Study of the progression of peptides in the nascent peptide tunnel of the ribosome.

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One of the restrictions encountered in performing *in-silico* modelling of molecules is the size of the system to be studied. In the laboratory we have developed efficient short-cut procedures for large systems such as the insertion of proteins in membranes.
In this study, we are interested in another large biological system, the ribosome tunnel. Indeed, understanding the progression of nascent peptides along the length of the tunnel is crucial to understanding the role of ribosome in the early steps of protein folding. The nascent polypeptide tunnel is a 100 Angstrom long tunnel bordered by more than 10 000 atoms of nucleic acids and proteins (the whole ribosome counts more than 200 000 atoms). As shown by Nissen *et al.*[1], the tunnel is not a straight tunnel but has two bends which we suggest may play a role in selecting the early fold of the nascent polypeptide.
In order to understand the progression of a nascent peptide in the tunnel of the ribosome, we analyzed the tunnel wall properties and forced the passage of isolated amino acids and short peptides through this tunnel. During this simulation, we followed the energy profile of interactions between the amino acid and the tunnel surface. All along the tunnel, we calculated the van der Waals and electrostatic change of interaction energy and analyzed the hydrophobicity potential. This revealed a hydrophobic attraction for all amino acids. In this hydrophobic profile, we can classify the amino acids in two families (the amino acids are classified by decreasing hydrophobic energy of interaction): Asn, Arg, Ser, Gly, Gln, Asp, His, Thr, Glu, Lys, Ala, Cys and Tyr, Val, Met, Trp, Ile, Leu, Pro, Phe. The electrostatic profile reveals a weak repulsion for the negatively charged amino acids and a weak attraction for the positively charged amino acids because of the presence of many phosphate groups inside the tunnel.[1].
In a future study we will simulate the progression of signal peptides in the tunnel of the ribosome because, as demonstrated by Agmon *et al.*[2] and Berisio *et al.*[3], these peptides interact inside the tunnel with the L22 protein to block the protein synthesis by inducing the transconformation of the L22 protein.
Besides its specific biological interest, a work such as this leads us to develop new *in-silico* procedures that should open the way to the simulation of ion, drug and peptide transport across membrane transporters, a largely unexplored domain.

[1] Nissen P., Hansen J., Ban N., Moore P. B. & Steitz T. A. (2000) *Science* vol. 289 pp. 920-930
[2] Agmon I., Auerbach T., Baram D., Bartels H., Bashan A., Berisio R., Fucini P., Hansen H.A., Harms J., Kessler M., Peretz M., Schluenzen F., Yonath A. & Zarivach R. (2003) *Eur. J. Biochem.* Vol.270 pp.2543-2556
[3] Berisio R., Schluenzen F., Harms J., Bashan A., Auerbach T., Baram D. & Yonath A. (2003) *Nat. Struct. Biol.* Vol. 10(5) pp.366-370