FREE-ENERGIES UNDERLYING ION BINDING AND TRANSPORT IN PROTEIN CHANNELS - FREE-ENERGY PERTURBATION SIMULATIONS OF ION BINDING AND SELECTIVITY FOR VALINOMYCIN

Por:EISENMAN, G (EISENMAN, G); AQVIST, J (AQVIST, J); ALVAREZ, O (ALVAREZ, O)
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Abstract

As a step to increasing the reliability of the calculation of free energies underlying ion binding and transport in protein channels, free energy perturbation simulations have been performed for the binding of alkali-metal cations to the cyclic depsipeptide molecule, valinomycin, and compared with experimental measurements of binding by two-phase salt extraction equilibria. Valinomycin was chosen because it forms regular 1:1 ion complexes through its ester carbonyl ligands of crystallographically known three-dimensional structure in which the cation is sufficiently enfolded by the molecule that the overall size, shape, and charge distribution of the complex is virtually the same regardless of the species of cation bound (i.e. the complexes are 'isosteric'). The experimentally measured selectivities are sufficiently similar, in a wide variety of solvent environments, that the differences in free energies measured between the different ion-valinomycin complexes in a convenient solvent can be taken as equivalent to the differences in free energies in vacuo. This enables the adequacy of Warshel's MOLARIS force field for computing ion-specific differences in binding to be tested and provides an opportunity for refining the estimates for the appropriate values of partial charge and Lennard-Jones 6-12 parameters for an ester carbonyl group.

Palabras clave

KeyWords Plus:TOBACCO NECROSIS VIRUS; CRYSTAL-STRUCTURE; MOLECULAR-DYNAMICS; NUCLEIC-ACIDS; FORCE-FIELD; MODEL; PERMEATION; REFINEMENT; PROGRAM; COMPLEX

Información del autor

Dirección para petición de copias: EISENMAN, G (autor para petición de copias)

+ UNIV CALIF LOS ANGELES,SCH MED,DEPT PHYSIOL,LOS ANGELES,CA 90024, USA.

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[1] UPPSALA BIOMED CTR,DEPT MOLEC BIOL,S-75124 UPPSALA,SWEDEN

+ [2] UNIV CHILE,FAC SCI,DEPT BIOL,SANTIAGO,CHILE

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ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK MILTON ROAD, CAMBRIDGE, CAMBS, ENGLAND CB4 4WF

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