# Combining human intervention and empirical data using interactive elastic network models

The main goal of the Interactive Molecular Simulation (IMS)[1] approach is to observe the conformational dynamics of a running molecular simulation. The instant visual feedback provides insightful monitoring as well as observation of structural changes imposed through the user's IMS manipulation.

The particular approach presented here is based on elastic Spring Network Models (ENM) as implemented in the BioSpring [1][2] simulation engine. It aims to simulate the overall flexibility of large biomolecular assemblies potentially echoing long timescale changes that would not easily be captured by molecular dynamics.

The UnityMol [3] visualization software has been augmented with a user interface to perform IMS experiments and test new interactive features with BioSpring, including the use of various types of empirical constraints. The research aims to build a protocol implementing structural and parametric data processing features to design adapted systems upstream and during IMS with a recorded monitoring of user inputs to warrant reproducibility. This framework will feature steering by predefined constraints (inspired by the Ambiguous Interaction Restraints (AIRs) method from the HADDOCK [4] docking program) for interactive docking experiments. These ambiguous force restraints guide the interaction while leaving the user free to explore different alternatives (metastable states).

A main objective of my thesis is to transpose the use of AIRs into an interactive approach. Another overall aim is to demonstrate that the combination of direct human intervention with ENM-based IMS guidance by empirical constraints is more time-efficient than traditional methods, while maintaining high docking pose quality.

[1] Tek, A., Chavent, M., Baaden, M., Delalande, O., Bourdot, P., Katz, B. F., & Ferey, N. (2012). Advances in human-protein interaction-interactive and immersive molecular simulations. In Protein-Protein Interactions-Computational and Experimental Tools. IntechOpen.
[2] Ferey, N., Delalande, O., & Baaden, M. (2012). Biospring: an interactive and multi-resolution software for flexible docking and for mechanical exploration of large biomolecular assemblies. JOBIM 2012-Journées Ouvertes en Biologie, Informatique et Mathématiques, 433-434.
[3] Z. Lv, A. Tek, F. Da Silva, C. Empereur-mot, M. Chavent and M. Baaden: Game on, Science - how video game technology may help biologists tackle visualization challenges PLoS ONE 8(3):e57990.
[4] Dominguez C, Boelens R, Bonvin AM. HADDOCK: a protein-protein docking approach based on biochemical or biophysical information. J Am Chem Soc. 2003 Feb 19;125(7):1731-7. doi: 10.1021/ja026939x. PMID: 12580598.