



Possible origin of life between mica sheets: does life imitate mica?

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The mica hypothesis for the origin of life proposes that life originated between the sheets of muscovite mica. This paper elaborates on two ways that life resembles what might have originated between mica sheets. First, enzymes: The configurations and dynamics of enzymes, with their substrates, cofactors, and sometimes transition metal ions, often resemble mica sheets, with their open-and-shut motions, acting on small molecules between them, sometimes assisted by transition metal ions. Second, organisms: Mica world had the potential to be a community or ecosystem of prebiotic organisms in a way unlike other models for the origin of life.

Keywords: muscovite; mechanochemistry; enzymes; protocells

1. Introduction

What are some of the characteristics of life that might give clues to the world in which life originated? Life is modular, composed of cells, organelles, and subcellular assemblies of macromolecules. Macromolecules and their assemblies typically have nanoscale motions that are involved in carrying out their functions. Life is communal, living in communities such as biofilms and other ecosystems. Charge transfer in living systems occurs primarily as flows of inorganic cations, mainly Na^+ , K^+ , and Ca^{++} , through membrane channels. Charge transfer also occurs as single electron movements in redox reactions and in electron tunneling or electron hopping, and as proton movements. Cells have high intracellular K^+ , ~ 100 mM, and a well-regulated water content. Cells' biopolymers are typically anionic. Lipid bilayers enclose cells and organelles. Entropy is low. Many cells are surrounded by rigid walls.

A mica world (Figure 1) provides many of the characteristics seen in life today. Such a world is hypothesized and described in Hansma (2010). Mica's nanometer-thick sheets are analogous to cell walls. Lipid bilayers form on the hydrophilic surfaces of mica sheets. Entropy is greatly reduced in the spaces between mica sheets, as diagrammed in Figure 5 in Hansma, (2010). The surfaces of mica sheets are anionic. Cations in the surrounding fluids exchange with these anionic surfaces. The close spacing of mica sheets provides compartment-

alization and the possibility of community for emerging life. The water content of mica is well controlled compared with the water content of clay minerals that shrink and swell when dry and wet. A *muscovite* mica world provides an environment high in K^+ . Muscovite mica's anionic sheets are bridged by K^+ , which hold the anionic mica sheets together, with one K^+ per 0.5 nm on the hexagonal lattices of pairs of mica sheets (Pauling, 1930). The origin of this K^+ has not been explained by other hypotheses about the origin of life.

Charge transfer in living systems is not particularly well described by a mica world. However, mica does provide an environment in which inorganic cations such as K^+ , Na^+ , Mg^{++} , Ca^{++} , and H^+ , are present, mobile, and exchangeable. These cations are present either between the mica sheets or in seawater, which is proposed, here and by others, to be the fluid where life originated. Redox reactions have been described in biotite mica (Burkhard, Ulmer, Redhammer, & Myer, 1999), which has more iron than muscovite mica. There are few reports of electron tunneling in mica or clay.

Many of the characteristics of mica are shared by clays, which have long been proposed as an environment in which life might have originated (Bernal, 1951). This is discussed also in Hansma, (2010). A mica world is consistent with many other origins hypotheses, including the RNA, lipid, and metabolic worlds. A mica world has the potential to unify origins hypotheses, because different

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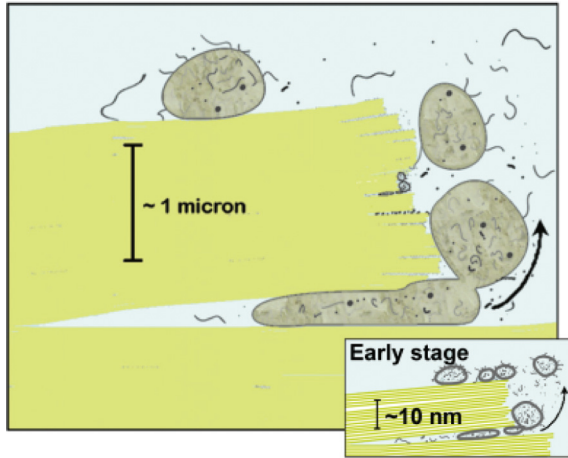


Figure 1. A mica world: diagrams of the possible origin of life between mica sheets. Protocells, the large gray structures, have a proto-cytoplasm that is distinct from the aqueous environment. Inset: at an early stage in the mica world, macromolecules and lipid vesicles are seen. The vesicles are filled with water and a few macromolecules. Note the scale change between early and later stages. Mica sheets are green. Green lines in the inset are individual mica sheets; white spaces between the green lines contain K^+ bridging adjacent mica sheets. Blue is the aqueous environment. Adapted from Hansma (2010).

molecular components and systems could simultaneously evolve in the spaces between mica sheets.

Mica also provides a new energy source for the origin of life – mechanical energy – to power the making and breaking of covalent bonds, the rearrangements of polymers (Figure 2), and the blebbing off of vesicles and protocells (Figure 1) in the earliest form of cell division.

1.1. Enzymes and organisms in a mica world

Enzymes and organisms in a mica world are proposed in this paper. A mica world could have been filled with

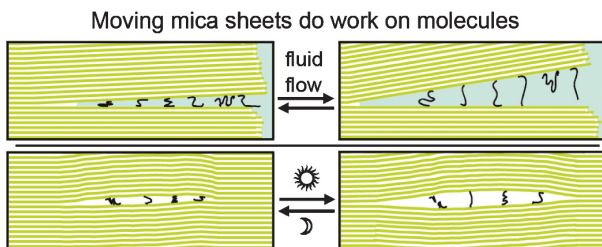


Figure 2. Mechanical energy from moving mica sheets may have provided an energy source for the origin of life. With mechanical energy doing work on molecules, no energy transduction is needed. Top panel: Mica sheets move open and shut in response to water movements, stretching and compressing polymer strands attached to them. Lower panel: Bubble between mica sheets functions as a heat pump in which hot and cold cycles cause the bubble to expand and contract, exerting forces on polymer molecules within the bubble. Adapted from Hansma (2010).

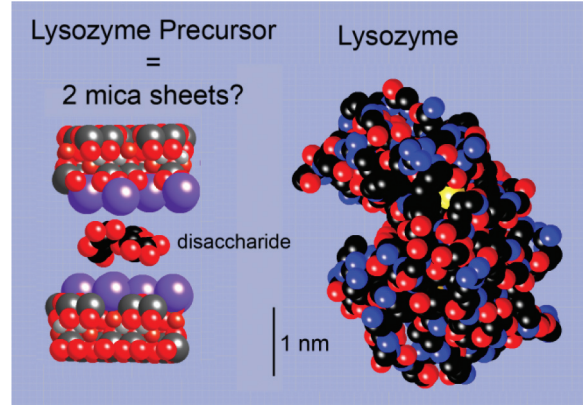


Figure 3. Mica sheets with a disaccharide (left) and a molecule of the enzyme, lysozyme (right). Enzyme motion may have originated from the motions of mica sheets. These models show the size of lysozyme’s cleft in relationship to the disaccharide mannose between muscovite mica sheets. The enzyme lysozyme cleaves polysaccharides. The disaccharide, mannose, is a dimer of glucose. Potassium ions are divided equally between the mica sheets. Atoms are colored as follows: Yellow = Sulfur, S; Purple-blue = Potassium ions, K^+ ; Black = Carbon, C; Reds = Oxygen, O, and Hydroxyl, OH; Grays = Silicon, Si, and Aluminum, Al; and Light blue = Aqueous environment. Models were prepared with CrystalMaker Software 2.3.6, using CPK van der Waals radii to define element sizes.

primitive enzymes of the sort proposed in Figure 3. A mica world could have functioned as a community or ecosystem of primitive organisms (Figure 1). Primitive organisms would be in the micron range of sizes, and primitive enzymes would be in the nanometer range of sizes.

1.2. Biomolecules on mica

The interactions of biomolecules with mica sheets have been explored extensively with the atomic force microscope (AFM). From this research, we know that inorganic cations affect both the strength and the extent to which DNA binds to mica (Hansma & Laney, 1996). We have seen DNA molecules swimming on the surface of mica and tethered DNA molecules flopping around on mica (Hansma, 2001). We have seen that many proteins adsorb to mica; in one case, a protein complex adsorbs asymmetrically (Hansma et al., 1998). We know that lipids readily form bilayers and multilayers on mica under water (Czajkowsky & Shao, 2002; Reviakine & Brisson, 2000). Bilayers form when lipid vesicles are deposited on mica, where they flatten and fuse with other vesicles and sometimes form multilayers. An early AFM image shows lipid layers on mica (Figure 4) (Hansma, Weisenhorn, Edmundson, Gaub, & Hansma, 1991). These many observations of biomolecules interacting with mica contributed to the hypothesis that life might have emerged between mica sheets.

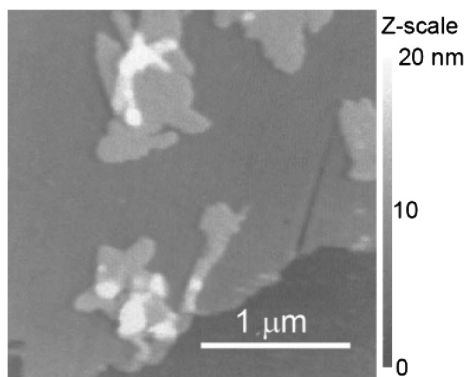


Figure 4. Lipids form bilayer and multilayer membranes on mica under water. This image shows a polymerized lipid film, but biological lipids form bilayers on mica when deposited as vesicles. Image adapted from Hansma et al. (1991). This image is an example of the ease with which biomolecules adhere to mica, as seen by atomic force microscopy.

2. Mica sheets as primitive enzymes

Enzymes and other active biomolecules are often described as ‘molecular machines.’ These molecular machines typically do mechanical work, as one would expect from a ‘machine.’ Lysozyme, for example, has a hinge-like motion around the cleft in Figure 3 (Choi et al., 2012; Radmacher, Fritz, Hansma, & Hansma, 1994). Enzymes push on their substrates with nanoscale internal motions. These internal motions arise from the *structure* of the enzymes, independent of the presence or absence of ligands or substrates (Bahar, Chennubhotla, & Tobi, 2007; Bahar, Lezon, Yang, & Eyal, 2010; Hammes-Schiffer & Benkovic, 2006). The existence of protein motion has been known since the late 1970s.

Where did life come up with these nanoscale motions? Perhaps from the spaces between mica sheets, which moved open and shut, doing mechanical work on the molecules between them. Mica’s work was powered by water movements and temperature changes. Enzymes’ work is now powered by chemical energy, typically in the form of ATP.

The mica hypothesis proposes that mechanical energy was one of the original energy sources for the origin of life and that chemical energy gradually replaced mechanical energy, to power the motions of enzymes and other active biomolecules, when direct mechanical energy from mica sheets became less available. Mechanical energy would have been an endless energy source.

Perhaps life originated with molecular machines powered by mica’s movements. Perhaps, with time, there was less energy available from moving mica sheets to power the molecular machines directly. This might happen if protobiotic and other material gradually filled the spaces between mica sheets. In any case, chemical energy emerged as the major form of energy to power the enzymes existing today, and these enzymes have

structures that cause them to have specific internal movements.

With mechanical energy, no energy conversion is needed, because the reacting molecules are simply pushed, mechanically, into the attractive regime of the free energy curve, as diagrammed in Figure 4A of Hansma (2010). Mechanical energy or mechanochemistry is better known for breaking bonds, but bond formation by mechanochemical synthesis is also known (Beyer & Clausen-Schaumann, 2005).

Enzyme molecules mimic mica’s up-and-down and open-and-shut motions. Many of life’s processes are carried out by enzymes in which the work is done by tiny motions of large enzyme molecules that have small molecules and inorganic cations sandwiched inside them. This combination of configuration and dynamics in enzymes closely resembles what is possible with mica sheets and the molecules sandwiched between them.

Where did life come up with this dynamic nanoscale configuration? Not in a primordial ‘soup.’ Not on a mineral surface. Not in a hot vent with strong convection forces or in the immobile confines of tiny icy compartments. The dynamic inorganic configuration that mostly resembles the dynamic configurations of enzymes and other biological assemblies is best illustrated in the spaces between mica sheets (Figure 3).

2.1. Ligand-assisted catalysis with transition metal ions

There is a growing belief about the origin of life, that ligand-assisted catalysis created many of the earliest biomolecules (Morowitz, Srinivasan, & Smith, 2010;

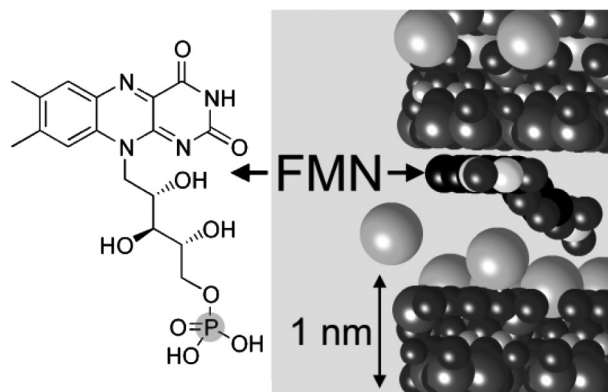


Figure 5. A cofactor, Flavin mononucleotide, FMN, between sheets of mica. This model of a cofactor between muscovite mica sheets bears a strong resemblance to enzyme–cofactor complexes and may be a precursor of what are now enzyme–cofactor complexes. The flavin rings are oriented on a sheet of mica without counterions, while the yellow phosphate on the end of the polymer chain is oriented toward a sheet of mica with potassium counterions, K^+ . For other atoms’ colors, and other details, see Figure 3 caption.

Srinivasan & Morowitz, 2009; Wachtershauser, 2007). This ligand-assisted catalysis often involved transition metal ions. Ligand-accelerated catalysis is highly enantioselective. Ligands bound to a transition metal can either speed up (catalyze) a reaction or slow it down (Berrisford, Bolm, & Sharpless, 1995). The ligands catalyzing reactions are in complexes with transition metals. Transition metal catalysts have been proposed as early participants in the origin of life, because transition metals are essential parts of many enzymes. Transition metals are present as impurities in and between mica sheets.

In the origin of life, many of the cofactors associated with enzymes today are believed to be the catalytic ligands that were involved with life's origins. Several of these cofactors are similar to nucleobases. These ligand cofactors include various redox cofactors such as nicotinamide adenine dinucleotide (NAD⁺), NAD⁺ phosphate (NADP⁺), flavin adenine dinucleotide (FAD), and coenzyme A (CoA) (Wachtershauser, 1988, 2007). Flavin mononucleotide (FMN), in Figure 5, is chemically related to FAD but has a simpler structure, lacking the adenine.

These cofactors may have catalyzed specific classes of reactions on surfaces (Wachtershauser, 1988). For example, pyridoxal phosphate (PLP) is a cofactor in transamination reactions that acts by forming a labile Schiff base between its carbonyl group and the amino group to be transferred. Indeed, life appears to operate by catalyzing classes of reactions with specific types of enzymes: when a new enzyme is needed, an enzyme performing the desired chemistry is recruited and modified to bind the desired substrate (Petsko, Kenyon, Gerlt, Ringe, & Kozarich, 1993). The alternate possibility appears *not* to be true: when a new enzyme is needed, the enzyme that already binds the substrate to be modified is *not* the enzyme that is modified to carry out the desired chemistry. This is the conclusion of research on the origins of a rare and probably recent metabolic pathway in bacteria (Petsko et al., 1993).

Cofactors between surfaces give more control of catalytic processes than cofactors on a single surface and the presence of two close-spaced surfaces confines the components of the reaction better than a single surface (Smith, Morowitz, & Copley, 2009). The spaces between mica sheets thus provide an unusually structured micro-environment for solid state synthesis. The spaces between mica sheets also provide an inorganic system that may be a precursor to the 'molecular motors' of living systems.

2.2. Peptides and saccharides

Peptides are simple to synthesize, compared with nucleic acids. This makes it likely that peptides were present in the earliest protolife. Beta strands are the most primitive peptide structure. The amino acid side chains in beta

strands point alternately up and down. How did peptides evolve this alternating up-and-down structure in the first place? A single mineral surface would not foster this bidirectional orientation. The structure that would foster this bidirectional orientation is a pair of mineral surfaces, such as a pair of mica sheets. In today's life forms, beta strands interact with adjacent beta strands to form parallel and antiparallel beta sheets.

The disaccharide molecule between mica sheets, in Figure 3, also shows a possible advantage, for confining small biomolecules, of a mica sandwich, as compared with a mineral surface or a swelling clay such as montmorillonite. The space between the mica sheets in Figure 3 is ~1 nm, while the spaces between sheets of swollen montmorillonite are 3 nm (Mathew & Luthey-Schulten, 2010). This disaccharide, mannose, has a twist between the two monosaccharides. This would make it likely to bind better to the surfaces of closely spaced mica sheets than to wider-spaced mineral sheets or to a single mineral surface.

2.3. Mica and clay minerals: nucleotide polymerization

Molecular dynamics (MD) simulations provide support for mica's possible role as a prebiotic enzyme. The clay mineral, montmorillonite, has been used as a catalyst and solid support for polymerizing activated nucleotides into oligonucleotides (Ertem, 2004; Ferris, Aubrey, Liu, & Orgel, 1996). Exciting new MD simulations show that the spaces *between* clay sheets are better for catalyzing polymerization reactions, as compared with their exposed surfaces (Mathew & Luthey-Schulten). Also, the correct biological polymerizations – 3'–5' linkages – form preferentially in the spaces between clay sheets, while unnatural polymerizations with 5'–5' linkages form preferentially on the exposed surfaces.

What does this have to do with a mica world? The montmorillonite clay simulations should be applicable to muscovite mica, because the clay and the mica have the same crystal structure and similar elemental compositions, except for the cations in the interlayer, which are primarily Na⁺ for montmorillonite clay and K⁺ for muscovite mica. The interlayer in the molecular dynamics simulations was water, with calcium ions, Ca⁺⁺, added for electrostatic and other reasons; neither Na⁺ nor K⁺ was present.

Mica also has fewer crystal defects than montmorillonite, which is why it forms such large sheets instead of being primarily in the form of clay. Therefore, the spaces between mica sheets are likely to facilitate nucleotide polymerization, like the spaces between montmorillonite sheets. Further analysis of mica vs. other minerals is provided in Hansma (2010).

Also, mica has an advantage over montmorillonite. In water, the spaces between sheets of montmorillonite

swell to a separation of 3 nm. For comparison, the mica sheets in the models of Figures 3 and 5 are only ~ 1 nm apart. At the 3 nm separation of water-swollen montmorillonite clay, uridine monophosphate (UMP) binds to the clay surface too weakly to diffuse in two dimensions on the clay surface. Mica does not swell in water. Instead, water slowly seeps in at the edges of the mica sheets, while the bulk of the sheet surface remains dry and bridged by K^+ . This would keep the mica sheets closer together, at least in the region where the water ends and the mica sheets begin splitting. In mica, with its closer-spaced sheets, UMP would remain closer to the mineral surface, as compared with montmorillonite. In this case, UMP might polymerize better, like AMP polymerizes between sheets of montmorillonite.

3. 'Mica world' as an ecosystem of primitive organisms

The mica hypothesis describes actual prebiotic *organisms*, where 'organism' is defined as 'anything resembling a living creature in structure, behaviour, etc.' A more detailed definition of such an 'organism' is:

any complex thing or system having properties and functions determined not only by the properties and relations of its individual parts, but by the character of the whole that they compose and by the relations of the parts to the whole. (<http://dictionary.reference.com/browse/organism>)

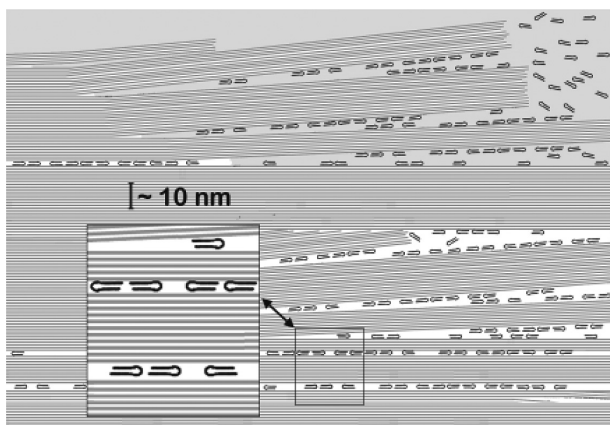


Figure 6. Mica provides massive redundancy and high error tolerance. Error tolerance is high in the spaces between mica sheets, as compared with prebiotic molecules in solution or on surfaces. Therefore, almost everything can go wrong. Error tolerance is one of the main requirements for the origin of life. This diagram envisages a self-replicating ribozyme inhabiting many spaces between mica sheets and diffusing in water to other spaces between mica sheets. Much of this mica world could be destroyed without eliminating all the molecules contained within it.

The spaces between mica sheets provide stable compartmentalization not possible with origins in vesicles, which are labile, or in ponds, or on surfaces, or in swelling clays. Thus, many types of prebiotic organisms might have formed in the stable compartments of a mica world that would not have formed elsewhere. Prebiotic organisms in a mica world could be encapsulated in lipid membranes, which are stable on mica under aqueous fluid (Hansma et al., 1991) and are probably also stable between mica sheets.

Without compartmentalization, life would not be able to develop a cell cycle or begin the process of speciation (Adamala & Luisi, 2011). This reference proposes that 'the division of protocells was triggered either by some inorganic catalyzing factor, such as porous surface, or protocells divided when the encapsulated contents reached some critical concentration.' According to the mica hypothesis, the division of protocells was triggered by pressure from moving mica sheets, as in Figure 1.

Mica sheets may also have been the original cell walls. Cell walls surround all bacteria and archaea, as well as plant cells.

3.1. Geometry controls chemistry in nanoscale systems

In the smallest compartments of living systems, such as cellular organelles, the kinetics of processes change with changes in the shapes and volumes of the organelles (Lizana, Konkoli, Bauer, Jesorka, & Orwar, 2009). One reason for this is that tiny changes in size or shape can cause large changes in the concentrations of reactants, because the volume depends on the cube of the radius, r^3 . This assumes that water moves readily in and out of compartments, while other molecules move slowly or not at all.

Signal transduction can also occur as a result of size changes, because size changes typically rearrange structures. Soft nanofluidic systems often behave in similar ways (Lizana et al., 2009).

Moving mica sheets would also be a system in which geometry could control chemistry, for any reactant that was associated with the surfaces of the mica sheets. When mica sheets moved closer together, they would partially enclose a smaller volume of fluid within which reactant would adsorb and desorb from the mica sheets. When the mica sheets moved farther apart, they would partially enclose a larger volume of fluid within which reactant would adsorb and desorb from the mica sheets.

3.2. Error tolerance

Almost everything will fail. Error tolerance is one of the main requirements for the origin of life (Dyson, 1999) and is essential for the continued existence of life.

The hypothetical error tolerance of a mica world is illustrated in Figure 6. This error tolerance comes from



Figure 7. This mica–water ‘sandwich’ shows the way in which mica provides an optimum ‘Goldilocks’ solution to the problem of too much water vs. too much dryness during the process of life’s origin. Mica is 50 × 75 mm. Dark areas are wet; light areas are dry. For other experimental details, see Hansma (2010).

the enormous redundancy of the 1 nm close spacing of the mica sheets, and from the large areas of the individual sheets. With a million sheets per millimeter, mica has vast numbers of spaces between its sheets, in close proximity, as well as centimeters of surface area per sheet. Assuming molecules can move by diffusion and water flow to different mica sheets and different regions within the spaces between mica sheets, a mica world would be likely to survive considerable mechanical or chemical destruction. The insulating properties of mica would also protect its interior regions over a wide range of temperatures and mica’s opaqueness to UV light would protect enclosed molecules from UV-induced damage.

With such large surface areas between pairs of mica sheets, there are ever-changing interconnections and separations between wet and dry regions of varying sizes and shapes (Figure 7). This is an interesting ‘Goldilocks’ just right solution to a problem in origin of life, that cycles of wetness and dryness are likely to be extreme, under many hypothetical prebiotic conditions, such as the surfaces of swelling clays. This is another example of mica’s high error tolerance, compared with molecules on surfaces or in solution. The cyclic wetting and drying between mica sheets is gentle, compared with the wetness of bulk water and the dryness of an environment exposed to air, in clays or on surfaces, for example.

‘Robust but fragile’ is a new concept in complexity theory (Carlson & Doyle, 2002). Living organisms and other systems such as jet planes are robust to a wide set of conditions that are common or anticipated, but they are fragile when confronted with a rare or unexpected condition. Robustness requires complexity. Simple mycoplasma bacteria with hundreds of genes survive only in well-controlled environments, while *E. coli* has thousands of genes and can live in a wide range of

environments (Carlson & Doyle, 2002). Is the hypothetical mica world robust and complex?

4. Is the mica hypothesis robust or fragile?

An opinion has been stated, that the mica hypothesis is a fragile thread, likely to break under the strain of a single experiment. It is not clear what this single experiment would be.

Mechanochemistry is one prediction of the mica hypothesis – that bonds are formed (and broken) by the mechanical energy of moving mica sheets. The first tests of this hypothesis are likely to fail. But, there are many variables in a mechanochemical experiment, including force, speed, distance, and a vast range of chemical conditions. Mechanochemistry is an entire research area, much more robust than a fragile thread.

Similarly, other predictions of the mica hypothesis are also research areas in themselves. For example, there is the prediction that the formose reaction, between mica sheets, will produce fewer products than in solution, due to confinement effects (Hansma, 2010). An attempt was made to test this, with the assistance of undergrad researchers. The attempt was unsuccessful, though through no fault of the hypothesis. The principal investigator needed to move away from the university and the undergrads scattered, as the research was beginning.

Testing even a simple prediction of the mica hypothesis is not simple. Polymer synthesis on clay mineral surfaces, for example, is measured in terms of synthesis per mg of clay (Joshi, Aldersley, Delano, & Ferris, 2009), even though the reaction depends on the surface area between clay sheets (Ertem, 2004). But most of the surface area of mica is not accessible, so the mass of mica is not a useful measure of its reactivity. And, of course, if mechanochemistry was involved in prebiotic syntheses in mica, then no experiments in a test tube will show this type of synthesis. Furthermore, the polymer syntheses on clays use activated monomers that are not expected to have been involved in the origins of life (Deamer, 2011). Experimental tests of the mica hypothesis are the subject of an upcoming book chapter (Hansma, 2013).

The mica hypothesis, like other hypotheses for the origins of life, is actually more like a network than a thread. Mica is the main hub, at the heart of the network, with connections to compartmentalization, mechanochemistry, and clay mineral surface chemistry, among other things. Other hypotheses for the origins of life continue to thrive, even though synthetic life has not yet been created. Perhaps, the mica hypothesis will fade away like the proteoid hypothesis (Deamer, 2011) or perhaps it will persist; but it is unlikely to be conclusively disproven.

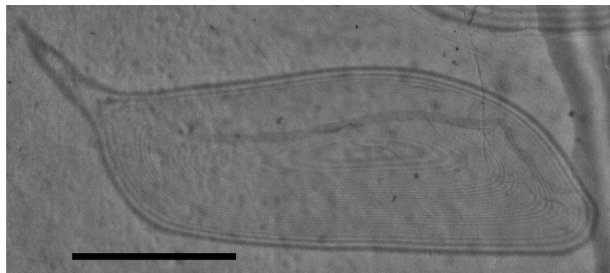


Figure 8. Did biopolymers evolve in a bubble defect in mica such as this one? High-grade muscovite mica in a dissecting microscope (Edmund Scientific Company, Barrington, NJ, USA) was photographed through a microscope objective with a Canon SD11 camera. The fringes on the right side are interference patterns near the edge of the piece of mica. Scale bar = 1 mm.

5. Concluding remarks

The mica hypothesis presents an orderly process for the origin and evolution of life. Research (Rutjens, van der Pligt, & van Harreveld, 2010) has shown that people are more likely to accept a natural origin of life when it is presented as an orderly process as opposed to a random process. Deus or Darwin? When threatened, the research subjects tended to prefer ‘Deus’ over ‘Darwin,’ unless Darwin’s evolutionary theory was ‘framed in terms of an orderly process with inevitable outcomes.’ This is not the objective of science – to soothe people; but the ‘Deus or Darwin’ research results are potentially useful for those interested in reducing hostility to science. These research results are useful for those interested in the interface between science and society, especially faith-based society.

Cytoplasmic K^+ concentrations are ~ 100 mM. Given the 0.5 nm spacing of K^+ bridging mica sheets, how far apart do mica sheets need to be separated to produce a K^+ concentration of ~ 100 mM? The answer is ~ 0.7 nm (Hansma, 2010). Did the earliest biomolecules evolve in wet mica chambers with ceilings sometimes as low as the diameter of a biopolymer? Such a chamber might have looked like the elongated structural defect inside mica in Figure 8. Such chemical confinement would tend to produce the unbranched protein and nucleic acid polymers, typically found in life today, as opposed to branched and bent polymers formed in an environment that is spatially and structurally less confined than the spaces between mica sheets.

References

Adamala K., & Luisi, P.L. (2011). Experimental systems to explore life origin: Perspectives for understanding primitive mechanisms of cell division. In J.Z. Kubiak (Ed.), *Results and problems cell differentiation* (2011/06/02 ed., Vol. 53, pp. 1–9). Berlin: Springer-Verlag.

- Bahar, I., Chennubhotla, C., & Tobi, D. (2007). Intrinsic dynamics of enzymes in the unbound state and relation to allosteric regulation. *Current Opinion in Structural Biology*, 17(6), 633–640.
- Bahar, I., Lezon, T.R., Yang, L.W., & Eyal, E. (2010). Global dynamics of proteins: Bridging between structure and function. *Annual Review of Biophysics*, 39, 23–42. doi: 10.1146/annurev.biophys.093008.131258.
- Bernal, J.D. (1951). *The physical basis of life*. London: Routledge & Kegan Paul.
- Berrisford, D.J., Bolm, C., & Sharpless, K.B. (1995). Ligand-accelerated catalysis. *Angewandte Chemie International Edition in English*, 34(10), 1059–1070. doi: 10.1002/anie.199510591.
- Beyer, M.K., & Clausen-Schaumann, H. (2005). Mechanochemistry: The mechanical activation of covalent bonds. *Chemical Reviews*, 105(8), 2921–2948.
- Burkhard, D.J.M., Ulmer, G.C., Redhammer, G., & Myer, G.H. (1999). Dynamic electrochemical assessment of redox reactions in natural micas between 613 and 1373 K at 105 Pa. *American Mineralogist*, 84, 493–505.
- Carlson, J.M., & Doyle, J. (2002). Complexity and robustness. *Proceedings of the National Academy of Sciences of the United States of America*, 99(Suppl 1), 2538–2545. doi: 10.1073/pnas.012582499.
- Choi, Y., Moody, I.S., Sims, P.C., Hunt, S.R., Corso, B.L., Perez, I., ... Collins, P.G. (2012). Single-molecule lysozyme dynamics monitored by an electronic circuit. *Science*, 335(6066), 319–324. doi: 10.1126/science.1214824.
- Czajkowsky, D.M., & Shao, Z. (2002). Supported lipid bilayers as effective substrates for atomic force microscopy. *Methods in Cell Biology*, 68, 231–241.
- Deamer, D. (2011). *First life: Discovering the connections between stars, cells, and how life began*. Berkeley, CA: University of California Press.
- Dyson, F.J. (1999). *Origins of life* (Rev. ed.). Cambridge: Cambridge University Press.
- Ertem, G. (2004). Montmorillonite, oligonucleotides, RNA and origin of life. *Origins of Life and Evolution of Biospheres*, 34(6), 549–570.
- Ferris, J.P., Hill, Aubrey R. Jr., Liu, R., & Orgel, L.E. (1996). Synthesis of long prebiotic oligomers on mineral surfaces. *Nature*, 381, 59–61.
- Hammes-Schiffer, S., & Benkovic, S.J. (2006). Relating protein motion to catalysis. *Annual Review of Biochemistry*, 75, 519–541. doi: 10.1146/annurev.biochem.75.103004.142800.
- Hansma, H.G. (2001). Surface biology of DNA by atomic force microscopy. *Annual Review Physical Chemistry*, 52, 71–92.
- Hansma, H.G. (2010). Possible origin of life between mica sheets. *Journal of Theoretical Biology*, 266(1), 175–188.
- Hansma, H.G. (2013). Possible origins of life between mica sheets: Testing the hypothesis. In B. Damer, J. Seckbach & R. Gordon (Eds.), *Genesis Engines: Computation and Chemistry in the Quest for Life’s Origin*. Dordrecht: Springer.
- Hansma, H.G., Bezanilla, M., Nudler, E., Hansma, P.K., Hoh, J., Kashlev, M., ... Smith, B. (1998). Left-handed orientation of histidine-tagged RNA polymerase complexes imaged by atomic force microscopy. *Probe Microscopy*, 1, 117–125.
- Hansma, H.G., Weisenhorn, A.L., Edmundson, A.B., Gaub, H.E., & Hansma, P.K. (1991). Atomic force microscopy: Seeing molecules of lipid and immunoglobulin. *Clinical Chemistry*, 37(9), 1497–1501. <http://dictionary.reference.com/browse/organism>.

- Hansma, H.G., & Laney, D.E. (1996). DNA binding to mica correlates with cationic radius: Assay by atomic force microscopy. *Biophysical Journal*, *70*, 1933–1939.
- Joshi, P.C., Aldersley, M.F., Delano, J.W., & Ferris, J.P. (2009). Mechanism of montmorillonite catalysis in the formation of RNA oligomers. *Journal of the American Chemical Society*, *131*(37), 13369–13374. doi: 10.1021/ja9036516.
- Lizana, L., Konkoli, Z., Bauer, B., Jesorka, A., & Orwar, O. (2009). Controlling chemistry by geometry in nanoscale systems. *Annual Review of Physical Chemistry*, *60*, 449–468. doi: 10.1146/annurev.physchem.040808.090255.
- Mathew, D., & Luthey-Schulten, Z. (2010). Influence of montmorillonite on nucleotide oligomerization reactions: A molecular dynamics study. *Origins of Life and Evolution of Biospheres*, *40*(3), 303–317. doi: 10.1007/s11084-010-9207-0.
- Morowitz, H.J., Srinivasan, V., & Smith, E. (2010). Ligand field theory and the origin of life as an emergent feature of the periodic table of elements. *Biological Bulletin*, *219*(1), 1–6.
- Pauling, L. (1930). The Structure of the micas and related minerals. *PNAS*, *16*(2), 123–129.
- Petsko, G.A., Kenyon, G.L., Gerlt, J.A., Ringe, D., & Kozarich, J.W. (1993). On the origin of enzymatic species. *Trends in Biochemical Sciences*, *18*(10), 372–376. doi: 0968-0004(93)90091-Z [pii].
- Radmacher, M., Fritz, M., Hansma, H.G., & Hansma, P.K. (1994). Direct observation of enzyme activity with the atomic force microscope. *Science*, *265*, 1577–1579.
- Reviakine, I., & Brisson, A. (2000). Formation of supported phospholipid bilayers from unilamellar vesicles investigated by atomic force microscopy. *Langmuir*, *16*(4), 1806–1815.
- Rutjens, B.T., van der Pligt, J., & van Harreveld, F. (2010). Deus or Darwin: Randomness and belief in theories about the origin of life. *Journal of Experimental Social Psychology*, *46*(6), 1078–1080.
- Smith, E., Morowitz, H.J., & Copley, S.D. (2009). Core metabolism as a self-organized system. In S. Rasmussen, M.A. Bedau, L. Chen, D. Deamer, D.C. Krakauer, N.H. Packard, & P.F. Stadler (Eds.), *Protocells: Bridging nonliving and living matter* (pp. 433–460). Cambridge, MA: The MIT Press.
- Srinivasan, V., & Morowitz, H.J. (2009). Analysis of the intermediary metabolism of a reductive chemoautotroph. *Biological Bulletin*, *217*(3), 222–232.
- Wächtershäuser, G. (1988). Before enzymes and templates: Theory of surface metabolism. *Microbiological Reviews*, *52*(4), 452–484.
- Wächtershäuser, G. (2007). On the chemistry and evolution of the pioneer organism. *Chemistry & Biodiversity*, *4*(4), 584–602. doi: 10.1002/cbdv.200790052.