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ORIGIN OF LIFE

The Power of Crowding for the Origins of Life

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Abstract Molecular crowding increases the likelihood that life as we know it would emerge. In confined spaces, diffusion distances are shorter, and chemical reactions produce fewer and more regular products. Crowding will occur in the spaces between Muscovite mica sheets, which has many advantages as a site for life's origins.

Keywords Muscovite mica · Molecular crowding · Origin of life · Mechanochemistry · Abiogenesis · Chemical confinement effects · Chirality · Protocells

Cells are crowded. Protein molecules in cells are typically so close to each other that there is room for only one protein molecule between them (Phillips, Kondev et al. 2008). This is nothing like a dilute 'prebiotic soup.' Therefore, by analogy with living cells, the origins of life were probably also crowded.

Molecular Confinement Effects Many chemical reactions are limited by the time needed for reactants to diffuse to each other. Shorter distances speed up these reactions. Molecular complementarity is another principle of life in which pairs or groups of molecules form specific interactions (Root-Bernstein 2012). Current examples are: enzymes & substrates & cofactors; nucleic acid base pairs; antigens & antibodies; nucleic acid - protein interactions. Molecular complementarity is likely to have been involved at life's origins and also benefits from crowding. Mineral surfaces are a likely place for life's origins and for formation of polymeric molecules (Orgel 1998). Here, too, there will be more reactivity if the solution above the molecular surface has a higher concentration of monomers.

Chemistry in confined spaces gives fewer different reaction products. Life has very few of the possible amino acids, sugars, and other small organic molecules. Chemical confinement is one explanation for this. For example, chemical confinement might reduce the number of products from the Formose reaction. The Formose, or Butlerov, reaction (Lambert, Gurusamy-Thangavelu et al. 2010) is a possible prebiotic reaction for synthesis of sugars, such as ribose for RNA; but the Formose reaction produces too many different types of sugars, and unnatural branched sugar polymers, resulting ultimately in a tarry mess. Confinement, especially on a

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crystalline mineral surface, might limit the number of different sugars formed, reduce the amount of branching in sugar polymers, and prevent the formation of complex tarry products.

Proteins in confined spaces are stabilized against denaturation (Zhou and Dill 2001). Confinement by pressure induces polymerization of actin and glycine (Cipolla, Gokina et al. 2002; Ohara, Kakegawa et al. 2007). Actin was not present at the origins of life, but polymerization of glycine and other small molecules is one of the challenges to be overcome in order for life to emerge. Confinement can increase yields in chemical syntheses. This was demonstrated for an imine synthesis in which smaller compartments gave higher product yields than larger compartments; compartment radii were 8 to 34 microns (Fallah-Araghi et al. 2014).

Chirality is another problem for life's origins. In life as we know it, amino acids are L, or left-handed, and sugars are D (right-handed). Normal chemical syntheses are achiral, producing equal quantities of D- and L-reaction products. How did life select sugars and amino acids of only one handedness out of these chiral mixtures? Crowding might favor the assembly of chiral polymers, because monomers of one handedness would pack closer, thus facilitating the synthesis of chiral polymers. Toy models are shown for preferential chiral packing to form dimers (Fig. 1a) and polymers (Fig. 1b).

Life's origin is one of the big unsolved problems in science. Crowding is a logical explanation for part of the problem of life's origins.

Where Might Crowding Occur at the Origins of Life?

Mineral surfaces are good for 2-dimensional crowding. The spaces between mineral surfaces are even better, providing parallel crystalline surfaces both above and below the prebiotic molecules. This might be an ideal place for solid phase synthesis, and a type of enclosure before the origins of cells (Fig. 2) (Hansma 2010, 2013). The layered mineral in Fig. 2 is mica, composed of nm-thick sheets. These mica sheets can be separated by as little as one water layer (Pashley and Israelachvili 1984) or expanded to a distance where pairs of sheets separate completely, turning one mica piece, or 'book,' into two. Often the mica becomes matted, with expanded spaces between many sheets.

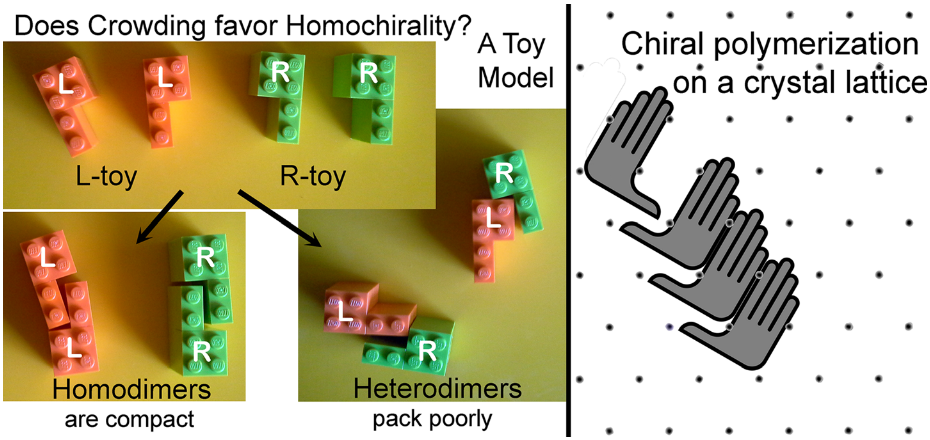

Fig. 1 Diagrams of homochirality induced by molecular crowding on surfaces. Left: Homodimers are more compact than heterodimers. Right: Homopolymer formation on a crystalline surface

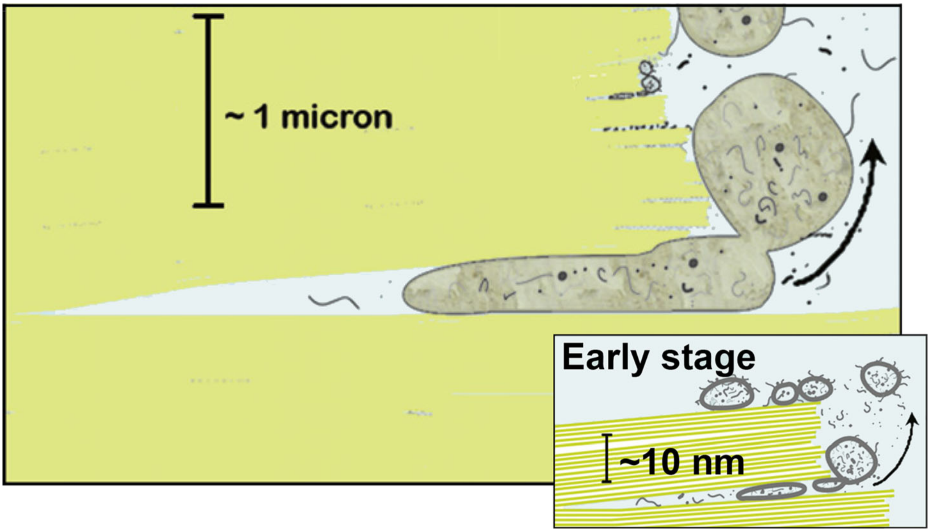

Fig. 2 Diagram of the origins of life between mica sheets. Variable spacing between mica sheets gives compartments to isolate and protect molecules, molecular assemblies, and protocells. Inset shows earliest stage of life's origins, with molecules, and small lipid vesicles filled with aqueous solution, instead of the 'proto-cytoplasm' in the protocells at a later stage. Moving mica sheets are shown to facilitate an early form of cell division, by pressing on protocells and vesicles, causing 'daughters' to bleb off. See (Hansma 2010, 2013)

Micas are old enough to have been the site for life's origins (Hazen, Papineau et al. 2008). Muscovite mica is perhaps the best choice for the origins of life on earth, because its mineral sheets are held together electrostatically with potassium ions, K+. All living cells have high intracellular K+ concentrations, and there have been few attempts to identify a source of high K+ at life's origins. Another idea is that the high K+ arose from origins of life at geothermal hot springs (Mulkidjanian, Bychkov et al. 2012).

Because mica sheets are cation exchangers (Gaines 1957), they also bind cations such as magnesium, Mg++, that interact with anionic polymers such as RNA and DNA in all living cells.

Mica is also present on Mars, which is a possible site for the origins of life on earth (Weiss, Kirschvink et al. 2000). Thus far, biotite is the only mica known to be on Mars (Bridges and Warren 2006). Its mineral sheets are held together primarily by iron ions, so life in biotite on Mars would not explain the high intracellular K+ in life on earth.

Mechanical Energy from Moving Mica Sheets Another advantage of mica for the origins of life is that work is done by mica sheets moving, open and shut, in response to fluid flows or temperature changes (Hansma 2009, 2010). This work is mechanical energy. At the sub-nanometer scale, mechanical energy can be used for chemistry - mechanochemistry - such as the formation (or rupture) of covalent bonds. Mechanochemical syntheses are the ultimate in crowding (Fig. 3). When atoms are forced into the attractive, or Van der Waals, regime of the energy profile, bonds will form.

On the nanometer scale, mechanical energy will rearrange polymers, creating different supramolecular structures. On the micron scale, mechanical energy will cause compression and expansion of protocells, such that they will bud off or rupture.

Much recent progress has been made in organic mechanochemical syntheses, driven in part by a need to reduce the use of chemical solvents. Mechanochemical syntheses include the

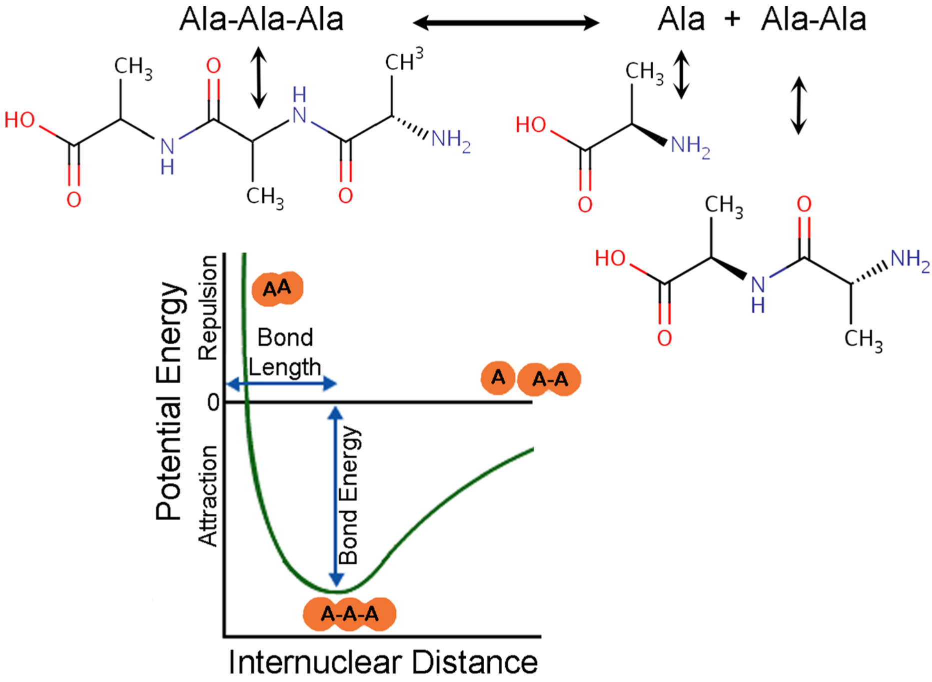

Fig. 3 Diagram of the idea that mechanical energy from moving mica sheets can form covalent bonds, such as the bonds between alanine residues in polyalanine. Orange circles indicate the relative distances between bonding nuclei in non-bonded (right), bonded (middle) and squeezed bonds (left). Mechanochemistry such as this is an extreme form of crowding that may have contributed to the origins of life

synthesis of peptides, nucleosides, optically active products, oxidations, reductions, condensations, nucleophilic reactions, and cascade reactions (Wang 2013). Other advantages of mechanochemistry are that: (1) yields can be higher; (2) nucleosides' and nucleobases' poor solvent solubilities are not a problem; (3) milder alkaline conditions can be used. Di- and tripeptides were synthesized with only sodium bicarbonate as the alkali (James, Adams et al. 2012). In addition to bulk mechanochemical syntheses, scanning probe microscopy (SPM) has been used to investigate single molecule mechanochemistry (Moriarty 2013). The single-molecule experiments by SPM have succeeded primarily in unfolding polymers and breaking bonds, e.g., (Oroudjev, Soares et al. 2002); mechanochemical syntheses are more challenging. Less than a decade ago, however, the entire field of mechanochemistry was limited primarily to the breaking of bonds (Beyer and Clausen-Schaumann 2005).

In summary, there are good reasons to believe that molecular crowding was essential for life's origins. This crowding could have occurred between Muscovite mica sheets, which resemble current life in many ways (Hansma 2010, 2013).

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