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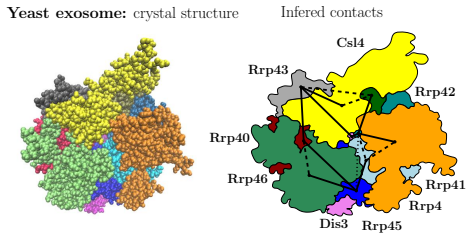


Master internship proposal

## Combinatorial optimization techniques leverage the reconstruction of atomic resolution models of large protein assemblies

**Context.** An antibody-antigen complex or an enzyme-inhibitor complex are example protein complexes involved in key biological functions, respectively the immune response and catalysis. The central problem in structural biology is to understand how the function of these molecular machines emerge from their structure and dynamics. These studies are especially challenging since they require structural data, which are pretty scarce: as of today, the protein data bank contains circa 100,000 structures, while millions of coding sequences are known. Even worse, few of these structures concern protein complexes–the vast majority concern isolated molecules.

**Goals.** The goal of this Master internship is to develop novel methods to design atomic resolution models of molecular assemblies involving from 3 to 10 subunits. In such cases, two complementary sources of information are usually available [ADV+07]: on the one hand, high resolution (i.e. atomic resolution) crystal structures of the isolated subunits; on the other hand, low resolution data for the whole assembly, typically coming from electron microscopy or mass spectrometry [ACCC15]. A natural strategy therefore consists of combining these sources of information [ACW15], to hopefully reach atomic resolution for the whole assembly. Doing so involves two mains steps, namely computing conformations of subunits compatible with low resolution data [CDM+15, RDRC16], and assembling these conformations to build the assembly [ACW15]. Both steps can be phrased as optimization and enumeration problems involving graphs, namely problems in the realm of graphical problems, and so graph algorithms techniques will be developed.

This internship will focus on the second step. The goal will be to analyze the existing methods and to introduce/develop some new original graph algorithm techniques.

**Background.** Theoretical computer science and/or bioinformatics/biophysics and/or applied mathematics.

**Misc.** Ideally, the MSc will be followed-up by a PhD thesis.

# References

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[ADV+07] F. Alber, S. Dokudovskaya, L. M. Veenhoff, W. Zhang, J. Kipper, D. Devos, A. Suprapto, O. Karni-Schmidt, R. Williams, B.T. Chait, M.P. Rout, and A. Sali. Determining the Architectures of Macromolecular Assemblies. *Nature*, 450(7170):683–694, Nov 2007.

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[RDRC16] A. Roth, T. Dreyfus, C.H. Robert, and F. Cazals. Hybridizing rapidly growing random trees and basin hopping yields an improved exploration of energy landscapes. *J. Comp. Chem.*, 37(8):739–752, 2016.