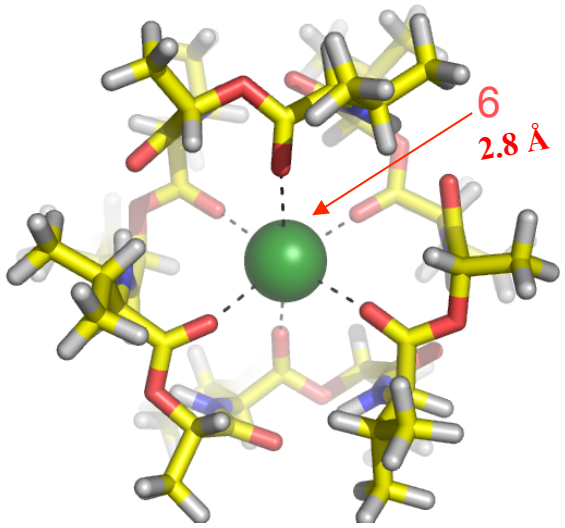
- K^+ selective (flexible or rigid cavity)
- Not K^+ selective (unless cavity size fits K^+)

1. K^+ equa-energy? Over-coordinate K^+ with CO to match $\mu^{ex}(aq)$
2. Na^+ rejection? Environment maintains specific, high n or specific cavity size
3. Same filter structure vs varied selectivity? Environment lets n (or cavity size) adjust

Biophys J (2007); Bostick & Brooks *PNAS* (2007)
J Mol Bio (2008); *JACS* (2008);
Ann Rep Comput Chem (2012)

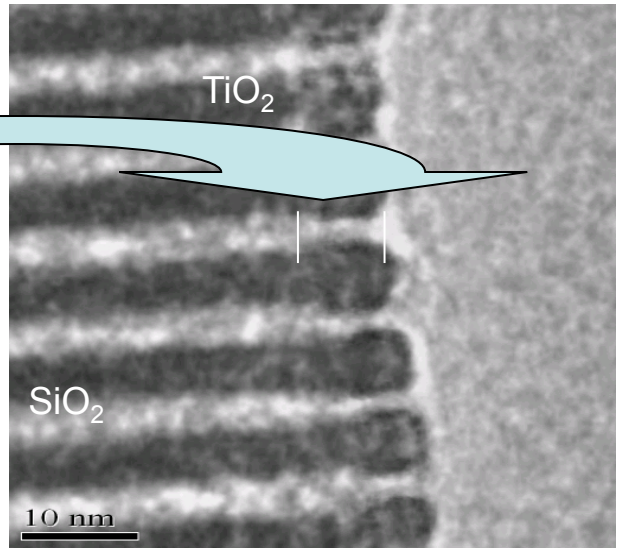
New hypothesis consistent with experiments:
Jiang & co *Nature* (2011)

Translate design to synthetic membranes?



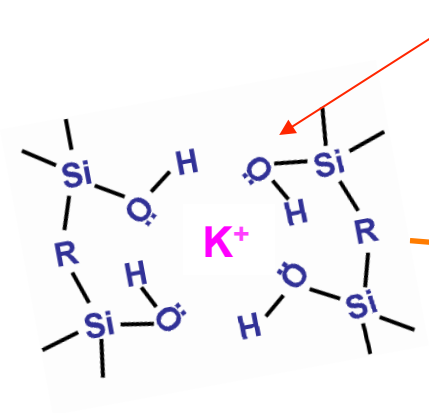
ε

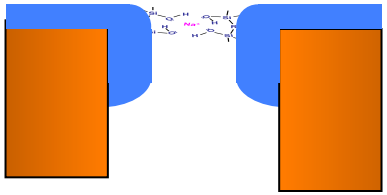
Inorganic Channels



4 x
1.5 nm

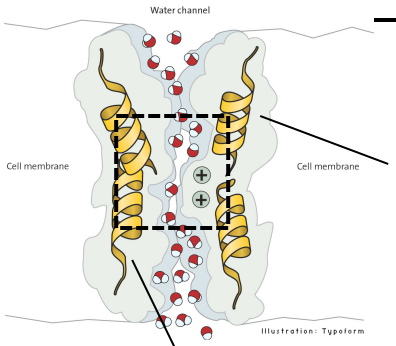
- Rigid ion-selective aperture?

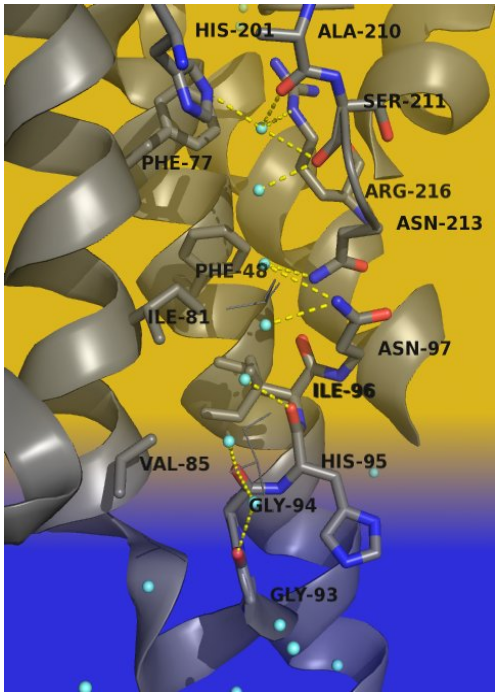




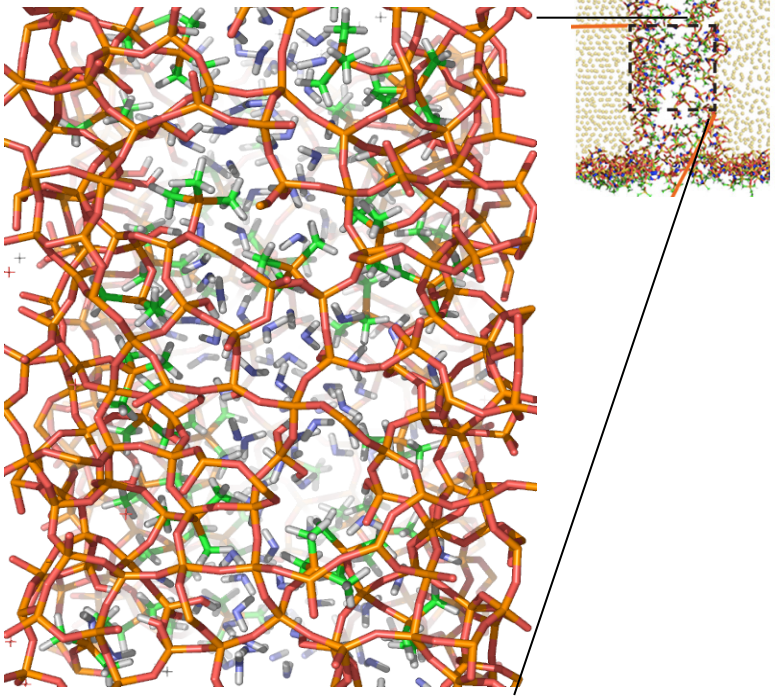
- Crowded ion-selective binding site?

Water Discrimination:
Fast water transport & ion rejection?





Aq water channel
(crystal structure)
(www.nobelprize.org)



Model inorganic pore
(simulation results)

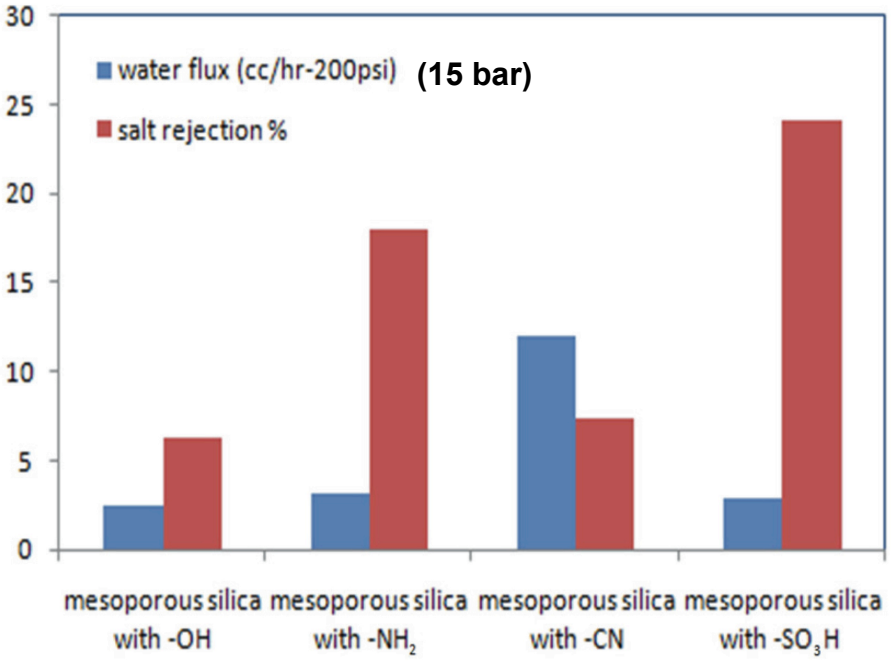
- thin, straight, narrow passage
- repulsive hydrophobic walls
- staircase of stabilizing dipoles (C=O, N-H)
- no symmetric dipole clusters

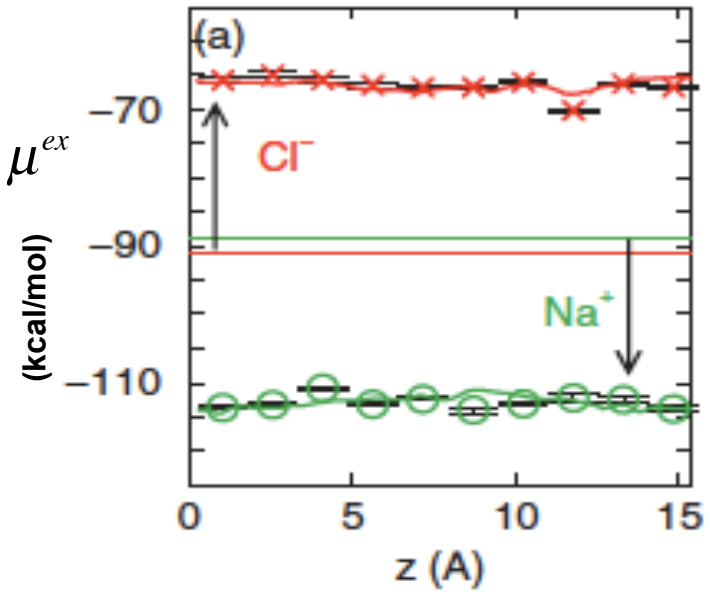
Leung, Rempe, Lorenz *Phys Rev Lett* 2006
Cygan, .. Leung, Rempe *Mat Res Bull* (2008)
Leung & Rempe *J Comp Theor Nanosci* (2009)

Water channels with wide polar pores

Fast water transport, poor ion rejection

- Atomic layer deposition modifies pore size & chemistry





with –OH
(reversed with NH_3^+)

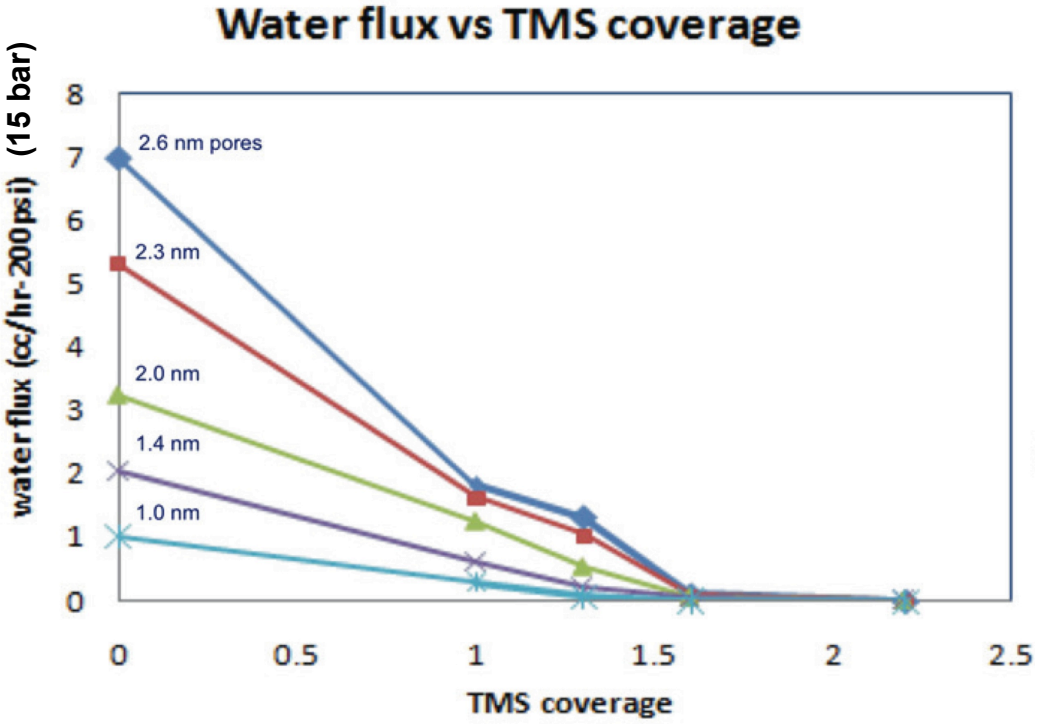
Over 1 nm polar pores:

- waters stabilized → high flux, little salt rejection
- predict alternating chemistry → full salt rejection

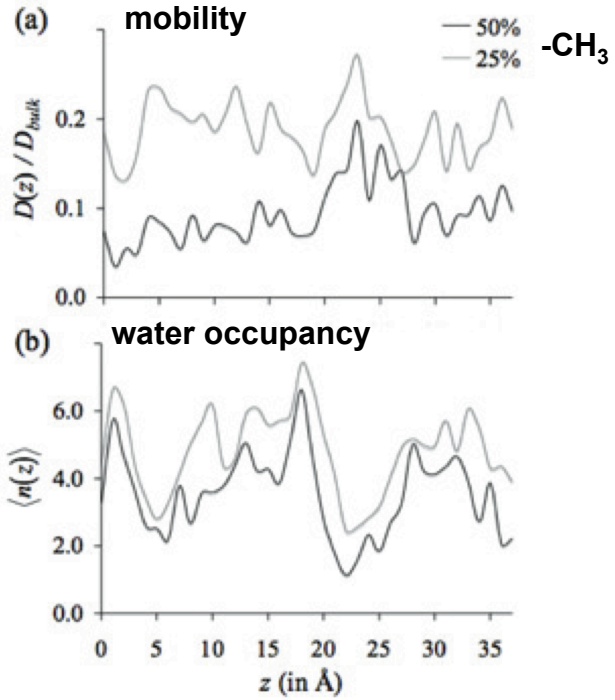
Leung, Rempe, Lorenz PRL (2006)

Water Channels with non-polar pores

Slow water transport, great ion rejection



$-Si-(CH_3)_3$

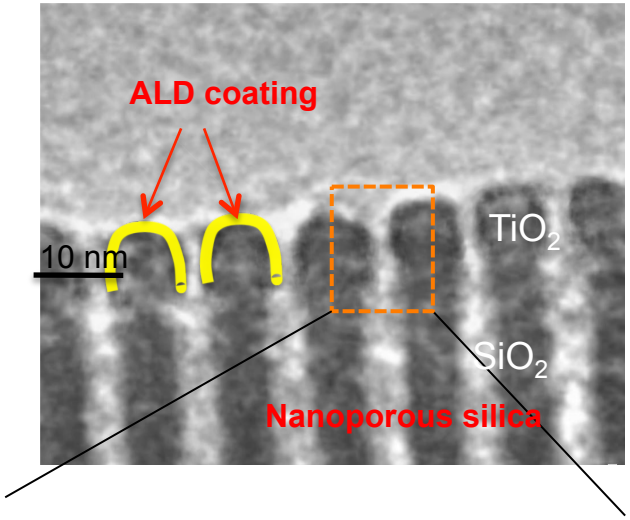


Over 1 nm hydrophobic pores:

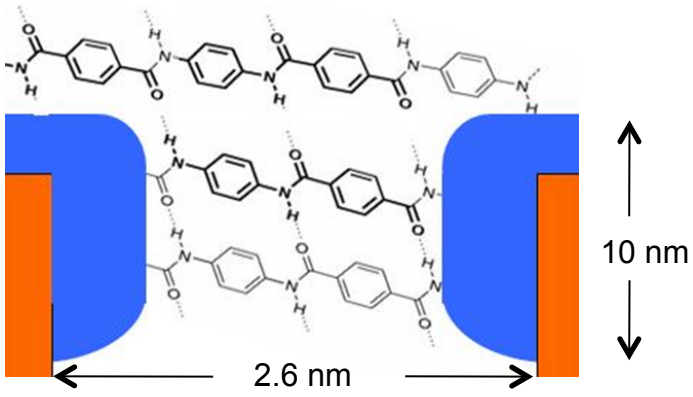
- ions rejected
- waters destabilized & immobilized

Molecular-layer deposition of polymer:

Translate key water channel designs?



- **C=O**, **N-H** dipoles stabilize water
- **hydrophobic** rings prevent sticking
- **no** symmetric dipole clusters for ions
- **narrow** passageway excludes hydrated ions



Molecular layer deposition near surface via plasma → fundamentally different membrane architecture:

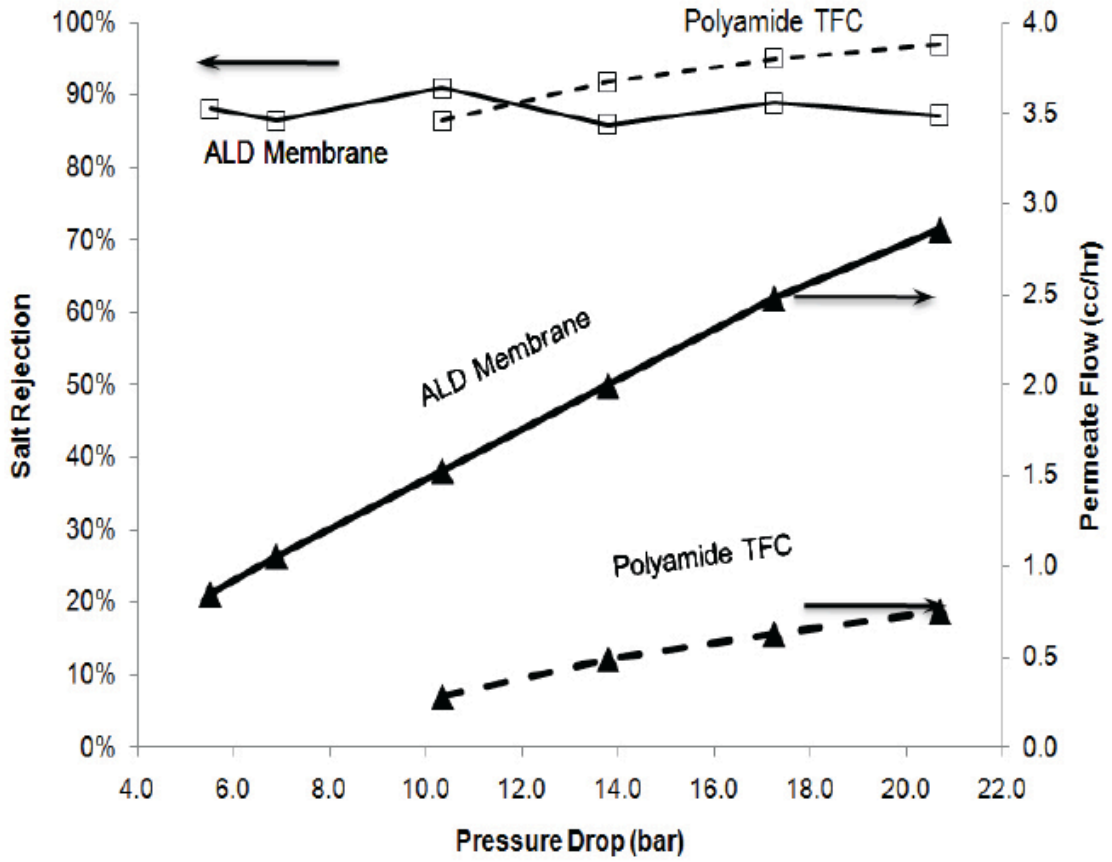
- TMOS (tri-methoxy silane)
- APS (amino-propyl silane)

Brinker Lab

J Membr Sci (2007)

JACS (2007)

ALD Biomimetic Membranes = behave differently than (TFC) membranes

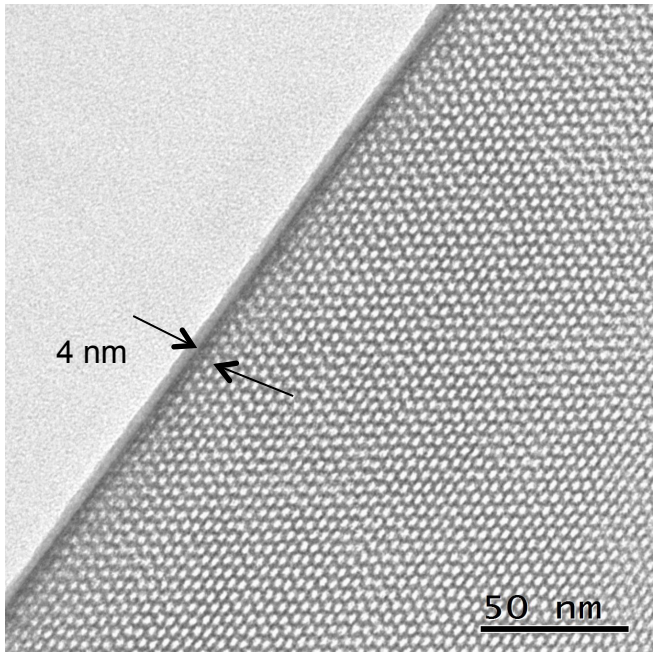


- **ALD: Rejection high even at low P**

→ **Different mechanism?**

- **0.1 M NaCl, osmotic Π = 2.1 bar, 1/κ = 1.2-nm**

What structural elements can be improved?

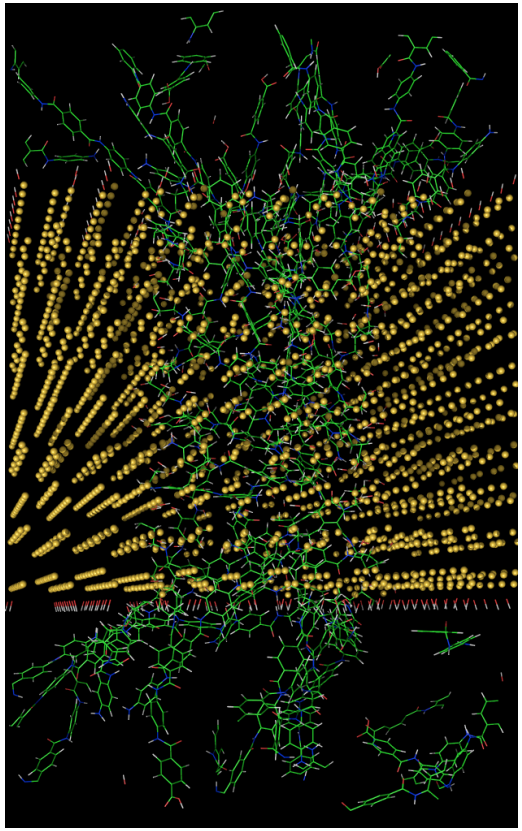


TEM image of thin membrane coating

- thin
- uniform
- robust

- Coordination chemistry?

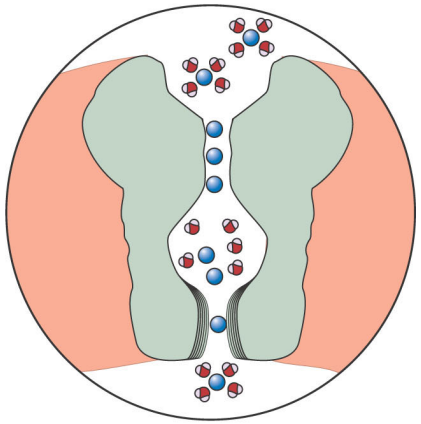
➢ room for improvement



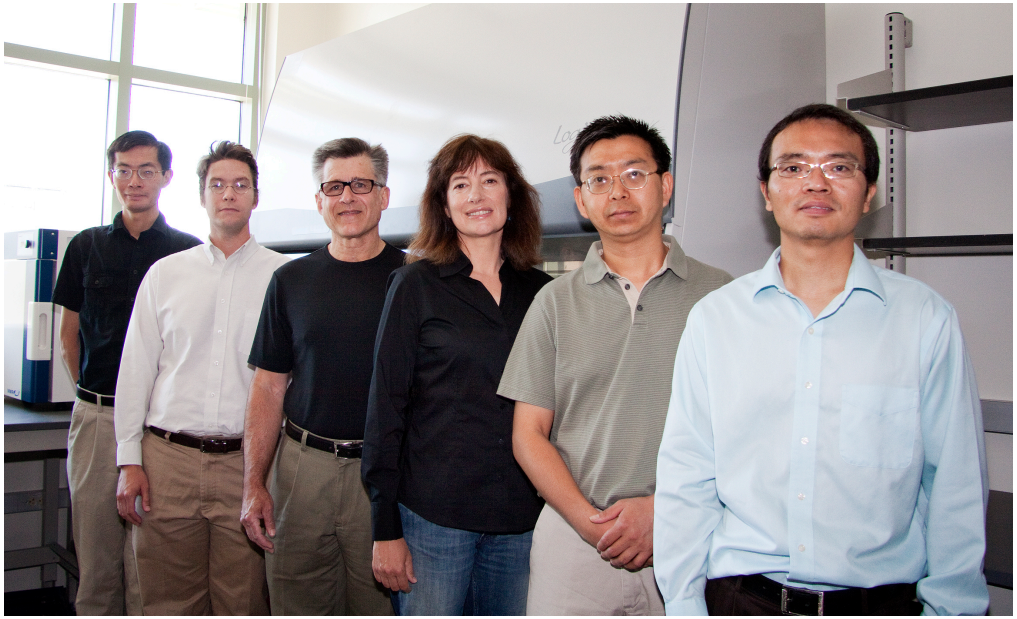
Simulated polymer ALD membrane

Summary: Membranes Designed to Mimic Protein Channels

- K^+/Na^+ discrimination & tunability (QM locally with new theory):
  - surroundings → maintain crowded (>6) binding site fit to K^+
  - surroundings → maintain rigid pore size fit to K^+
- Specific water selectivity & reject ions (fabricated ALD):
  - narrow
  - polar/non-polar mix
  - no ion binding sites
- General biomimetic features (fabricated EISA/PA-ALD):
  - thin & straight
  - uniformly active
  - robust structure



Team




Sandia National Laboratories
University of New Mexico
R&D 100

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  1. **DOE: Sandia's Water Desalination Program**
  2. **DOE: Sandia's LDRD program (BST, ERN)**
  3. **NIH: Nanomedicine Center**
- **Compute time**
  1. **Sandia Computing: Red Sky**
  2. **National Centers: NCSA, NERSC**

- **Theory Collaborators**

- **David Rogers (postdoc → U S Florida)**
- Dian Jiao (postdoc → UT)
- **Sameer Varma (postdoc → U S Florida)**
- Dubravko Sabo (postdoc → NYU)
- Chris Lorenz (postdoc → King's College)
- Mangesh Chaudhari (postdoc)

- Kevin Leung (SNL)
- Peter Feibelman (SNL)
- Lawrence Pratt (Tulane)

- **Experimental Collaborators**

- **Jeff Brinker (SNL, UNM)**
- **Ying-Bing Jiang (UNM postdoc → UNM)**
- Zhu Chen (UNM postdoc → Ford)
- **Shaorong Yang** (UNM postdoc → CNM)
- Seema Singh (UNM postdoc → SNL)
- Caroline Rempe (UNM student → U Tenn)
- Todd Alam (SNL)
- Tom Mayer (project manager SNL→ UNM)

Prior Simulation Studies of Fast Separations

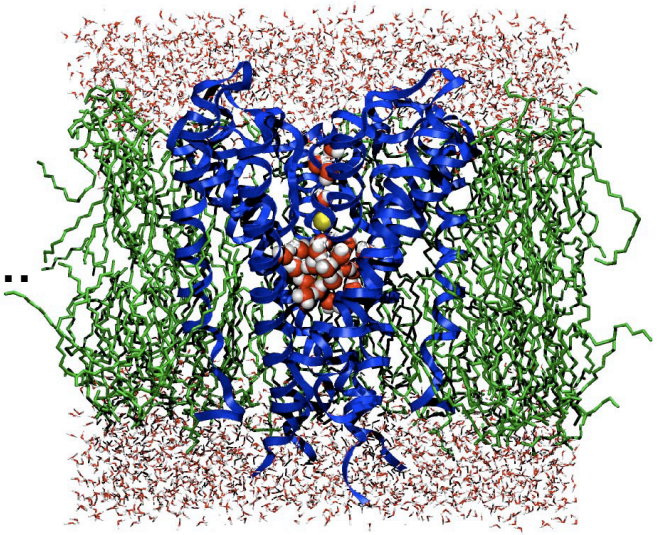
- ***J of General Physiology*:**
  Perspectives on Ion Selectivity (2011)

  Noskov, Roux, Allen, Asthagiri, Pratt, Rempe, …

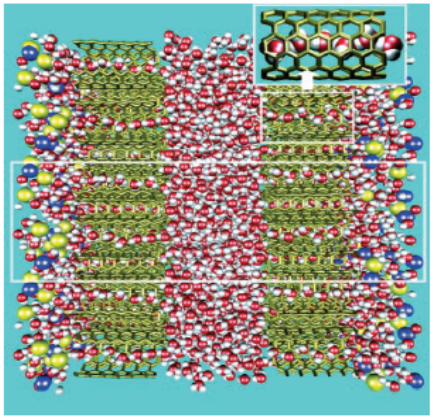
  Corry, Bostick, Brooks, Weaver, Green
  Sansom, Domene, Carloni, Aqvist, …

- **Aquaporins**
  - De Groot, Grubmuller
  - Tajkhorshid, Schulten
  - Warshel

- **Other Pores**
  - Hummer, Patel, Leung, Aluru
  - Corry, Roux
  - Lynden-Bell



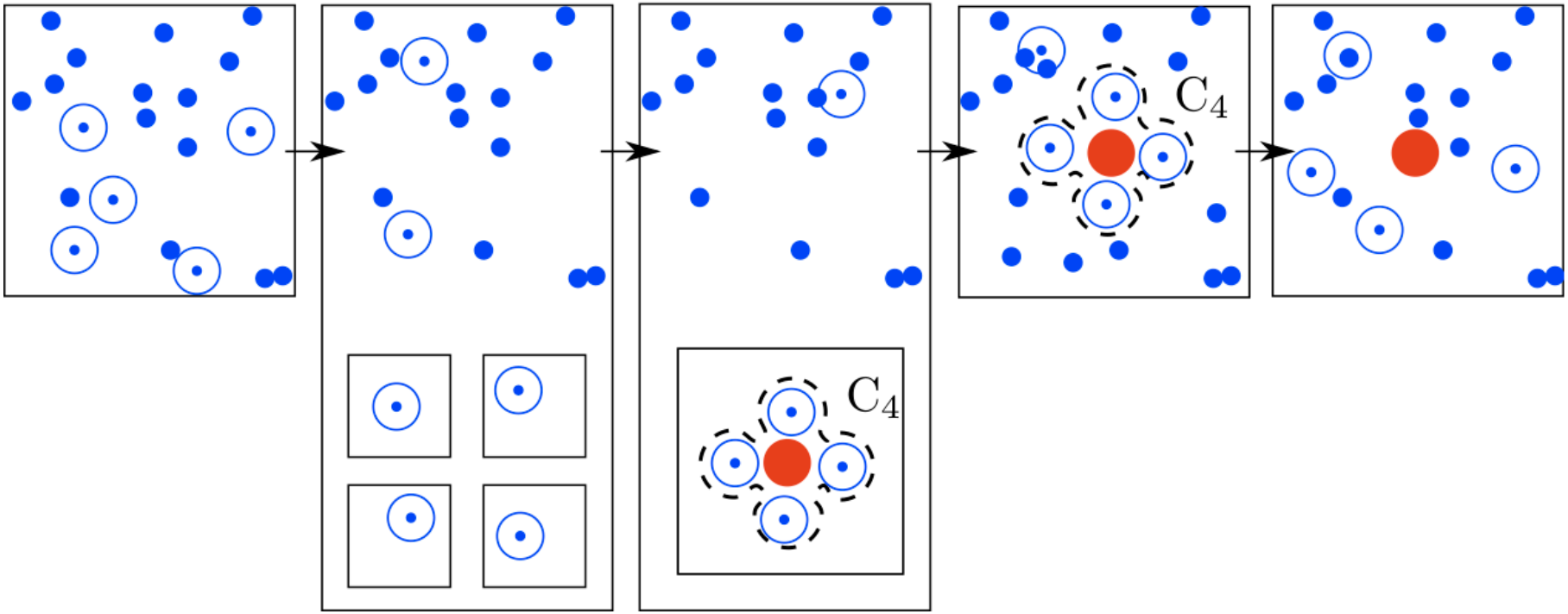
Rogers & Rempe, *J Stat Phys* (2011)



Hummer & co *PNAS* (2003)

Treat Ion Binding & Solvation via QM Efficiently

$$\beta\mu_{\mathrm{X}}^{(\mathrm{ex})} = -n\beta\mu_{\mathrm{L}}^{(\mathrm{ex})} - \ln[K^{(0)}(C_n){\rho_L}^n] + \beta\mu_{\mathrm{X}\cdot\mathrm{L}_n}^{(\mathrm{ex})} + \ln p_{\mathrm{X}}(C_n)$$



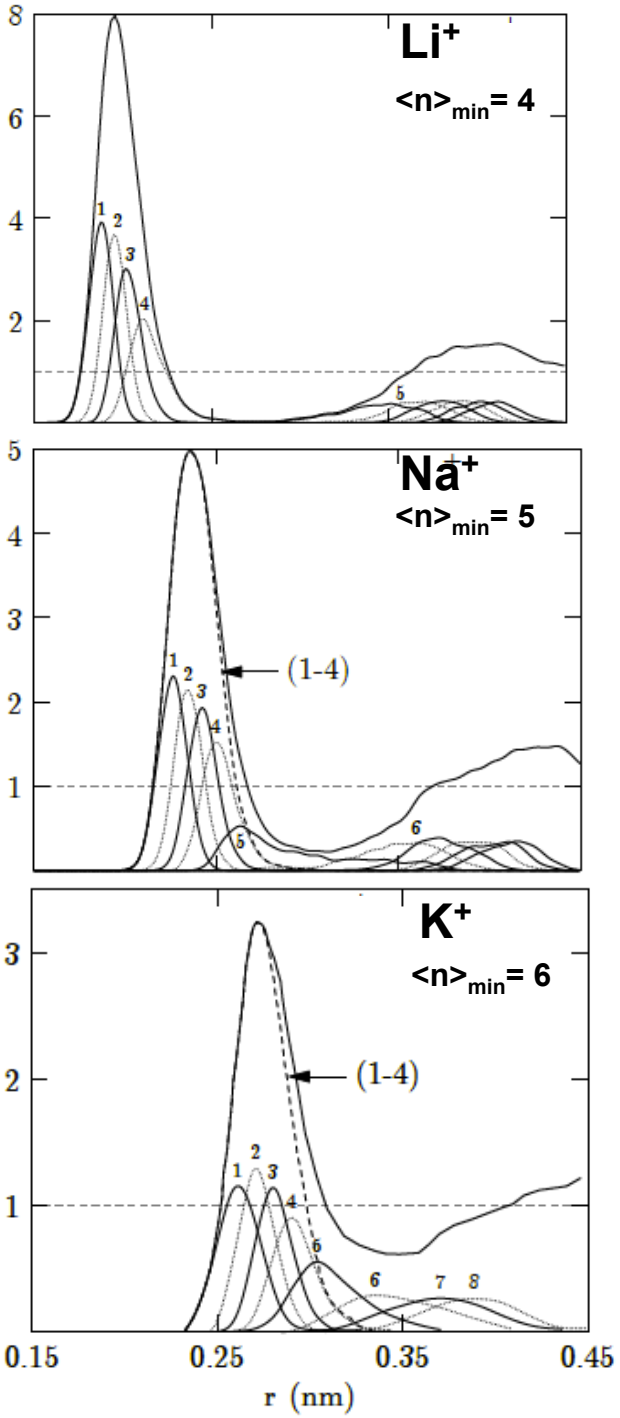
Quasi-chemical theory (QCT) advantages:

→ study binding sites with QM

→ study environment ('architectural constraints')

JPCB (2011); *Ann Rep of Comp Chem* (2012)

Lessons: Ions (aq)
(full QM)



- **Ions differ:**
  - Structure, DG
- **Common structural theme:**
  - **n = 4** directly coordinating
  - Non 'split-shell' convenient
- **Higher *n* in proteins?**
  - n = 4 within 2.8 A (water)
  - n = 8 within 2.8 A (channel)

How do channels discriminate between ions?

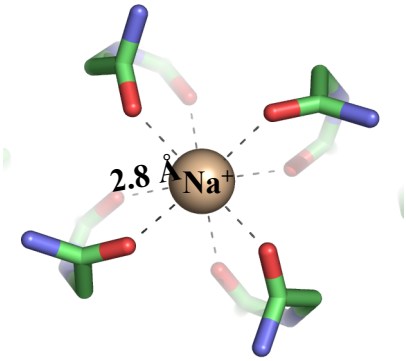
Agreement with exp
*Neilson
*Soper

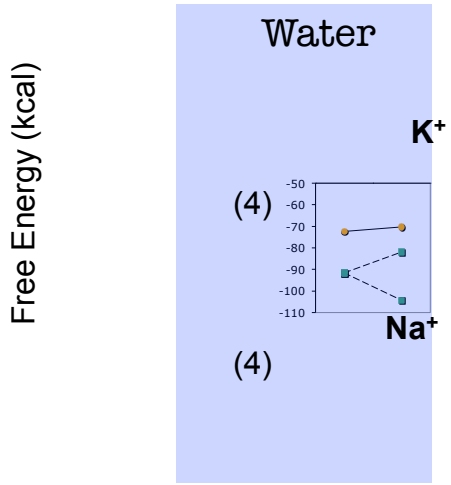
***Ann Rep Comp Chem* (2012)**

Varma & Rempe *Biophys Chem* (2006)

Environment maintains a specific binding site coordination that fits K^+

K^+ Channels





(8)

(8)

• K^+ selective
(flexible or rigid cavity)

(5-6)

• Not K^+ selective
(unless cavity size fits K^+)

Environment → maintain crowded (> 6) ligands → K^+/Na^+ discrimination:

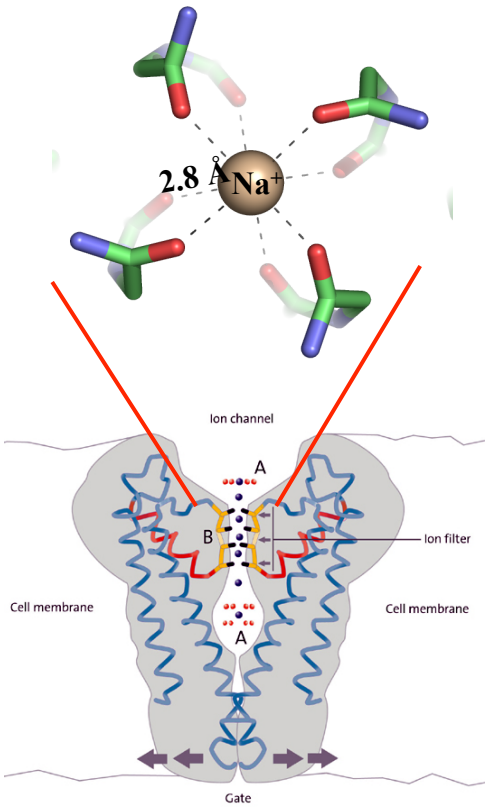
***Same chemistry → environment tunes binding site composition → varied function**

Biophys J (2007); [2]Bostick & Brooks *PNAS* (2007)
J Mol Bio (2008); *JACS* (2008); *Ann Rep Comput Chem* (2012)

Jiang & co *Nature* (2011) Environment of multiple binding sites

Translate design for mineral water

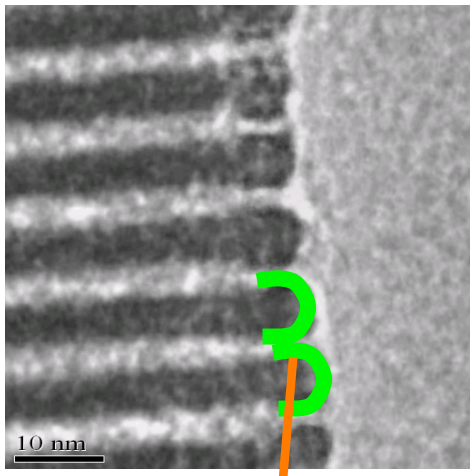
Natural Channels[1]



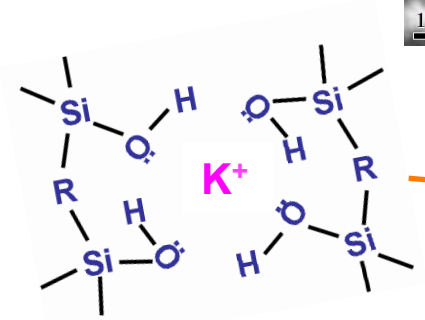
Bio mechanisms

Engineered Mimicry

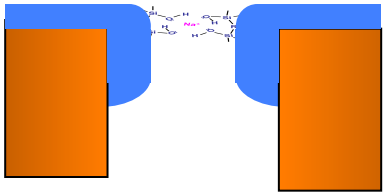
Inorganic Channels



4 nm x 1.5 nm



•[3] Plasma-limited ALD + molecular imprinting?



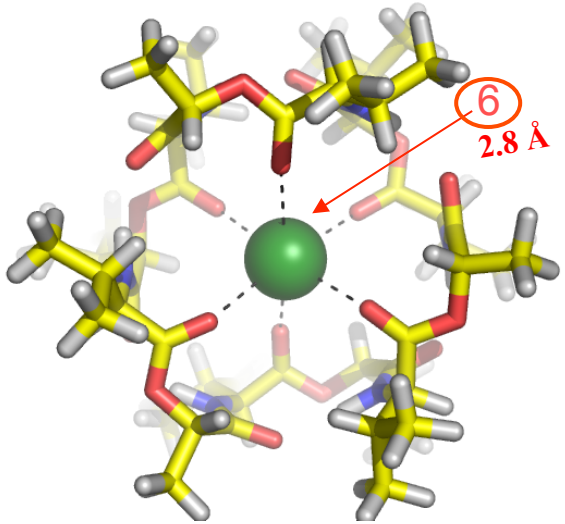
Nanoscale design parameters to target[1]:

"The caress of the surroundings"[2] to maintain crowded ligands in fluctuating cavity

[1]*Biophys J* (2007); [2]Jordan *Biophys J* (2007); [3]Jiang, Brinker, *et al. JACS* (2006,2007)

Translate design for mineral water

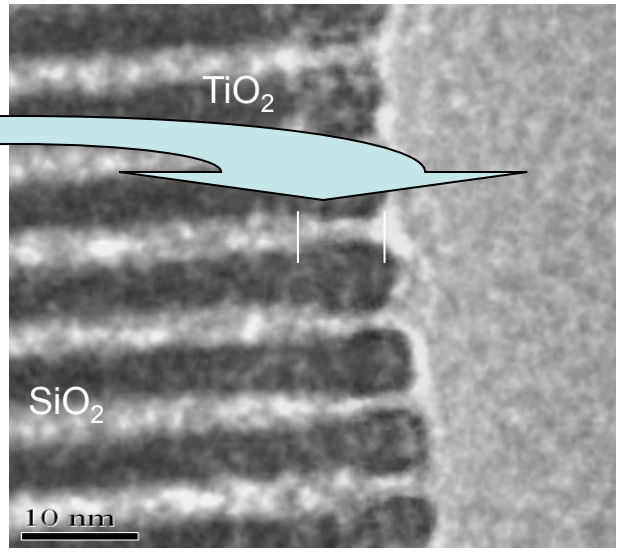
Natural K-selective Molecule



- **Specific cavity** fits K^+, not Na^+
- **H-bonds** & ring maintain cavity size
- **Environment** may disrupt H-bonds, selectivity

Valinomycin, JMB (2008)

Inorganic Channels

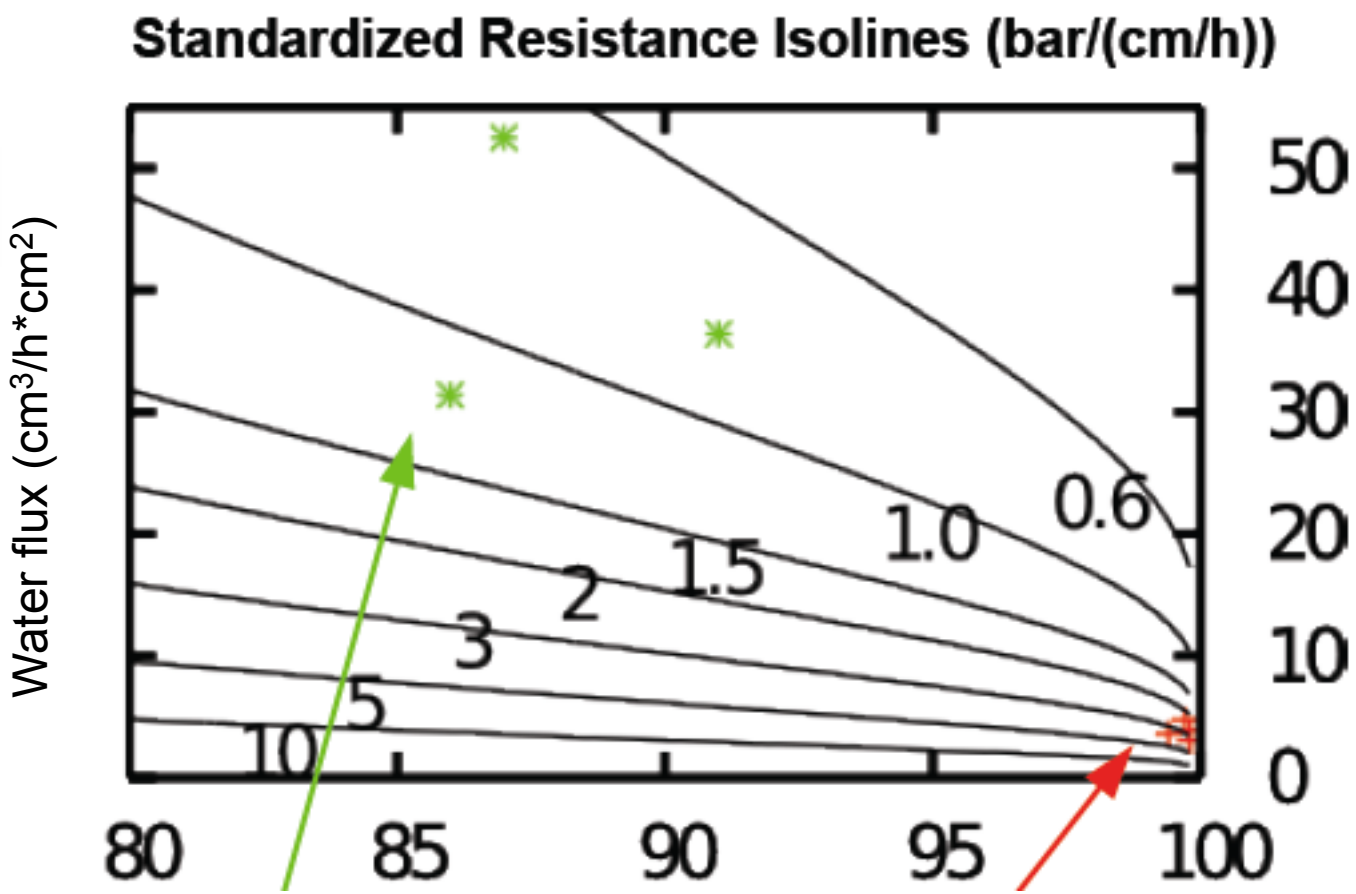


4 x
1.5 nm

- **Rigid Ion-selective aperture?**

- **Two ways to discriminate K^+ over Na^+:**
  - Environment → overcoordinate to fit K^+ → pore size can fluctuate
  - Environment → fixed cavity fits K^+ → any number of ligands that solvate K^+

ALD Biomimetic membrane: 5-fold less resistance than Commercial



Gold standard: FilmTec