Towards Co-evolution of Membrane Transport and Metabolism

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Protocellular boundaries were inextricably connected to the metabolism they encapsulated: to be inheritable, early metabolism must have led to an increased rate of growth and division of vesicles and, similarly, transport through vesicle boundaries must have supported the evolution of metabolism. Even though explaining how this coupling emerged and evolved in the absence of the complex machinery of modern cells is one of the key issues in studies on the origin of life, little is known about the biochemical and biophysical processes that might have been involved. This gap in our knowledge is a major impediment in efforts to construct scenarios for the origin of life and laboratory models of protocells. A combination of experimental and computational studies carried out by us and our collaborators is aimed at helping to close this gap.

Properties of membranes might have contributed to the selection of RNA as an early biopolymer. A kinetic mechanism was proposed (Sacerdote & Szostak, 2005) in which ribose was supplied more quickly than other aldopentoses to primordial cells for preferential incorporation of ribonucleotides into nucleic acids. This proposal is based on a finding that ribose permeates membranes an order of magnitude faster than its diastereomers, arabinose and xylose. Our computer simulations, which yield permeation rates in excellent agreement with experiment, and kinetic modeling explain this phenomenon in terms of inter- and intramolecular interactions involving exocyclic hydroxyl groups attached to carbon atoms of the pyranose ring (Wei and Pohorille, 2009). They also constrain scenarios for the formation of the earliest nucleic acids (Wei and Pohorille, 2013). In one scenario, sugars permeate protocellular walls and subsequently are used to synthesize nucleic acids inside protocells. As long as this process proceeds at the rate faster than 6×10^{-3}/s, ribose derivatives will be available for synthesis easier than their diastereomers. If nucleosides or their activated derivatives are synthesized outside protocells and subsequently transported across protocellular membranes the kinetic mechanism does not apply because all diastereomers, which have their sugars in the furanose rather than pyranose form, permeate the membrane at approximately the same rate.

Properties of membranes might have been also coupled to metabolism involving peptides. Recently, Adamala and Szostak (2013) have shown that a dipeptide inside fatty-acid vesicles catalyzes the formation of another dipeptide that binds to vesicle walls and, by doing so, promotes their growth at the expense of other vesicles. This coupling of metabolism, permeability of vesicles and their growth is the first demonstration of evolutionary advantage imparted by small, membrane-bound peptides. Building on this work we have calculated the rate at which different blocked amino acids are delivered to a protocell for synthesis of dipeptides. We have further shown that the dipeptides are located at the water-membrane interface rather than in the center of the bilayer. On these basis it is anticipated that other dipeptides containing aromatic, but not necessarily hydrophobic amino acids (e.g. tyrosine) could have the same catalytic effects. Insight from these studies allows for estimating the rate of vesicle growth and the rates of dipeptide synthesis required to keep the system in balance. These results, in combination with our earlier studies, lead to a general scenario for evolution from membrane-bound dipeptides to ion channels in the origin of life.

References

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