Master « In Silico Drug Design »
2ème année

PROPOSITION DE STAGE
Année Universitaire 2016/2017
A envoyer à Mme Pr Camproux
anne-claude.camproux@univ-paris-diderot.fr

Nom du Responsable du Laboratoire ou de l'Entreprise: Professor John Pyle

Affiliation administrative : Department of Chemistry, University of Cambridge

Adresse précise du Laboratoire : Lensfield Road, Cambridge CB2 1EW, United Kingdom

Nom du Responsable de l'équipe d'accueil (EA) : Rachel MacDonald
E-mail : rmm73@cam.ac.uk

Responsable du stage : Professor David J. Wales

email: dw34@cam.ac.uk
Telephone: +44 (0)1223 336354
FAX: +44 (0)1223 336362
WWW: http://www-wales.ch.cam.ac.uk

Spécialité du stage : Recherche ☐

Indiquez par quelques mots clés, l'orientation scientifique du sujet :

Complex peptide/ARN, tat/TAR HIV-1, docking, « factorised superposition approach », échantillonnage de minima, « basin-hopping method », « disconnectivity graph », « parallel tempering », fonction de partition, thermodynamique

---

Titre du stage :

Studies of binding for a peptide to RNA.

Ce sujet constitue-t-il un premier pas vers un travail de thèse : Ne sait pas

---

Description du sujet (quelques lignes):

The project would involve studies of binding for a peptide to RNA.

HIV-1 tat protein binds specifically to HIV-1 TAR RNA. The purified protein forms a one-to-one complex with HIV-1 TAR RNA.
Tat binding in vitro is dependent upon the presence of 3 non-base paired U residues which produce a 'bulge' in the TAR RNA stem-loop structure.
Deletion of the uridine residues in the bulge or substitution with guanine residues produced RNAs with a 6 to 8-fold lower affinity than wild-type TAR.
Mutations that alter the sequence of the 6 nucleotide-long loop at the tip of TAR RNA structure, and mutations which alter the sequence of the stem whilst preserving Watson-Crick base pairing, do not affect tat binding significantly. There is a direct correlation between the ability of Tat to bind to TAR RNA and to activate HIV transcription. Viral LTRs encoding TAR sequences known to bind tat weakly, are not stimulated efficiently by tat in vivo.
We would investigate binding using a variety of computational tools, ranging from simple scoring functions to fully atomistic approaches.
A key aim is to use the factorised superposition approach to see how the binding energy converges, and check the free energy differences predicted between mutants against experimental values.
