Hydration mimicry of Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+} ions in the ion-channel

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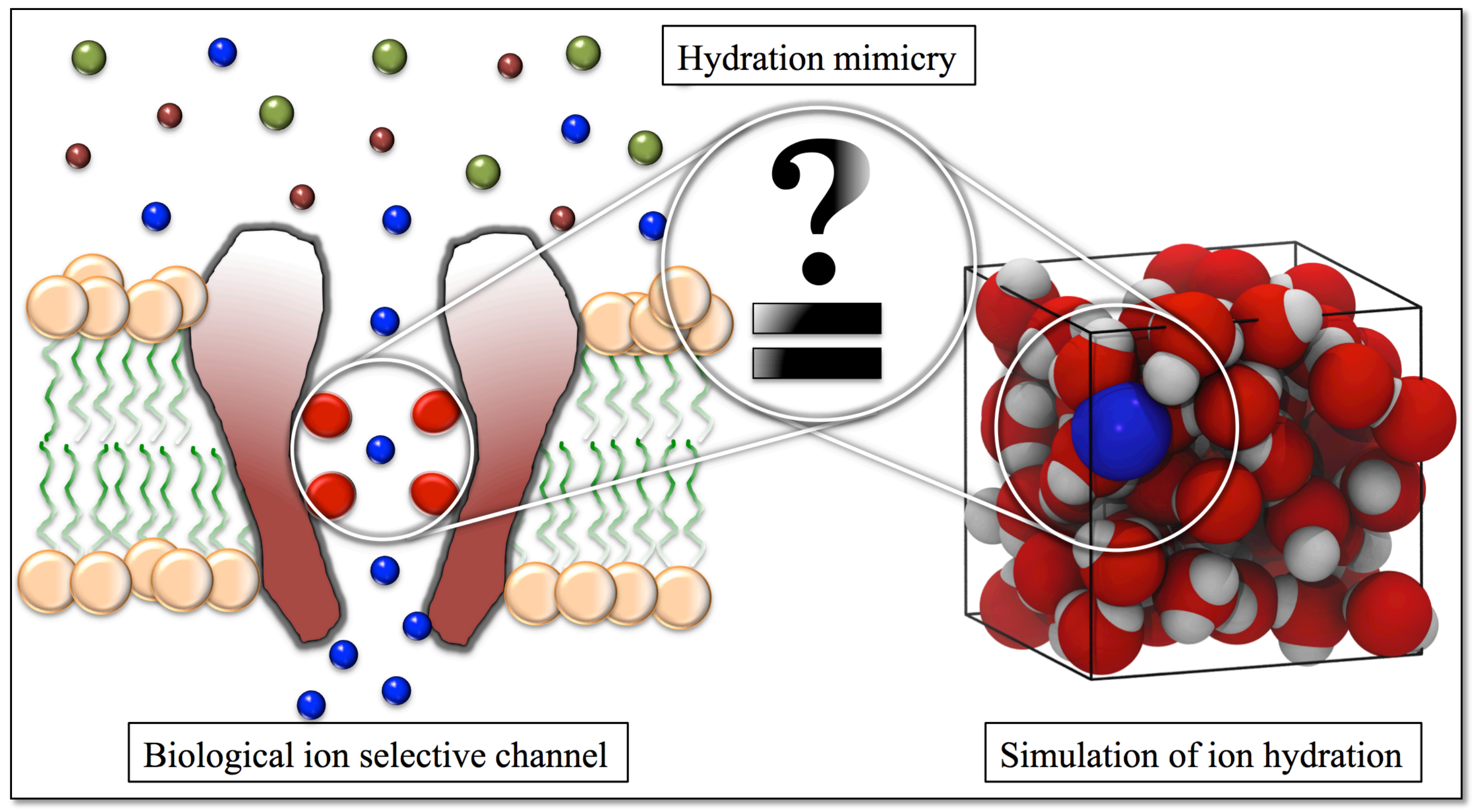
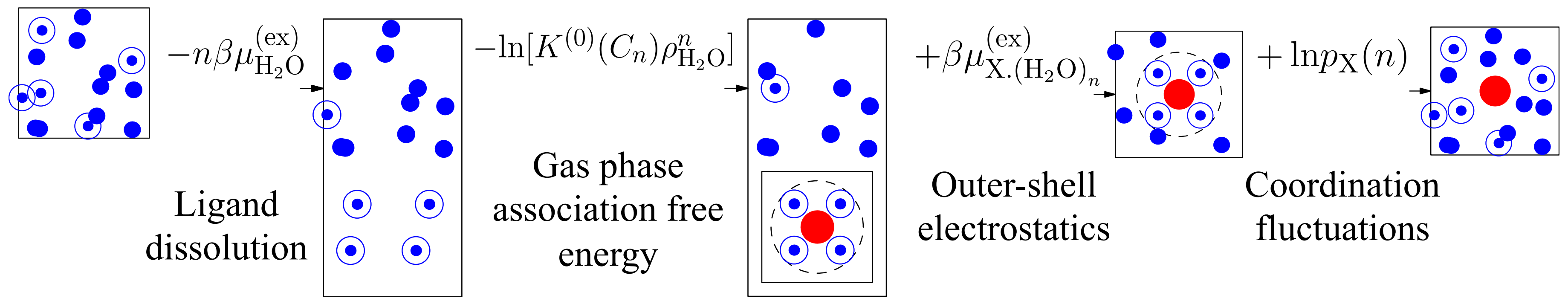
SAND2014-20447C

INTRODUCTION

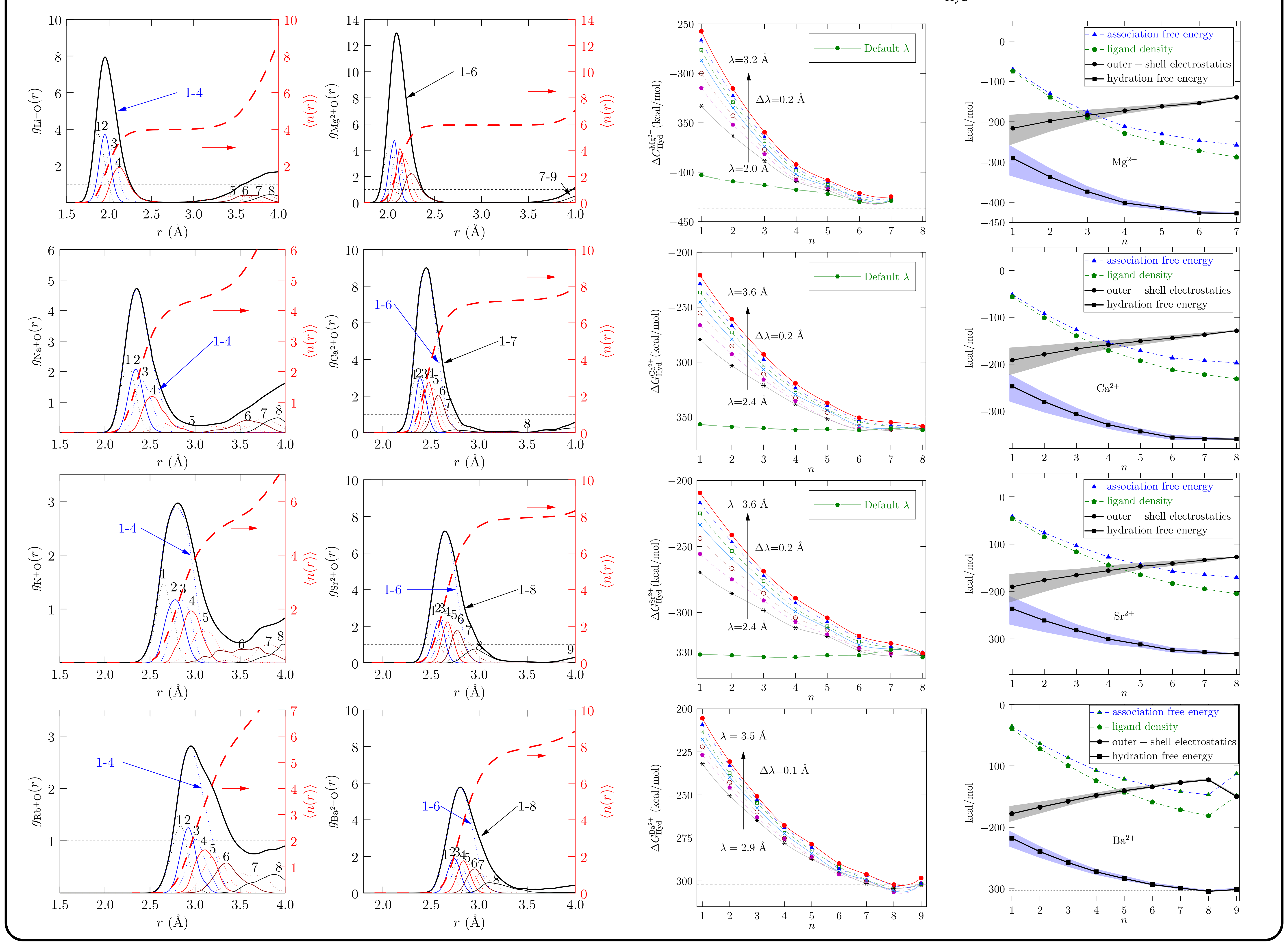
Ion hydration is biologically important as a reference environment for ion transport across cellular membrane. Cells like those in the brain, heart and muscle exert exquisite control over ion concentration gradients across their membranes for electrical signaling. Cellular mechanisms of ion transport may be useful for designing better membranes for power generation and water purification. Here, we combine ab-initio simulations, electronic structure calculations and statistical mechanical theory to interrogate the hydration structures and free energies of divalent cations. The predicted hydration free energies are compared with experimental values. We also address a long-standing puzzle about whether or not ion channel binding sites mimic the hydration structure of specific ions to promote their transport. Our studies focus on Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+} ions.



QUASI-CHEMICAL THEORY (QCT)



$$X^{2+} + nH_2O \rightleftharpoons X(H_2O)_n^{2+} \qquad K_n^{(0)} = \frac{\rho_{X(H_2O)_n^{2+}}}{\rho_{X^{2+}}\rho^n_{H_2O}}$$


Radial distribution function and running coordination number

Effect of QCT parameter selection on ΔG_{Hyd}

Decomposition of QCT terms

METHOD

- VASP *ab-initio* molecular dynamics simulation package
  - System: Single ion in 64 water molecules, NVT, T= 330 K, p=1 atm
- Gaussian 09 was used for electronic structure calculations
  - TPSS basis set, PCM model, pseudo-potentials for core electrons.
- Graphics are produced using VMD and Chimera

Our study focused on hydration structure and evaluation of hydration free energy using quasi-chemical theory. Near neighbor distribution yields structural insights which are relevant to deduce local coordination structure.

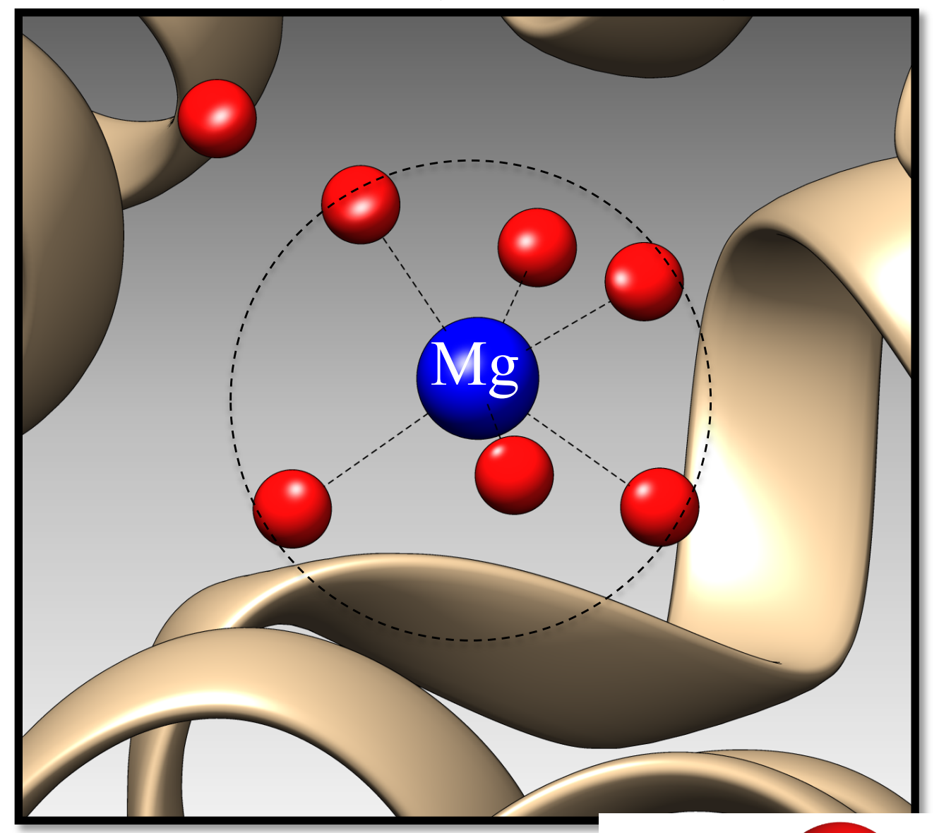
This is the first time such an extensive study was carried out on divalent ions using quasi-chemical theory.

PUBLICATIONS

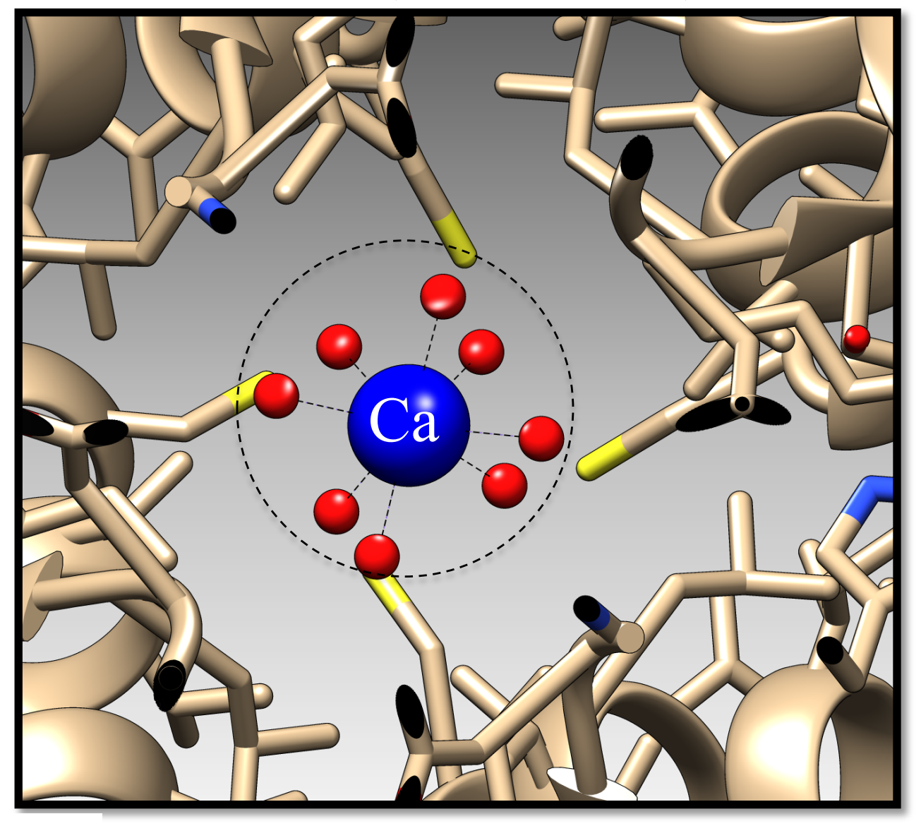
1. "Octa-coordination and Hydrated Ba^{2+}(aq) ion," M. I. Chaudhari, M. Soniat and S. B. Rempe, *Submitted to* ***Phys. Chem. Chem. Phys.*** **(2014)**
2. "Hydration of Sr^{2+} and the Potassium Channel Blocking Site," M. I. Chaudhari and S. B. Rempe, *In preparation for* ***Biophysical Journal***
3. "Hydration Studies of Biologically Relevant Divalent Cations: Magnesium (Mg^{2+}), Calcium (Ca^{2+}), Strontium (Sr^{2+}) and Barium (Ba^{2+})", M. I. Chaudhari, J. M. Vanegas and S. B. Rempe, *In preparation for an invited article in* ***Acct. Chem. Res.***

HYDRATION MIMICRY

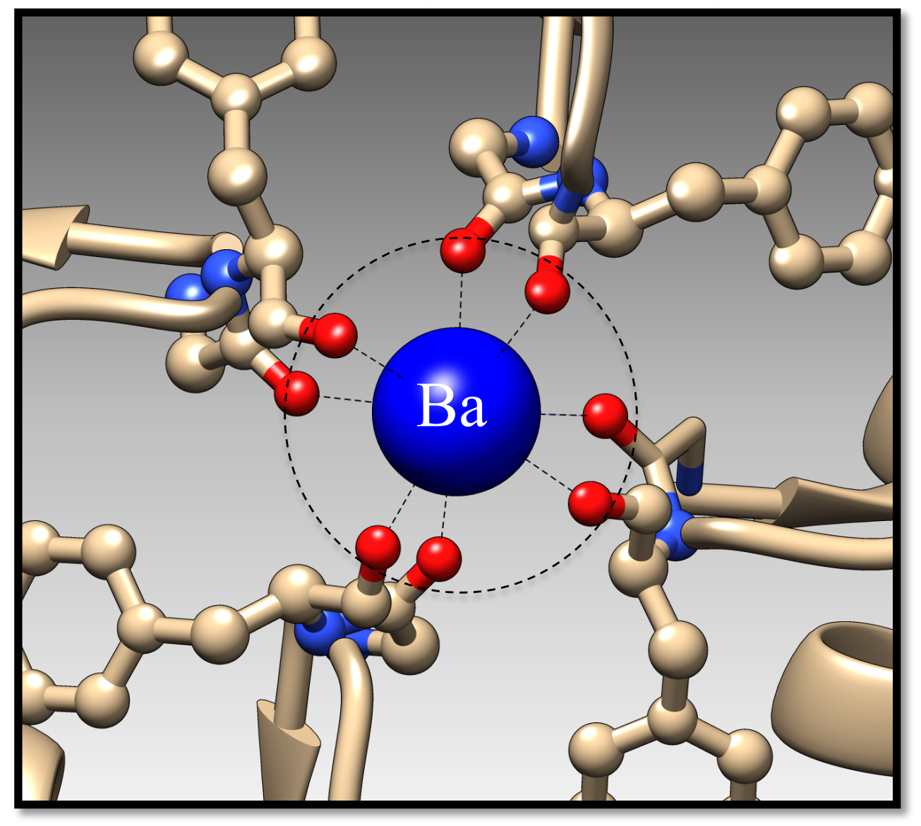
$[Mg(H_2O)_{6+1}]^{2+}$ cluster in Mg-ion channel (PDB:4U9L)

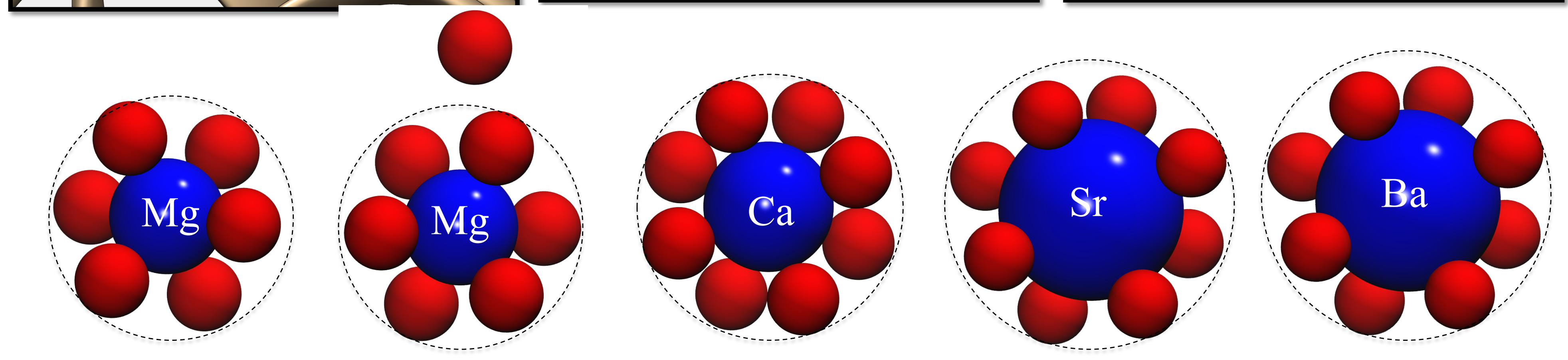


$[Ca(H_2O)_8]^{2+}$ cluster in Ca-ion channel (PDB:4MS2)



[Ba(-O)8]2+ ion at binding site in K-ion channel (PDB:4PDR)





Optimized clusters of ion and water in the dielectric continuum of water are comparable to ion structures inside the ion channels.

CONCLUSIONS

- QCT predicts hydration free energy that is comparable to experimental values provided complete inner shell environment is specified
- Ion channels (Calcium, Magnesium and Potassium) mimic hydration structure at the binding sites allowing selective transport through membranes.
- K-channel blockers Ba and Sr shown 8-fold coordination structure as most stable structure in water (similar to binding site configuration).
- Calcium and Magnesium channels are huge and allow hydrated ions to go through based on size of ion-water clusters.

ACKNOWLEDGEMENT

We gratefully acknowledge funding from the Sandia National Laboratories LDRD program. Sandia National Laboratories is a multi-program laboratory managed and 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. SAND-2014