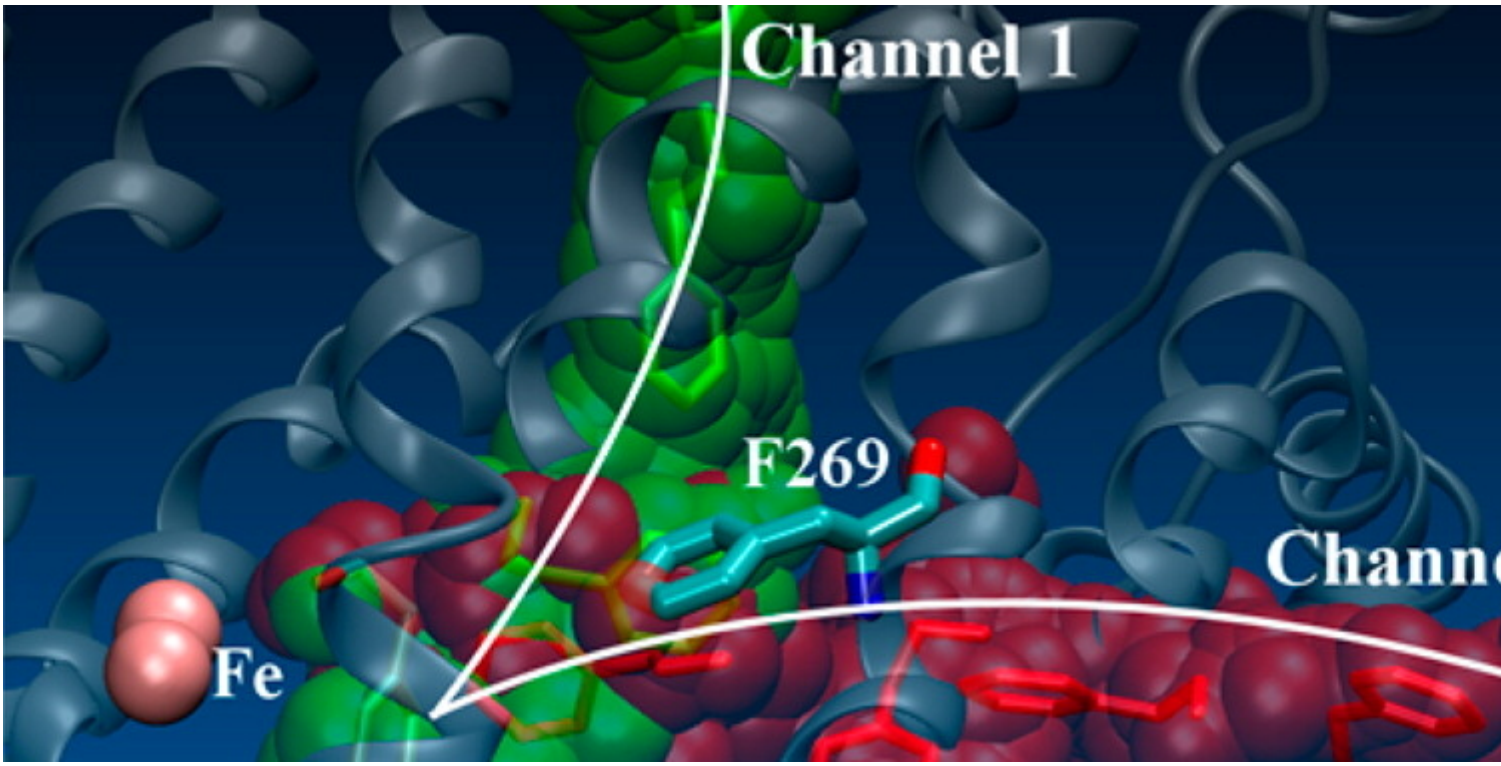
PELE: Monte Carlo methods for protein/DNA-ligand interactions



A key line of research in the lab is the development of PELE (Protein Energy Landscape Exploration), a fast and accurate Monte Carlo software for mapping protein(and DNA)-ligand interactions.

Summary

PELE combines a Monte Carlo stochastic approach with protein structure prediction algorithms, and is capable of accurately reproducing long timescale processes in only few hours of CPU (typically no more than an overnight computing period). For example, we can map de free (non-biased) ligand diffusion and binding, such as the one performed with extensive molecular dynamics techniques, at a fraction of the computational cost. Moreover, when combining PELE with markov state models (MSM), we recently obtained absolute binding free energies at an affordable manner (*Journal of Chemical Theory and Computation* (2013) **10**:282-288)

Several applications and benchmark studies have been performed, including a recent induced fit external benchmark by AstraZeneca (*Journal of Chemical Information and Modeling* (2016) **56**: 774-787). In addition, in the last Community Structure-Activity Resource (CSAR) blind competition, PELE was described as “an impressive accomplishment”, with top performance in all targets.

PELE has been developed mostly witn an Advanced-ERC grant and is accessible (at no charge) at pele.bsc.es

Objectives

Main current ongoing development projects in PELE include:

1. Improving backbone dynamics through internal coordinates perturbations
2. Faster and more reliable sampling protocols (for induced fit and global sampling)
3. New scoring functions and free energy calculations for ligand binding (using MSM, FEP, etc)
4. Application studies with industrial partners (for example with AstraZeneca)

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