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# BEAGLE

## Science Highlight

**Ion selectivity of the bacterial NavAb channel: Gaining insight from microsecond timescale molecular dynamics simulations.**

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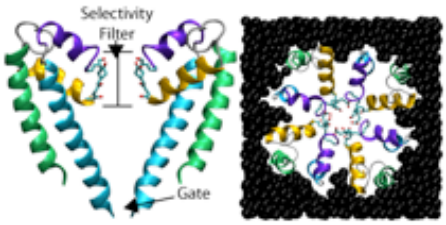
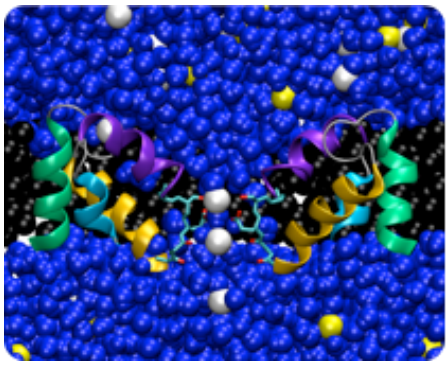
The selectivity filter of NavAb is not as narrow as the selectivity filter of the known potassium-selective channels, in most places there is room for the penetrating ion to remain solvated, and cations may pass each other in some places, potentially leading to a multitude of non-serial pathways for conduction. To provide non-static picture of the ion channel, and to study the mechanism of ion conduction and ion selectivity through the selectivity filter of the pore in a statistically based manner, microsecond-timescale molecular dynamics simulations of ion conduction were performed on the Beagle supercomputer. While these timescales are frequently achieved on dedicated machines like DE Shaw Research's Anton, they are less commonly attained using local clusters and were unheard of in the recent past. The long timescales of the simulation, along with the versatility of using parallel versions of traditional molecular dynamics code (NAMD), allowed us to use a protein that was truncated to provide a model of the selectivity filter in a stiff supporting lattice (figure), rather than requiring a complete pore in a lipid membrane, reducing necessary system size by nearly half. The effect of cations in solution, their concentration and applied voltage on the selective conduction of sodium and potassium through the NavAb selectivity filter has been studied.




Left, the crystal structure of the pore domain of NavAb (PDB ID : 3RVY) with front and back segments removed for clarity. Note that the gate at the bottom on the pore domain is closed preventing ion conduction. Right, bird's eye view through the top of the truncated model of NavAb.



Side view of the truncated model of NavAb used for simulations of ion conduction with the front and back segments removed. Water (blue) and sodium (white) penetrate the pore, however chloride (yellow) does not.

The cell membrane separates a cell from its environment, but there are many kinds of transport proteins that can allow ions, water, and small molecules to cross. Ion channels are a type of transport that allows ions to pass into or out of the cell, some of these only allow a specific anion or cation type to pass, others are less selective. In humans voltage-gated, ion-selective ion channels are part of many pathways, including action potentials of nerves, muscles, and many signaling pathways. The first voltage-gated potassium channel was solved over ten years ago, but other ion-selective channel families have been more elusive. Two summers ago, the first crystal structure of a putative sodium-selective, voltage-gated ion channel, NavAb, was published. The pore domain has a narrow region called a selectivity filter, a large water-filled cavity, and at the bottom it has a gate that is opened and closed by the voltage sensors (see figure).

Additional information on Beagle can be found at: Beagle Website

## Scheduling Policy and Access to Beagle

- For normal priority jobs, there are no limits to the number of nodes, submitted or running jobs, or walltime used. To find more details about specific queue type: qstat -q
- For the new low priority settings, the restrictions are a walltime of four hours or less, and nothing more than 10 nodes. Basically, we're scheduling normal priority jobs first, then filling in the gaps with lower priority jobs. The smaller the job, the easier it'll be to schedule, so the quicker it will move from queued to running.
- Nothing needs to be specified in the submit script. Low priority configurations are handled on the server side on a per-project basis. Any project that has been designated as having a low-priority allocation will automatically have those settings assigned when Moab reads the project code/name when the job is submitted.
- Scheduling is based on a fair-share system, with four queues to meet the varying needs of our users. Details can be found at: Beagle Scheduling Policy

## Resources

- *Beagle Wiki* Get detailed usage information from the Beagle team
- *Beagle Support* Contact the Beagle experts for help
- *Globus Online* for file transfer Get started moving files to/from Beagle using this fast service
- *Other CI resources* Learn about other computing resources available at the Computation Institute

## Beagle Related Publications

- Supercomputing for the parallelization of whole genome analysis, Megan J. Puckelwartz, Lorenzo Pece, Viswateja Nelakuditi, Sharlene Day, Thomas Cappola, Euan Ashley
- Molecular autopsy for sudden death using whole genome sequencing, Megan J. Puckelwartz, Lisa Dellefave-Castillo, Don Wolfgeher, Viswateja Nelakuditi, Mark T. Campbell, Jessica R Golbus

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