

# Free energy perturbation simulations of cation binding to valinomycin

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Experimental values of the free energies of cation binding to the cyclic depsipeptide molecule, valinomycin, obtained from Pedersen-type salt extraction measurements, provide data against which it is possible to test the adequacy of the procedures and force fields of the molecular dynamics algorithms, MOLARIS and GROMOS. These data are then used to assess appropriate values for the partial charges of the ester carbonyl oxygen and carbon. Valinomycin was chosen because it has only one kind of ion-binding ligand and because the cation is sufficiently enfolded by the molecule in the ion-complexes that the overall size and shape of the complex is virtually the same regardless of the species of cation bound. For such an 'isosteric complex', 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 by two-phase salt extraction experiments into dich