back-scattered from interstellar hydrogen atoms, Lallement et al. (1) have detected a small (about 4%) difference between the flow directions of neutral hydrogen and helium in the region where the interstellar medium and the heliosphere interact. Well away from the heliosphere, the helium and hydrogen in the interstellar medium should move in the same direction at the same speed. But nearer to the heliosphere, the two gases are expected to behave differently. Helium is not affected much by the interaction with the outer parts of the heliosphere, whereas hydrogen is slowed and can also be deflected sideways by any lateral asymmetry in the shape of the heliosphere, such as that produced by the interstellar magnetic field.

Lallement et al. point out that the most plausible cause of the observed deflection is a lateral asymmetry caused by the interstellar magnetic field. The physical picture is complex, but based on their observations and results from numerical simulations, the authors present a convincing picture. They determine the angular direction (but not the sense) of the projection of the magnetic field on the sky. The fact that the magnetic field is sufficiently strong to change the shape of the heliosphere also places constraints on its magnitude, although the authors do not discuss this point.

Radio emissions observed by the Voyagers over the past 12 years have recently been interpreted as constraining the direction of the local magnetic field (I). This approach yields a different direction from that found in (1), but it is less direct.

The observations reported by Lallement et al. (1) substantially improve our understanding of both the nature of the interaction of the Sun with its local interstellar environment and the structure of the local interstellar medium. Future in situ measurements of the magnetic field, perhaps from Voyager 1, may allow its magnitude and the full three-dimensional vector to be determined.

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also nicely illustrates how an apparently complex cellular process can be reduced to the simple rules of chemical thermodynamics.

The hydrophobic core of a cell membrane is sandwiched between the polar head group layers of its constituent phospholipids (see the figure). Given this structural complexity, one might expect that the energetic contribution of an amino acid would depend on its position along the test segment—and it does, at least for some amino acids. A larger energetic penalty is incurred when polar and charged amino acids are placed near the center of the membrane. This makes perfect sense, because close to the polar head group layers electrostatic forces help to stabilize the positive charge of arginine or lysine side chains. And if there is a gradient of water molecules tending to penetrate the membrane surface, then polar side chains closer to the edge will gain an energetic advantage through partial hydration by even one or two water molecules. Tryptophan and tyrosine are especially interesting because they are energetically unfavorable at the membrane center, but energetically favorable near the head group layers. In other words, there are energy wells near the edge of the membrane for these particular amino acids. This finding offers a simple explanation for why tryptophan and tyrosine are usually found near the membrane-water interface of membrane proteins (4). In their energy wells, these amino acids confer stability to a protein’s transmembrane helix.

Let’s return to the question of how the translocon knows what to do with the polypeptide segment that sits inside of it. The authors offer a simple explanation based on the apparent equilibrium behavior of the system. If the translocon allows the peptide segment to sample the lipid environment while it is being transported across the membrane, then the peptide is presented with a choice: It can either dissociate from the translocon and insert itself into the membrane or it can remain adherent to the translocon and continue across the membrane. The final outcome is dictated by the amino acid composition and sequence of the peptide. The basic idea—that the peptide segment samples its environment and is essentially at equilibrium with the membrane and the translocon channel—is elegant in its simplicity. The idea also seems compatible with the crystal structure of a prokaryotic homolog of the endoplasmic reticulum translocon, which is closed, but is proposed to open from the side into the membrane (5).

What do these results tell us about transmembrane helix stability and membrane protein structures? They suggest that far more powerful membrane helix prediction algorithms can be developed, because the biological hydrophobicity scale, together with position-dependent energy terms for each amino acid, provides a rich data set with which to analyze protein sequences. Such predictions might seem to be of limited use because most helical membrane proteins simply contain the most hydrophobic amino acids (isoleucine, leucine, phenylalanine, and valine) in the center of their transmembrane segments (6). What is most impressive is that the authors decompose S4 into individual amino acid energy terms and demonstrate that the probability of insertion is essentially predictable. The key to prediction is to understand energetic counterbalance (hydrophobic amino acids work against polar amino acids through additivity of energy terms) as well as positional dependence (the energy penalty for arginine peaks sharply near the center of a transmembrane helix).

Analysis of the protein structure database has led us to expect that helical membrane proteins should always have maximally stable transmembrane helices. The new studies (1, 2) show that this does not have to be the case. If specific functions are required, less stable transmembrane helices are possible. It is intriguing to ponder what nature might have in store for us in our quest to understand the structures and mechanisms of membrane proteins. Oddities like voltage-dependent ion channels might be just the tip of the iceberg.

Two important aspects of transmembrane-helix stability. (Left) Hydrophobic amino acids of membrane proteins are favored inside the lipid membrane interior, whereas hydrophilic amino acids are favored in the aqueous exterior. Whether a transmembrane α helix is stable inside the membrane depends on a net energy balance. Hydrophilic and even charged amino acids become inserted into the membrane if they are forced to do so by a sufficient number of hydrophobic amino acids. This idea of energetic counterbalance is illustrated by a tug-of-war between hydrophobic amino acids (phenylalanine, leucine, and isoleucine) and a hydrophilic amino acid (arginine). (Right) The energy cost for transferring a positively charged amino acid such as arginine from water to the membrane depends on its depth in the membrane. The “energy hill” is sharply peaked and is mostly concentrated within a distance of ~8 Å on either side of the middle of a 30 Å–wide hydrophobic core.

References