

Molecular Self-Assembly and Nanomanipulation – Two Key Technologies in Nanoscience and Templating**

By Wolfgang M. Heckl*

If at some time in the future we will want to build objects out of single atoms and molecules so that we can manufacture them with molecule assembly machines then we must think about which techniques need to be mastered in order to move things on the scale of atoms or molecules.

The first task will be to position the atoms and molecules, and the second will be to know if they have been correctly positioned. The scanning probe microscope has given us a wonderful method of seeing and working down to the single atom level. The tip of the microscope is so designed that in some cases it can also be used for positioning.

When searching for a parallel assembly technique for atoms and molecules one is well advised to look at the methods of nature. Nature uses the method of self-assembly. Several examples are shown below to illustrate that self-assembling systems can be used as templates, to structure, order, and position given entities as may be required in futuristic applications. That one cannot always predict precisely the outcome of a self-assembly process is first illustrated by a short story.

This story took place in the 1950's, perhaps in an English garden. It was a beautiful romantic summer evening, the moon had risen, a young lady sat on a park bench and an old man came along the path. The young lady looked at the old man and said: "Imagine Albert, if we had a child together. It would have your brain and my beauty." The old man was wise enough to answer, "but Marilyn, just imagine how it would be if the opposite happened". He knew about the stochastic nature of self-organisation and it is no different when we talk about the passing on of hereditary information. It is then dependent upon whether we are speaking of a deterministic self assembly process and if the individual units will be dominant or recessive. On the nanoscale we often cannot be precise, even though we know that molecules interact with each other across weak hydrogen bonds in the A-T-G-C- pattern. We do not know what results: whether it is a deterministic process or if it is a process which is unpredictable, with unexpected consequences.

There is a vision in the distant future that one day it will be possible to create whatever we dream of, like a *deus ex machina*, using molecular components and atoms. We would like to have a machine: "the vision is that small active units assemble themselves together. They do it in countless nanofactories without human aid. By them every desired material, every substance required would be put together atom by atom, molecule by molecule. (taken from Wolfgang M. Heckl in „Das Nanoschnitzel, Vision und Wirklichkeit in der Nanotechnologie,“ Bayerischer Rundfunk, Fernsehen 2003 „The nanosteak, the vision and reality of nanotechnology“ Bavarian TV 2003). The vision goes a few steps further. Here is an example from the area of medicine, from the science fiction novel "Prey" by Michael Crichton. It imagines that self assembled nanoparticles can be used as a camera: "I have in this syringe nanocameras only two billionths of a millimetre long. Compare the size with a red blood cell. You can see that our cameras look like tiny octopuses. I will now inject millions of these cameras into the blood stream of our patient. The cameras will form a swarm and immediately show a picture of the vein. They can even show a single blood cell. This method makes it possible to see into the smallest blood vessels, even the capillaries of the finger tips."

The complexity of nature arises from self organisation. A simple example is a school of fish. Each individual does not think for itself, it is governed only by group dynamics: keep a constant distance from the neighbouring fish, do only what the neighbour fish does. The result is that the shoal behaves like a single complex individual which moves itself in a way

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in which none of the individuals could have intended. This is peculiar to emergent systems which self-assemble. Such a primitive form of self assembly is much more than crystal growth. In his novel "Prey" Michael Crichton plays with such a shoal of hybrids: living beings in this case viruses which hybridise with inorganic self assembling machines.

These machines present a danger which is currently being strongly publicly discussed. The danger belongs in the realms of science fiction. It must however be discussed scientifically because it is being discussed publicly. Scientists no longer have the position of researchers who can say that they have everything under control and won't argue against public concerns.

There will be however the opportunity to use nanomachines for something positive, e.g. the removal of toxic substances from a waste disposal site, to make new non-toxic materials from the waste atoms and molecules, even to build useful substances. The nanomachines could be first frozen and stored perhaps in ice cubes or polymer matrix and transported. At a certain temperature they could be set free to do their work. A fantastic scenario.

Self-assembling nanomachines are not unusual. One example is the muscel system comprised of actine and myosin proteins. One of these proteins acts as a machine and makes nano meter long steps along the protein strand, this occurs each time a muscle is moved. Another example is given by the ribosome present in each cell, which is actually a nano-assembling machine which reads the DNA and translates the

code into protein. It works wonderfully in nature. The difficulty is to mimic the idea and to use it in practicable technology. This type of Nanobionic requires a second type of evolution. This evolution II is the hole idea of Nano.

Jean-Marie Lehn defined Self-organisation as a spontaneous emergence of supramolecular structures arising from individual components, such as atoms and molecules, under certain conditions. The proteins, such amazingly complex structures, are a very good example of this, as also are single macromolecules or polymers.

How does self-assembly on the nanoscale work? Taking DNA as an example: In experiments we have observed that DNA bases, the letters of the genetic code, self-organise into a two dimensional molecular crystal when applied in liquid solution onto a mineral surface. This amazing spontaneous formation of order, the arising of something new from the single molecular components occurs in a μ second or less with 10^{16} molecules per square centimetre. This is a phenomenon which could never be imitated if it had to be built molecule by molecule according to a fixed plan. This can only happen by a natural process of self-assembly. If DNA or RNA bases are allowed to self-organise on a surface it is always the case that hydrogen bonds form between the molecules and hold the structure stable. Self-assembly of DNA molecules is one of the most important themes for research because it leads to an explanation for the origin of life, one of the greatest research challenges of our century. In fact, the origin of life was nanotechnology 4.8 billion years ago.

Table 1. Self-assembling molecules to form two-dimensional crystals on surfaces.

Molecule	Sum formula	rel. Molecular mass	Subl. -Enthalpy [kJ/mol]	measured Subl.-Temp. [°Celsius]
Adenine (A)	C ₅ N ₅ H ₅	135,1	126,3	205
Guanine (G)	C ₅ N ₅ OH ₅	151,1	186,2	270
Cytosine (C)	C ₄ N ₃ OH ₅	111,1	167	220
Thymine (T)	C ₅ N ₂ O ₂ H ₆	126,1	131,3	153
Uracil (U)	C ₄ N ₂ O ₂ H ₄	112,1	126,5	168
2-Thiouracil (2-TU)	C ₄ N ₂ O S H ₄	128,2	129	155
Glycine (Gl)	C ₄ N O ₂ H ₅	75,1	136,5	130
PTCDA(Perylene-tetra-carbonic acid)	C ₂₄ O ₆ H ₈	392,3		310
Coronen	C ₂₄ H ₁₂	300,35		100
Trimesic Acid	C ₉ O ₆ H ₆	210,1		181
Indigotine	C ₁₆ H ₁₀ N ₂ O ₂	262		in 8-CB solvent
Quinacridone	C ₂₀ H ₁₂ N ₂ O ₂	320		in 8-CB solvent
Alizarine	C ₁₄ H ₈ O ₄	240		in 8-CB solvent
Alizarine Krapplack				in 8-CB solvent
Hemine (Protoporphyrine)	C ₃₂ H ₂₈ ClFeN ₄ O ₄	616		in 8-CB solvent
6-, 8-, 10-,12- Cyanobiphenyle				From solution

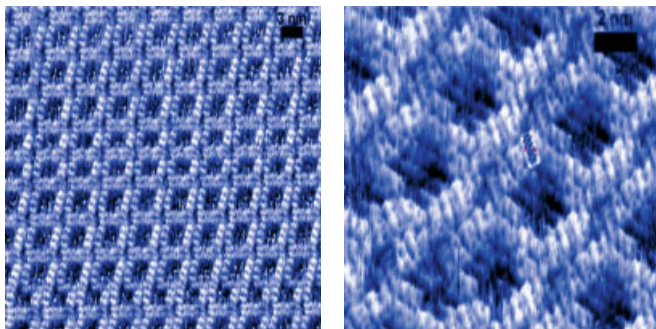


Fig. 1. 8-Cyanobiphenyl-cavities for an organic host-guest system

An essential factor in the development of life forms is chirality, without it life does not exist. We could experimentally recognise this very early on with the help of a scanning tunnel microscope, DNA bases grow either right or left handed on mineral template surfaces. The importance is that a chiral break in symmetry must occur for single nucleic and amino acids to give rise to life in nature. We have investigated a whole series of molecules which self-assemble to form such two dimensional crystals on surfaces. They have molecular weights of up to 616 atomic units e.g. hemine, a protoporphyrin molecule (see Table 1).

Several more recent examples of molecular self organisation from our current work are described below: Trimesic acid, a benzene ring with three additional carboxyl groups, the dye molecule Coronene and the semi-conducting quinaclidone molecule (see Fig. 1).

The first molecules investigated with the scanning tunnel microscope were liquid crystal molecules. The phases separate, the liquid crystal takes different structures and there is a phase boundary between them. That is actually the first molecule which was directly seen by the real space method back in 1988 by Foster and Frommer. Other structures can be formed from liquid crystals. For example one is of particular interest because it is open-pored and therefore is a two-dimensional guest system in which one can store hosts.

Carmines is a red substance known to every artist. It crystallises spontaneously in two-dimensions by solid-solid wetting on a surface. There are of imperfections in the structure, however the self-assembly process works very well.

Quinacridon is another pigment with a linear type structure. Each molecule has two hydrogen bonds bridging the neighbouring molecules. A one-dimensional chain can be made. Tunnelling spectroscopy reveals that these chains are semi-conducting, and so can be used as molecular wires. The wires can be moved and repositioned with the tip of the microscope to assist the self-assembly process. Specific structures can be made such as a condenser geometry or a structure where three conducting structures come together in a transistor geometry. It is however a huge challenge to connect these structures with the outside world; that is to electrodes. Two layers can be placed on top of each other to form a crossed pattern.

If the conductors grow in different directions a technique we have termed "Molecular Combing" can be used to align the molecular wires.

The most successful Host-Guest system is a two dimensional lattice prepared in our laboratories using trimesic acid. In the literature a three dimensional crystal of trimesic acid has been described. In 1998 our molecular mechanics simulation illustrated how this molecule could form a two dimensional layer on a solid surface. From this we could predict the formation of a trimesic acid lattice with an open-pored template structure. The substrate we first used was silicon and this led to some very disappointing results because the adsorption energy is too high and so the expected open-pored, self-organised, crystalline two-dimensional lattice did not arise. We concluded therefore that the substrate needs to have a much lower adsorption energy, a possible suitable substrate was found to be graphite. Using graphite an open-pored structure was formed where six molecules held together by stereospecific hydrogen bonds form a cavity with a distance between the cavities of around 2 nm. We have termed the structure a "chicken-wire" structure since it resembles the macroscopic fence. We have also succeeded in making a "Flower" structure where smaller cavities are formed next to the larger ones. In this structure six trimesic molecules form a ring with six more molecules hexagonally surrounding them. Here additional hydrogen bonds form in trigonal geometry and not only in the geometry with 180° rotation.

The open cavities, i.e. the "guest" positions, can be filled with guest molecules. An interesting experiment can be done here. By application of the tip of the scanning tunnel microscope to a trimesic molecule in a guest position the molecule can be switched from the corresponding top position to a down position. In addition to this vertical transposition we have also resolved a horizontal switching process. There are six docking positions for a trimesic molecule in such a ca 2 nm sized cage. The six positions can be actively rotated

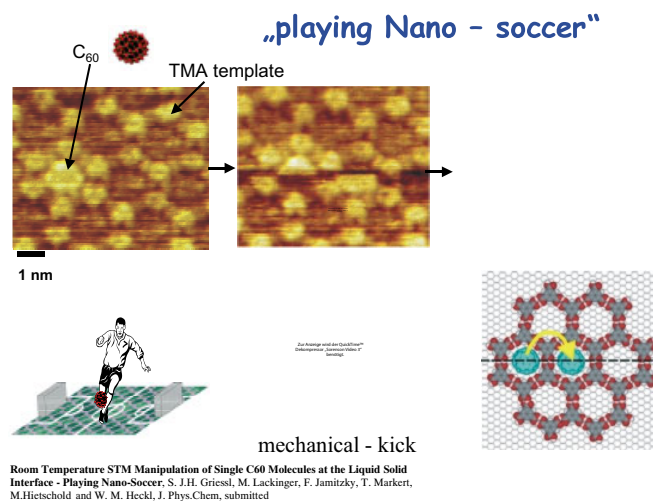


Fig. 2. Room temperature STM manipulation of single C60 molecules at the liquid solid interface – playing nano-soccer.

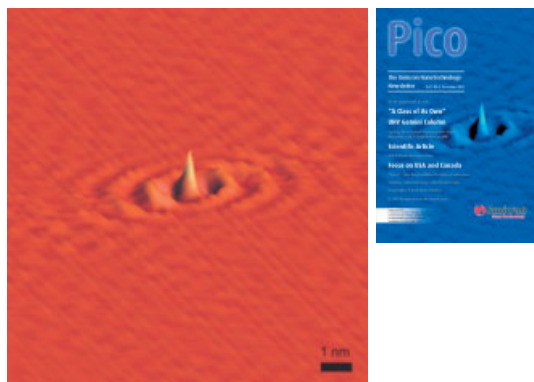


Fig. 3. The structure of the trimesic network can be regarded as a two-dimensional zeolite.

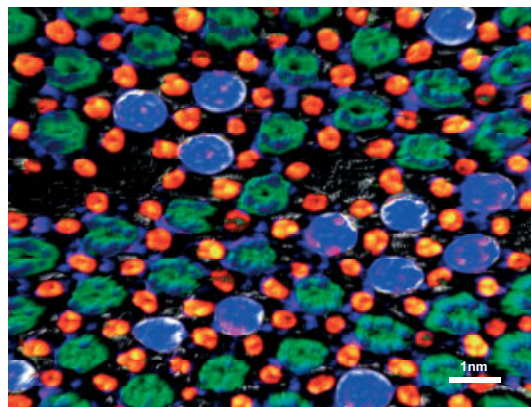


Fig. 4. Coronene molecules (blue), "kicked" out by a nanomanipulation technique.

from the outside. This corresponds to an elementary molecular switch.

Other molecules which are very interesting are carbon cage molecules, e.g. the C₆₀-molecule, also known as Buckminster fullerene. They have exactly the right size to fit perfectly in the cavities of our molecular template trimesic network. One of these football shaped molecules has been placed in the middle of one of the template rings, and can be "kicked" into the guest position of the neighbouring ring. This shows that manipulation on the molecular scale is possible (Fig. 2).

Another molecule of particular interest is coronene. Quantum mechanical effects can be directly observed, the Fresnell-oscillation and the scattering of surface electron waves on the single molecules even at room temperature. Interference effects can even be observed between two closely neighbouring molecules (Fig. 3).

In Figure 4 coronene molecules (blue) have been "kicked" out by our nanomanipulation technique, an elementary reaction. There is however space around the molecule within its cavity, and it is therefore at least able to vibrate (green are bound coronene molecules and blue are vibrating molecules). This has been reported in the literature. Gimzewski has reported a case of molecules either remaining still or turning depending upon where they are attached. This was described as a molecular motor. We believe that these and our molecules quite simply vibrate. The term "rotate" is inconsistent with the second law of thermodynamics.

Returning now to the original theme. I believe that the emergence of living systems has been a result of self-assembly on the nanoscale, essentially the self-assembly of nucleic and amino acids. We have been working for many years investigating

these early stages in the evolution of life by using primeval soup scenarios on mineral surfaces, for example how nucleic and amino acids can self-assemble to form layers on minerals such as pyrite and so represent the first step towards life. Darwin knew that the key was the formation of a protein or polypeptide de novo. An abiotic situation needs to be imagined with no bioreactors present that could have manufactured these molecules. Our method is to drop a solution of nucleic and amino acids on a mineral surface. This imitates the scenario where a lake of primeval soup evaporated on hot stones. We have called the method the Sizzling technique, because of the noise made by the water lapping on the hot rocks. A completely spontaneous two-dimensional ordering of organic molecules occurs under the simplest conditions in a fraction of a second. The mineral surface acts as a template for the self-assembly of the nucleic acids which in turn acts as an organic template for amino acids. This is the coding mechanism: nucleic acids form the code for amino acids which subsequently hydrogen bond on top of them, able to polymerize now into enzymes and other proteins (Fig. 5).

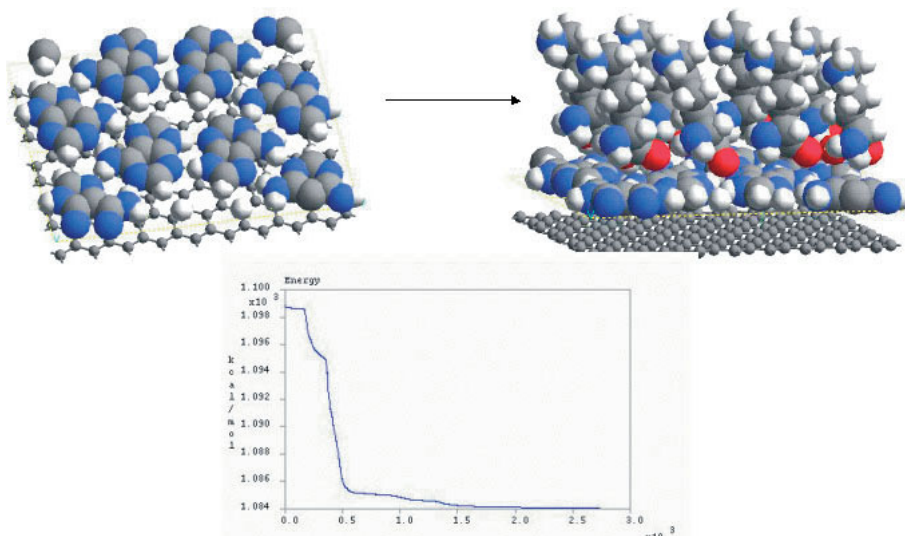


Fig. 5. Spontaneous two-dimensional ordering of organic molecules on a mineral surface, acting as a template.

In cells there is a three dimensional process. The DNA is read in the ribosomes and for each triplet of nucleic acids an amino acid is built into the forming protein in this "molecule assembler". Nucleic acids code for amino acids by direct stereospecific interactions. In our experiments there are no ribosomes, but there were also none at the beginning of life. There were molecules floating in the primeval lake and we imitate the phenomenon of self-assembly in our "historic" experiments. We cover a surface with nucleic acids, then with

amino acids and peptide like systems are formed. The formation of the peptide bond is fundamental to the formation of enzymes from amino acids. This is a de novo polypeptide synthesis. A cycle of coded enzyme and amplifications arises by itself. We hope therefore to have shown experimentally nothing less than the origin of the molecular assembly of life, the principles of its spontaneous emergence from the simplest natural components.
