

## Integrating multiscale modeling and simulations with scalable high performance computation

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Despite significant advances in high performance computing resources, the complexity of simulating protein dynamics limits the problems that can be investigated *in silico*. The crux of the problem lies in rapid exploration of protein conformational ensemble. The iFold server (<http://ifold.dokhlab.org>) presents an efficient alternative approach: coupling the fast discrete molecular dynamics (DMD) conformational sampling algorithm with multiscale modeling. DMD is among of the fastest techniques for conformational sampling; accessing biologically relevant length and time scales by utilizing a multiscale protein modeling approach – using simplified models for probing conformational dynamics, followed by high-resolution reconstruction of trajectories for detailed analyses. The iFold server provides a premier web-based resource for high-throughput analyses of protein dynamics using DMD, utilizing local Linux cluster computing resources. This approach is highly scalable and global cyber-infrastructure resources can be added for supporting massive simulation requirements. Customizable complex simulation modes such as protein folding, unfolding, thermodynamic scan,  $P_{Fold}$  scan and simulated annealing are possible using iFold. In summary, amalgamating multiscale modeling and simulation tools at the iFold server with high performance computing resources has allowed probing protein dynamics at unprecedented scales.

### References:

1. **S. Sharma**, F. Ding, and N. V. Dokholyan, "Multiscale modeling of nucleosome dynamics." *Biophysical Journal*, 92: 1457-1470 (2007).
2. **S. Sharma**, F. Ding, H. Nie, D. Watson, A. Unnithan, J. Lopp, D. Pozefsky, N. V. Dokholyan, "iFold: A platform for interactive folding simulations of proteins." *Bioinformatics*, 22: 2693-2694 (2006).
3. N. V. Dokholyan, F. Ding, **S. Sharma**, "Multiscale molecular modeling." *Proceedings of the German Conference on Bioinformatics, submitted* (2007).
4. F. Ding, N. V. Dokholyan, "Simple but predictive protein models." *Trends in Biotechnology*, 23(9):450-5 (2005).