

## **Modeling electrostatics in molecular biology: application to motor domain motion along microtubule**

Emil Alexov

Computational Biophysics and Bioinformatics, Department of Physics, Clemson University,  
Clemson, SC 29634

Electrostatics plays major role in molecular biology because practically all atoms carry partial charge while being situated at Angstroms distances. Many biological phenomena involve the binding of proteins to a large object. Because the electrostatic forces that guide binding act over large distances, truncating the size of the system to facilitate computational modeling frequently yields inaccurate results. Here we report a multiscale approach that implements a computational focusing method that permits computation of large systems without truncating the electrostatic potential and achieves the high resolution required for modeling macromolecular interactions, all while keeping the computational time reasonable. We tested our approach on the motility of various kinesin and dynein motor domains. We found that electrostatics help guide kinesins as they walk: N-kinesins towards the plus-end, and C-kinesins towards the minus-end of microtubules. In case of dynein, we show that electrostatic binding energy forms a guiding funnel that navigates the stepping of the long “legs” of dyneins at the right binding pocket on the microtubule. Furthermore, we demonstrate that the running length and velocities of dynein and dynein mutants are correlated with the magnitude of the binding energy. Our methodology enables computation in similar, large systems including protein binding to DNA, viruses, and membranes. Lab webpage: <http://compbio.clemson.edu>