

Molecular Self-Assembly and the Origin of Life

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*„All things began in order, so shall they end, and so shall they begin again;
according to the ordainer of order and mystical mathematics of the city of
heaven“*

Sir Thomas Browne 1658

Keywords:

Origin of Life, Molecular Self-Assembly, NanoScience, supramolecular architecture, two-dimensional, genetic code, template, DNA, protein, polypeptide, Scanning Tunneling Microscopy, STM, molecular simulation, mineral, Self-Organisation, adsorption, crystal, structure determination, organic thin film, chiral symmetry break

Abstract:

The formation of highly ordered monolayers of the purine and pyrimidine DNA bases through physisorption mediated molecular self-assembly at the solid-liquid interface is an example for the spontaneous creation of order. We have proposed a functional role of this process for the emergence of terrestrial life which may also lead towards the construction of genetically based supramolecular architectures for modern technical applications.

We present the structure determination of DNA base molecules self-assembled on mineral template surfaces after thermal evaporation of their aqueous solutions (“sizzling” technique) as well as by Organic Molecular Beam Epitaxy under UHV-environment. We show how the two-dimensional molecular packing structure of these films can be determined by the combination of real space data from Scanning Tunneling Microscopy (STM) and the reciprocal space data from Low Energy Electron Diffraction (LEED). Together with molecular force field calculations and the determination of the preparation parameters and thermodynamic variables, such as adsorption energy, clear models can be derived as a result.

Primitive information coding two-dimensional systems may be used to construct peptide libraries, thus reducing the complexity of the ribosomal RNA-mediated process of polypeptide synthesis in nature. We present the concept for a peptide

library in the framework of the need for a primitive molecular assembler. Purine-pyrimidine arrays adsorbed on naturally occurring mineral surfaces might act as templates for the biomolecular assembly of amino acids.

Nanoarchitectonics is a new interdisciplinary field within the NanoSciences, which investigates the principles responsible for the formation of higher-ordered functional structures starting from their nanoscopic building blocks like atoms and molecules. Such a bottom up approach is new within the field of contemporary technology, which has used very successfully the top down strategy for the miniaturization of fabrication processes during the last hundred years. However, nature has always worked bottom up, where the principles of self-assembly lead to crystal growth in the inorganic world, and, via molecular self-assembly, to functional structures in biology. For instance, the three-dimensional architecture of a nanomachine called the ribosome comprises the natural molecular assembler, which organizes the transition from the DNA informational blueprint into polypeptides and other functional units. To understand and make technological use of the underlying mechanism of this process is one of the major goals of modern Proteomics, where the relation between the DNA base sequence and the respective protein must be mastered. One approach to this question is to simplify the process by transferring it into a two-dimensional scenario, thus reducing the complexity of the three-dimensional architecture to an in-plane problem. Such a reduced coordination space may also be adequate for a primordial soup scenario, where the spontaneous self-assembly of abiotically produced organic compounds may be facilitated. The formation of highly ordered monolayers of the purine and pyrimidine DNA bases through physisorption mediated molecular self-assembly at a solid-liquid mineral interface and the subsequent stereospecific adsorption of amino acids is an example for the spontaneous creation of nanoscale order. We have proposed a functional role of this process for the emergence of life that may also lead towards the construction of genetically based supramolecular architectures for modern technical applications [1-4].

1. Key Questions for the Emergence of Life

There are a number of key questions in the context with models for molecular self-assembly and the emergence of life, amongst them the following which have widely been discussed within the literature [5-14]:

- Which key molecules are necessary for the first steps toward self-assembled molecular nanoscopic systems capable to reproduce and undergo some type of molecular evolution towards creation of higher-ordered structures? How are these elementary building blocks being synthesized in the absence of any biological machinery?

- What type of primordial synthetic chemistry comprises a possible route to answer this question and is there evidence enough from primitive earth simulation experiments, from analysis of extraterrestrial debris or from spectroscopic analysis of interstellar gases?
- Where are plausible locations, such as terrestrial and subterranean areas of geothermal activity or marine/non-marine (tidal) pool systems (to allow molecular sizzling) or submarine hydrothermal systems, for such a self-assembly?
- What is the origin of the observed biological homochirality when simple chemical synthesis normally leads to racemic mixtures? Is the reason for the required symmetry break that leads the route to life in evolutionary forces (for example selective enzymes at some stage)?
 Might purely physical forces such as the known parity violation process in the radioactive β -decay play a role?
 Can minute energy differences between two isomers (on the order of $\sim 10^{-17}$ kT for biomolecules) be responsible for a bias towards homochirality?
 Might the interaction with external chiral forces such as left or right handed polarized light drive the crystal growth towards one side?
- How can the circular relationship between a coded enzyme and its code arise when each is needed for the synthesis of the other?

2. Directed Molecular Self-Assembly

Molecular self-assembly has been defined as the spontaneous emergence of highly organized functional supramolecular architectures from single components of a system under certain external condition [15]. Such conditions may include for example a suitable template, where molecules can adsorb to and the appropriate environmental conditions, such as the right mixture and concentration of molecules in a solvent like water, temperature etc. In contrast to molecular chemistry, that has established its power over the covalent bond, non-covalent intermolecular forces prevail in this field of supramolecular chemistry. The energetic and stereochemical properties of non-covalent intermolecular forces such as electrostatic interactions, van der Waals forces and, most prominent, hydrogen bridge bonding act like the joints of Lego game pieces because they direct the monomeric building blocks to spontaneously assemble into supramolecular structures with inherent higher order. The stereospecific hydrogen bridge bonds determine the structure that comprises the blueprint for this type of transition from monomers to two-dimensional polymeric flat crystalline organic layers. In nature, the main example for coded self-organization is the DNA-double helix. Molecules capable of making hydrogen bridge bonds, such as the DNA-bases may self-organize into two-dimensional crystals as shown in Fig. 1. Here the steric arrangement of functional groups such as the possible H-bridge donors N-H, O-H and the possible H-bridge acceptors such as N, O moieties are

responsible for the specific periodic DNA-base surface. The electrostatic potential of adenine, where N-H and H interactions are used to build a monolayer, is shown here as an example. It has been calculated in an ab initio molecular orbital calculation to exactly display H-bond acceptors (in blue) and H-bond donors (in red) [16]. Such a potential map can be considered as a representation of the chemical activity of the molecule. The arrangement of the molecules shown here is only one possible pattern, which fulfils the periodic space-filling requirement of an energetically minimized two-dimensional crystal structure. Subsequent experimental observations must verify the proposed models.

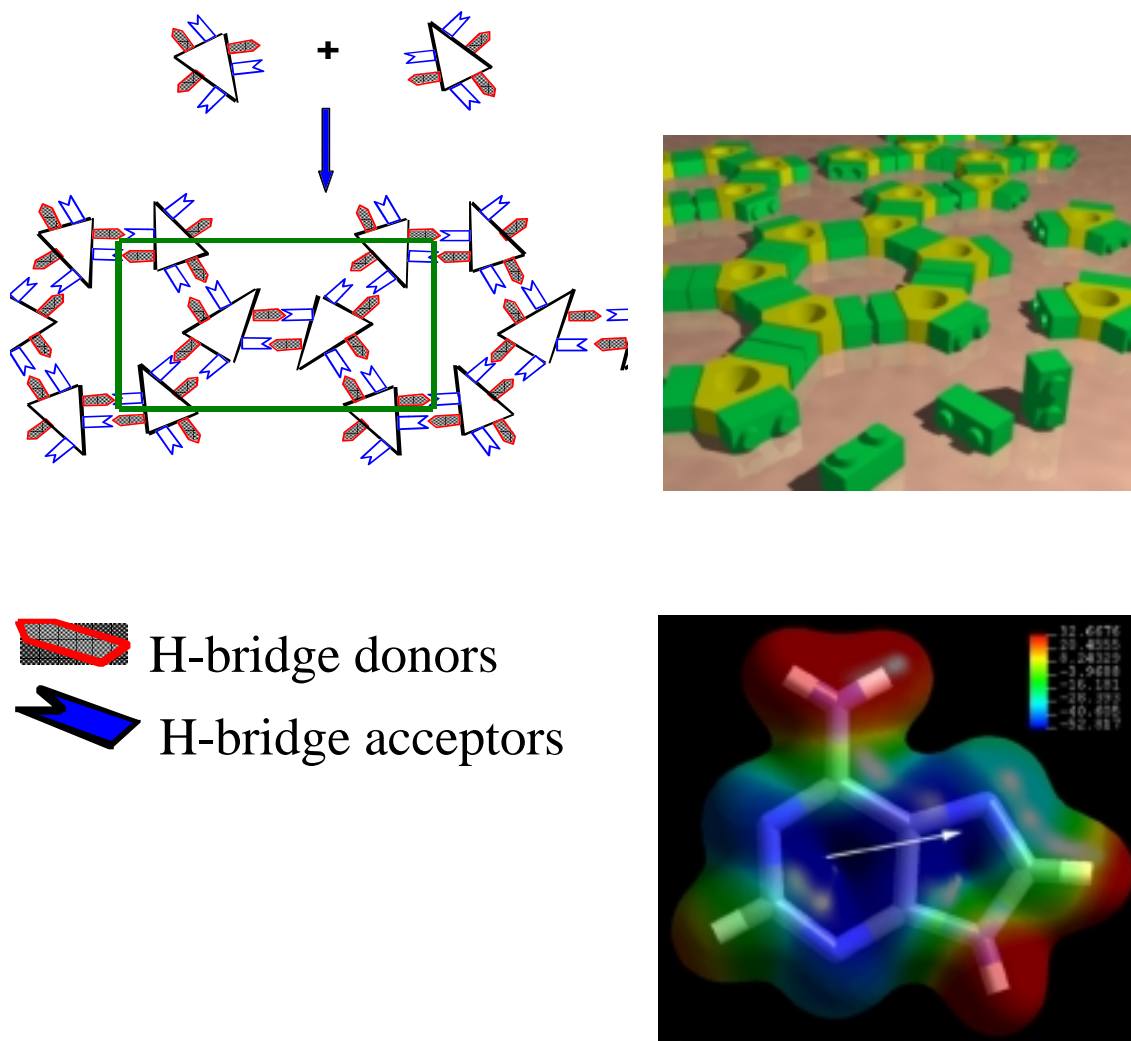


Fig.1 Schematic of recognition directed molecular self-assembly of monomeric DNA-based molecules into a two-dimensional organic crystalline layer.

3. Direct Microscopic Verification of self-assembled DNA-bases on Mineral Template Surfaces

With the advent of scanning tunneling microscopy [17] it was possible to observe directly DNA base molecules with possible hydrogen bridge donors and acceptors to self-organize into such periodic organic molecular layers on mineral template surfaces [18,19]. Since then a large number of studies of these self-assembled DNA-base systems have been published (for a comprehensive overview refer to [2]).

To mimic a primordial situation, where molecules (for example of the primordial soup) are dispersed in liquid solution and come into contact (for example by tidal movements) with the surface of a mineral template, also possibly present within a shallow sea scenario, the sizzling technique [19] has been applied to initiate the self-organization of the molecules. Here the molecules are dissolved in water and applied to a slightly heated (up to 130 °C) mineral template surface providing the energy to facilitate the two-dimensional crystal growth via molecular surface diffusion (Fig. 2). In order to be error tolerant, with respect to the right docking position of a new molecule adsorbing to a growing two-dimensional seed crystal, it is important that the molecular interactions are of weak second order chemical bond nature. Simultaneous occurring growth and dissolution processes are shifted towards the formation of the molecular crystal because the mineral template forces a seed crystal to grow due to the fixation of molecules upon physisorption. The key to the spontaneous emergence of these supramolecular structures is the appropriate energetic interplay between intermolecular interactions in two dimensions. The in-plane molecular H-bonding is responsible for creating the repetitive motive of the base layer. This is comparable to the pattern, which arises through complementary H-bonding in the three-dimensional DNA-polymer. The physisorption energy of the mineral surface determines to what exact surface atomic positions adsorption occurs. Clearly, this relates to the question of whether clay minerals [6,14], sulfur containing minerals with catalytic possibility [20,21] or other mineral surfaces may have played the actual role as inorganic template. From our experimental point of view the mineral should have a surface energy low enough to facilitate physisorption in contrary to chemisorption where the growth of two-dimensional organic crystals is hindered by the restricted surface mobility of the molecules. Therefore, and in order to be able to do STM, we have mainly used the conductive natural crystalline mineral surfaces graphite (001) and molybdenite (001).

In the following example the concept of organic monolayer structure determination as shown in Fig. 3 has been applied to adenine physisorbed to graphite [22]. Here the real space STM technique provides high resolution microscopic images of the molecules on a local scale and is combined with the low energy electron diffraction (LEED) technique or surface X-ray diffraction [23] providing a reciprocal space image of the average two-dimensional molecular crystal structure. Together with molecular modelling force field calculations [24,

25] and the determination of the preparation parameters and thermodynamic variables, such as adsorption energy measured by thermal desorption spectroscopy (TDS), clear models can be derived as a result. Fig. 4 shows the adenine on graphite layer in a high resolution STM image together with the LEED pattern. Single molecules can be identified to form a periodic molecular arrangement with a rectangular unit cell with vectors $a = 22.1 \text{ \AA}$ and $b = 8.5 \text{ \AA}$ with. The flat lying centro symmetric adenine dimers with p2gg symmetry heteroepitaxially grow on the mineral surface with 4 molecules per coincident unit cell with

$$\begin{pmatrix} a \\ b \end{pmatrix} = \begin{pmatrix} 9 & 0 \\ 2 & 4 \end{pmatrix} \cdot \begin{pmatrix} g_1 \\ g_2 \end{pmatrix}$$

metric, where g_1 and g_2 are the hexagonal arranged graphite unit cell vectors of 2.46 \AA in length. The coordination number for a molecular dimer is 6, representative for the dense packed energetically minimized stable structure where each dimer is surrounded by 6 next neighbor dimer molecules. Each molecule is surrounded by 3 neighboring molecules with the maximum number of 6 hydrogen bonds per molecule. This type of arrangement also leads to cyclic hydrogen bonding which stabilizes the monolayer via π -electron cooperativity.

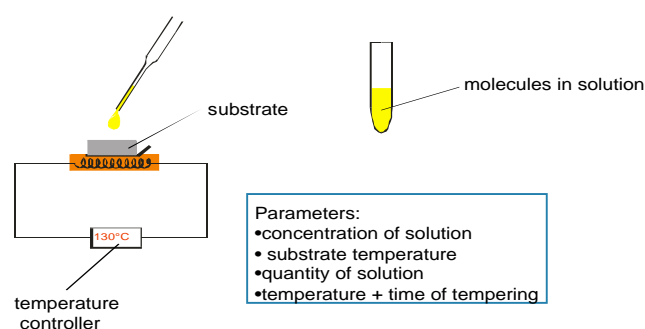
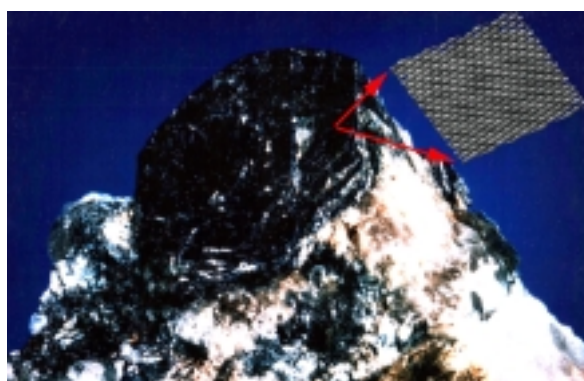


Fig. 2 Schematic of the sizzling technique applied to mimic the possible spontaneous self-assembly of two-dimensional molecular crystalline layers onto mineral surfaces within a primordial soup scenario where the elementary building blocks of life may be dissolved. Here a natural molybdenite crystal is shown together with the atomic scale resolution STM image of the surface.

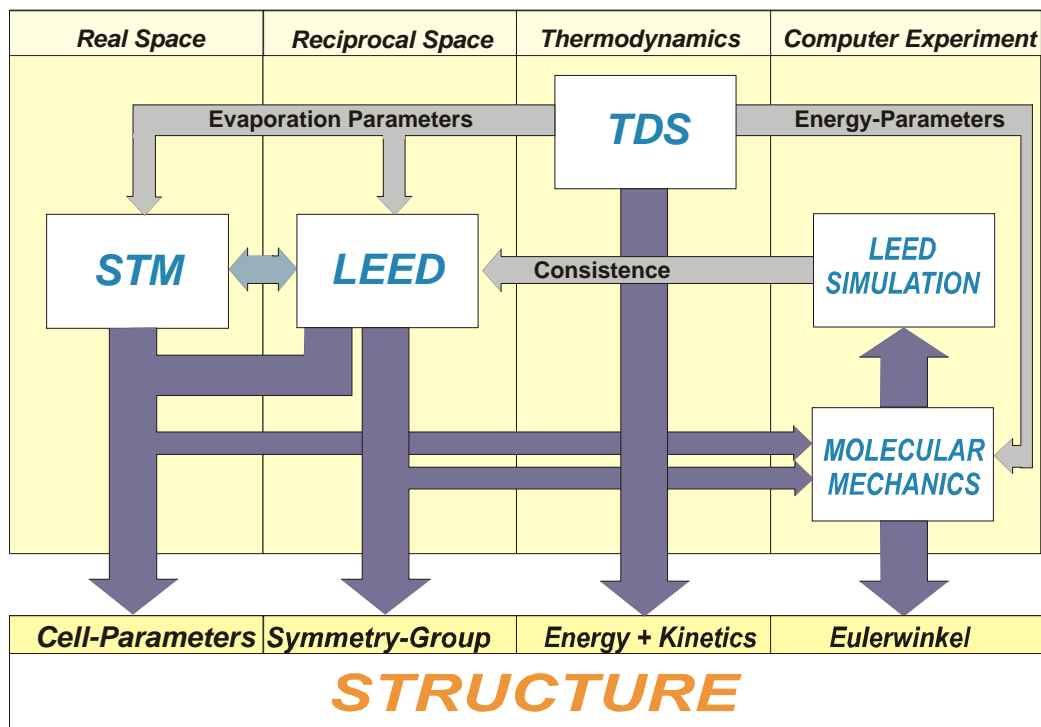


Fig 3 Concept for the structure determination of self-assembled molecular layers by the combination of different complementary techniques.

In some cases the spontaneous molecular self-assembly from liquid solution leads to localized chiral symmetry break, which may have some role in the origin of biomolecular optical asymmetry. Sowerby et al. [1] have observed such a spontaneous symmetry break for example upon adsorption of adenine on molybdenite. Although the adenine molecule is achiral by the usual definition whether a stereochemical center is present or not, there are two mirror-symmetric possible ways when the molecules adsorb to the (symmetric) mineral template surface. Whenever the unit cell is oblique, it exists in possible left handed and right handed molecular crystals within the definition of two-dimensional chirality of not being superimposable by any translations or rotation in two dimensions.

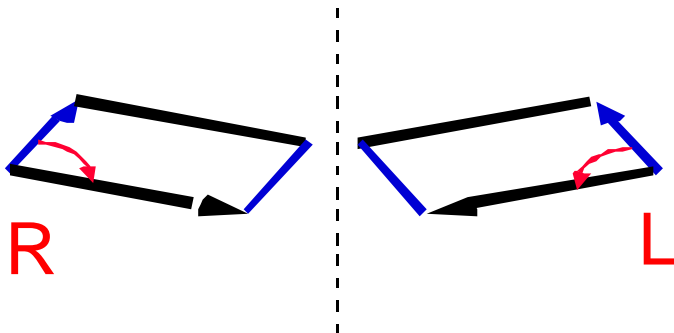


Fig. 4. Two dimensional chirality of right and left handed molecular crystals

Whether such a symmetry break upon adsorption may gain a bias towards one handedness over the other due to a force from an external source, such as for example polarized light, is not known to date. STM however is the only technique to observe such differences on the local scale and the possibility that purine-pyrimidine arrays assembled in such a chiral fashion on naturally occurring mineral surfaces might act as chiral organic templates for subsequent biomolecular assembly of higher-ordered compounds is intriguing.

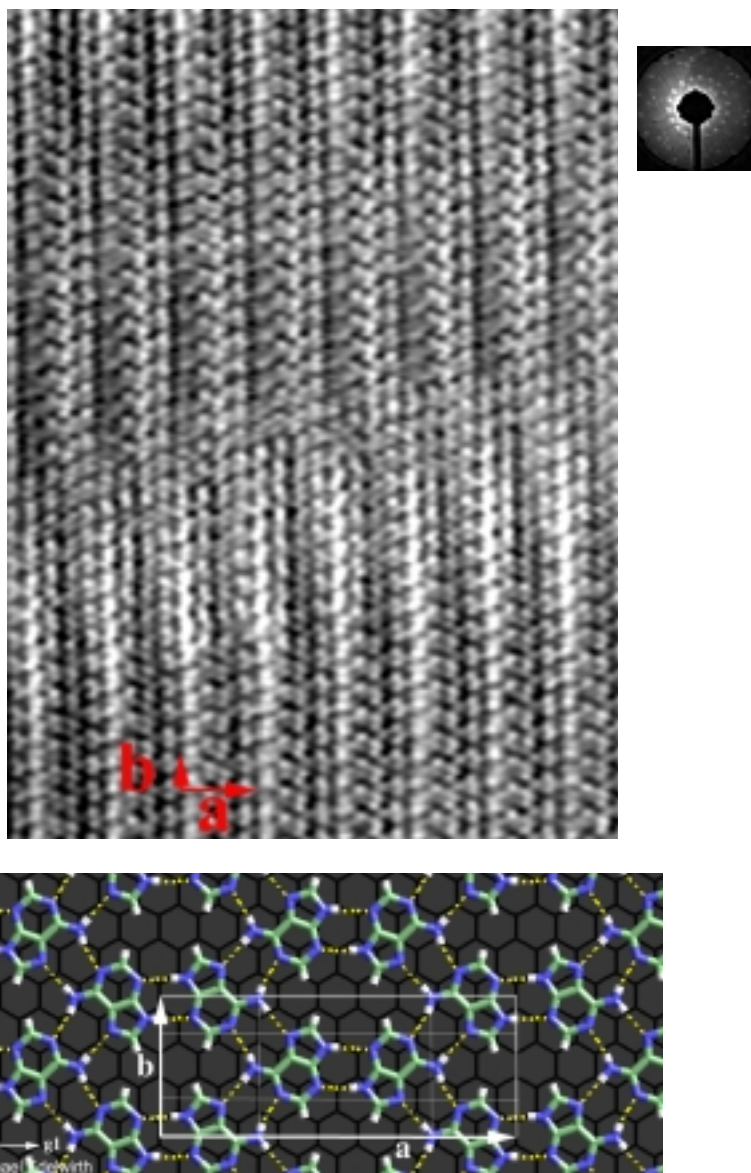


Fig. 5. Scanning tunneling microscopy image of a spontaneously self-organized adenine monolayer physisorbed to the mineral surface of graphite, together with the structure (below) determined from reciprocal space LEED-analysis (diffraction pattern show above right) and direct space STM image with rectangular unit cell with vectors $a = 22.1 \text{ \AA}$ and $b = 8.5 \text{ \AA}$.

4. Genetically Based Supramolecular Architectures from Self-Assembled DNA-Bases Coding for Amino Acids

We have presented an organic template model [2] where the key features are summarized in Fig. 5. As shown above for adenine, the spontaneous molecular self-assembly of DNA-base molecules from liquid solution on a mineral surface may lead to a (localized chiral?) organic template surface, capable of stereospecific interaction with subsequently adsorbed amino acids which may self-organize on top of the templating nucleic acid layer. Thus the construction of supramolecular complexity through the control of the intermolecular bond, preferentially the H-bond is achieved. The proposed architecture may facilitate the polycondensation of the amino acid monomers and lead to polypeptides, leaving the surface after loss of the ammonium proton upon formation of the peptide bond, which can then no longer form a stabilizing H-bond to the base template. As a consequence, this process is capable of catalyzing the formation of polypeptides in liquid.

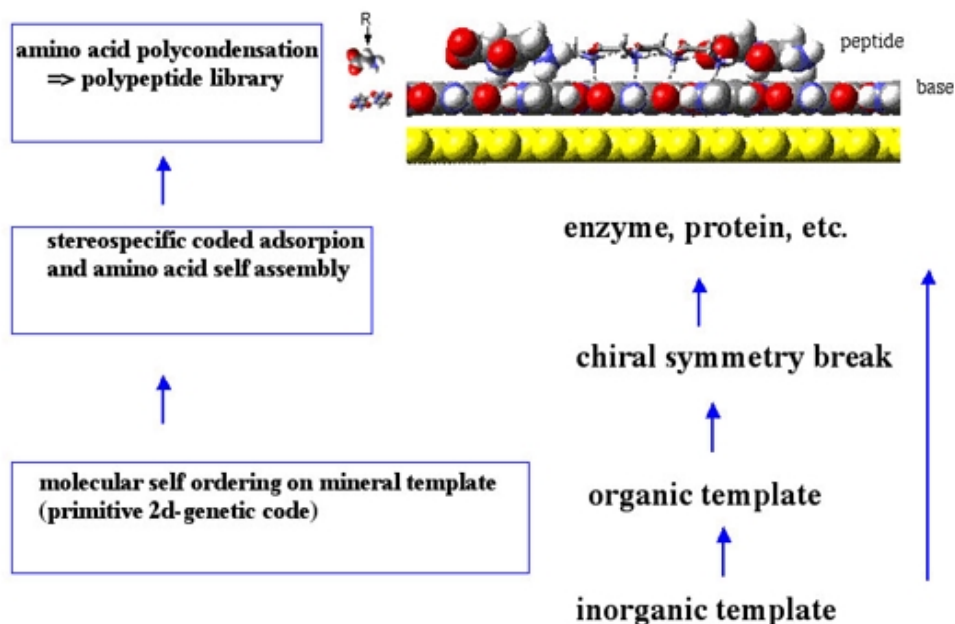


Fig. 6 Model for the assembly of polypeptides based on a 2d-DNA-base library at the solid-liquid interface

Such a scenario can be regarded as primitive self-programmable, self-assembling two-dimensional genetic matter. An aperiodic mixture of different nucleic acids has been observed and may be used to construct a variable peptide library [1,4], thus reducing the complexity of the ribosomal RNA-mediated process of polypeptide synthesis in nature. Whether the two-dimensional DNA-base layer can act as a primitive coding mechanism depends on the exact adsorption process of amino acids on top of the

nucleic acid layer. This has recently been tested by predicting the adsorption of lysine on a flat adenine template surface via molecular mechanics simulation [26]. Here the lysine molecules order as shown in Fig. 6 with calculated adsorption energy of 13 kcal/Mol. The energetic landscape for this process exhibits a very quick and steep descent to a stable energetic minimum in total energy, which demonstrates the robustness of the proposed process. It has recently been shown experimentally, that the adsorption of different nucleic acids to graphite surfaces is specific, demonstrating the influence of the energy of adsorption, which is the prerequisite for a rational coding mechanism [27]. A coding-like discrimination of amino acids by purine bases adsorbed on an inorganic surface has just been shown [28].

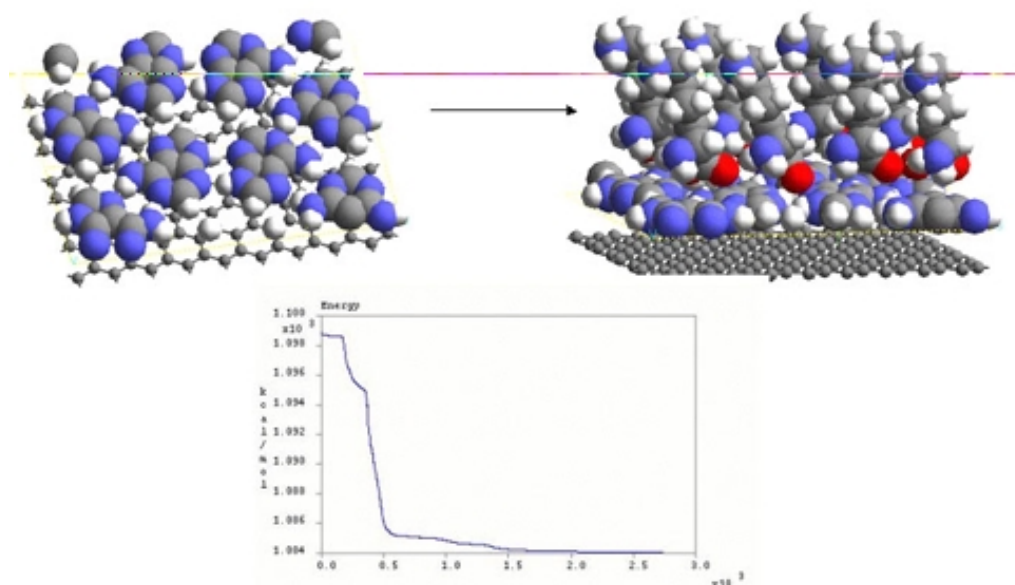


Fig. 7 Molecular mechanics calculated model of the observed self-assembly of nucleic acid adenine (left) and subsequent self-assembly of amino acid lysine on top of the templating nucleic acid layer (right). Bottom shows the development of the energetic hypersurface over time.

5. Conclusion

The application of near field microscopy techniques, namely scanning tunneling microscopy (STM), to self-assembled two dimensional nucleic acid crystals has allowed for the first time real space analysis of these systems with molecular scale resolution. This has stimulated the development of new concepts regarding the possible role of molecular self-assembly in the de novo emergence of higher-ordered supramolecular architectures, comprised of today's DNA and protein building blocks and eventually guiding a route to life under prebiotic conditions. We have suggested that purine and pyrimidine monolayers could be candidates for a stationary phase in organic molecule separation systems, and as templates for the assembly of higher-ordered polymers at the prebiotic solid-liquid interface. In some cases, such as adenine on molybdenite, a symmetry break can be observed which may have some role in the origin of biomolecular structural asymmetry. In the future it should be possible to test experimentally whether the proposed scenario actually may lead to the necessary compounds.

Acknowledgments:

The theory described in this paper has been developed over a number of years as the result of a collaboration with Dr. Stephen Sowerby and Professor George Petersen of the Department of Biochemistry, University of Otago, New Zealand. I am grateful to my collaborators for reading the manuscript and for their suggestions. My students, M. Edelwirth, F. Jamitzky, F. Trixler and F. Griessl, have also contributed with various images.

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