In silico evaluation of the influence of the translocon on partitioning of membrane segments

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Résumé en anglais	Background The locations of the TM segments inside the membrane proteins are the consequence of a cascade of several events: the localizing of the nascent chain to the membrane, its insertion through the translocon, and the conformation adopted to reach its stable state inside the lipid bilayer. Even though the hydrophobic h-region of signal peptides and a typical TM segment are both composed of mostly hydrophobic side chains, the translocon has the ability to determine whether a given segment is to be inserted into the membrane. Our goal is to acquire robust biological insights into the influence of the translocon on membrane insertion of helices, obtained from the in silico discrimination between signal peptides and transmembrane segments of bitopic proteins. Therefore, by exploiting this subtle difference, we produce an optimized scale that evaluates the tendency of each amino acid to form sequences destined for membrane insertion by the translocon. Results The learning phase of our approach is conducted on carefully chosen data and easily converges on an optimal solution called the PMIscale (Potential Membrane Insertion scale). Our study leads to two striking results. Firstly, with a very simple sliding-window prediction method, PMIscale enables an efficient discrimination between signal peptides and signal anchors. Secondly, PMIscale is also able to identify TM segments and to localize them within protein sequences. Conclusions Despite its simplicity, the localization method based on PMIscale nearly attains the highest level of TM topography prediction accuracy as the current state-of-the-art prediction methods. These observations confirm the prominent role of the translocon in the localization of TM segments and suggest several biological hypotheses about the physical properties of the translocon.

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