IMPRS on Multiscale Biosystems

Project description

Title: GPI-anchored proteins: a mysterious encounter of three disparate types of biomolecules witnessed by molecular dynamics simulations.
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In collaboration with: Prof. J. Heberle (FU)

Project description: Many proteins are attached to the outer leaflet of eukaryotic cell membranes by so-called Glycosylphosphatidylinositol(GPI)-anchors. These are relatively complex glycolipids that are post-translational modifications of proteins and can occur, apart from an invariant core structure (see Figure 1(b)), in many different variants. GPIs have been attributed a variety of biological roles [1], yet without a clear molecular scale picture of how they function. They are thought, e.g., to enhance protein mobility and thus to be relevant for sorting and trafficking of proteins on cell membranes (Figure 1(c)), but also their contributing to signal transduction has been suggested.

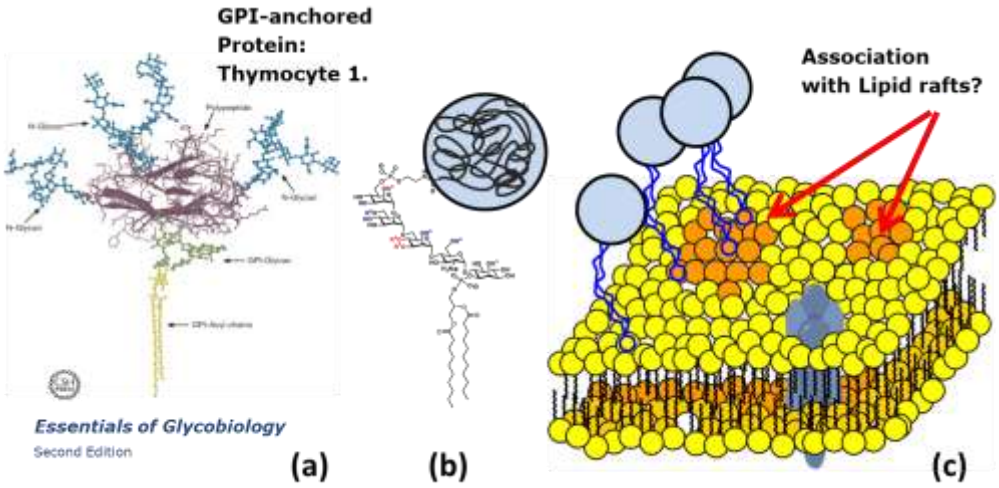

Figure 1: (a) Example of a GPI anchored protein (Thymocyte 1) with lipid (yellow), GPI backbone (green) and polypeptide part (purple). Blue: N-linked protein glycosylations. (b) reduced view highlighting the composition of the conserved carbohydrate backbone connecting to the lipid tail the protein part is kept schematic. (c) In membranes, GPIs are often thought to facilitate lateral diffusion as compared to membrane embedding (grey), for quick association of the anchored proteins with, e.g., lipid rafts (backbone part kept in blue).

Experimental insight into the behavior of the close proximity of protein, carbohydrate and lipids is rather limited. The goal of the project is therefore to create and investigate several atomistic computational models of GPI-anchored proteins in order to shed more light on how GPI anchoring influences the nearby composition of the membrane, the spatial degrees of freedom of the protein, its mobility and structure. The student can make use of an existing numeric library of saturated and unsaturated phospholipids, phospho-inositols, cholesterol, ions and GPI anchors in order to study a broad variety of scenarios. The example of Thymocyte 1, for instance (see Figure 1(a)), may serve as a case study where the properties of the bare protein, its glycosylated and GPI-anchored forms can be compared systematically.

Required background: The prospective student should have a good background in biochemistry and physical chemistry. Interest in numerical/theoretical methods is advantageous.

Paper to read before the interview:

1. Paulick, M. G.; and Bertozzi, C. R. The Glycosylphosphatidylinositol Anchor: A Complex Membrane –Anchoring Structure for Proteins. 2008. *Biochemistry* **47**:6991—7000.

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