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Emergence of Complex Chemistry on an Organic Monolayer

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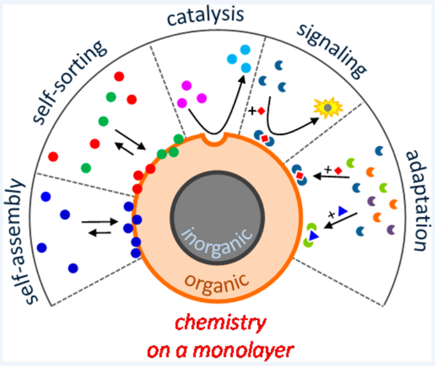

CONSPECTUS: In many origin-of-life scenarios, inorganic materials, such as FeS or mineral clays, play an important role owing to their ability to concentrate and select small organic molecules on their surface and facilitate their chemical transformations into new molecules. However, considering that life is made up of organic matter, at a certain stage during the evolution the role of the inorganic material must have been taken over by organic molecules. How this exactly happened is unclear, and, indeed, a big gap separates the rudimentary level of organization involving inorganic materials and the complex organization of cells, which are the building blocks of life.

Over the past years, we have extensively studied the interaction of small molecules with monolayer-protected gold nanoparticles (Au NPs) for the purpose of developing innovative sensing and catalytic systems. During the course of these studies, we realized that the functional role of this system is very similar to that typically attributed to inorganic surfaces in the early stages of life, with the important being difference that the functional properties (molecular recognition, catalysis, signaling, adaptation) originate entirely from the organic monolayer rather than the inorganic support. This led us to the proposition that this system may serve as a model that illustrates how the important role of inorganic surfaces in dictating chemical processes in the early stages of life may have been taken over by organic matter. Here, we reframe our previously obtained results in the context of the origin-of-life question.

The following functional roles of Au NPs will be discussed: the ability to concentrate small molecules and create different local populations, the ability to catalyze the chemical transformation of bound molecules, and, finally, the ability to install rudimentary signaling pathways and display primitive adaptive behavior. In particular, we will show that many of the functional properties of the system originate from two features: the presence of metal ions that are complexed in the organic monolayer and the multivalent nature of the system. Complexed metal ions play an important role in determining the affinity and selectivity of the interaction with small molecules, but serve also as regulatory elements for determining how many molecules are bound simultaneously. Importantly, neighboring metal ion complexes also create catalytic pockets in which two metal ions cooperatively catalyze the cleavage of an RNA-model compound. The multivalent nature of the system permits multiple noncovalent interactions with small molecules that enhances the affinity, but is also at the basis of simple signal transduction pathways and adaptive behavior.

1. INTRODUCTION

The question of how life emerged is still unanswered and will presumably also remain so. The only verifiable fact is the current manifestation of life, based on the cell as the basic structural and functional unit and for that reason referred to as the building block of life.[1] Numerous hypotheses have been developed in order to explain how a complex organic structure such as the cell could have emerged from the few chemical ingredients that were present in the early stages of Earth.[2−7] In many of these hypotheses, adsorption processes of organic small molecules on inorganic materials, such as FeS or mineral clays, are considered to have played an important role.[8−10] Wächtershäuser defined surface metabolism as a primary step in chemical evolution emphasizing the ability of adsorbed molecules to react in a two-dimensional surface reaction system.[10] Indeed, it has been shown experimentally that adsorption onto such materials provides for a means to concentrate selectively small organic molecules, catalyze their chemical transformation, and facilitate polymerization reactions of nucleotides and amino acids.[11−13] However, although these studies clearly point to a likely role of inorganic surfaces in directing chemical processes in the early stages of life, it leaves the question open as how this role of the inorganic surface could have been taken over by organic material, which is the characteristic feature of life as we know it (Figure 1). Generally, it is hypothesized that condensation reactions on the inorganic material would at some point have led to the formation of molecules (lipids, RNA, peptides) able to structure themselves and take up catalytic roles independently from the surface.[11,14,15] However, a critical feature of many organic protocells such as vesicles and other self-assembled structures based on peptides, RNA, and so forth is that their formation relies on noncovalent interactions, which are relatively weak. Consequently, the self-assembly of the organized state typically requires relatively high concentrations of the building blocks. In addition to that, the labile nature of these aggregates poses relatively strong restrictions to the chemical environment (pH,

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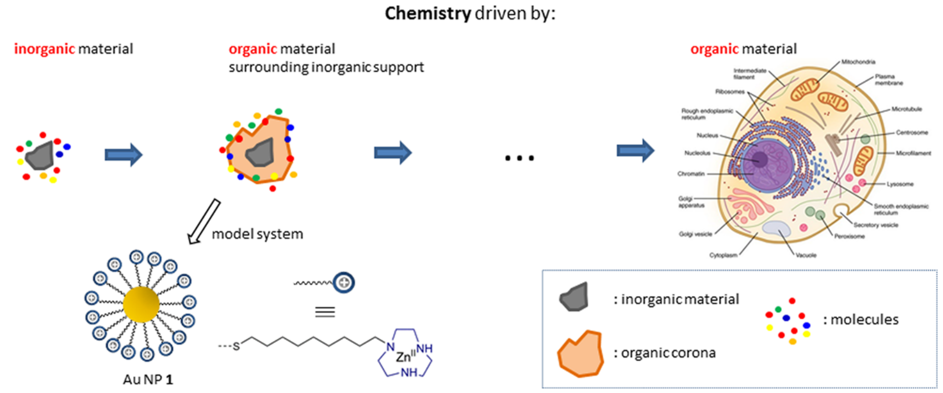

Figure 1. Schematic representation of the transition from chemical processes sustained by inorganic materials toward chemistry sustained by an entirely organic structure such as the cell. It is generally assumed that in the early stages of life inorganic materials played an important role in concentrating small molecules and catalyzing their chemical transformation. Here, we propose a hybrid inorganic/organic structure as an intermediate next step for the transition from inorganic to organic sustained chemical processes based on the observation that a corona of organic molecules surrounding an inorganic core can exhibit the same identical functions as those typically assigned to the inorganic surface. Au NP **1** is proposed as a model system for studying the properties and potential of an organic monolayer to dictate chemical processes. The illustration of the cell was created by the OpenStax College (Human Anatomy and Physiology).

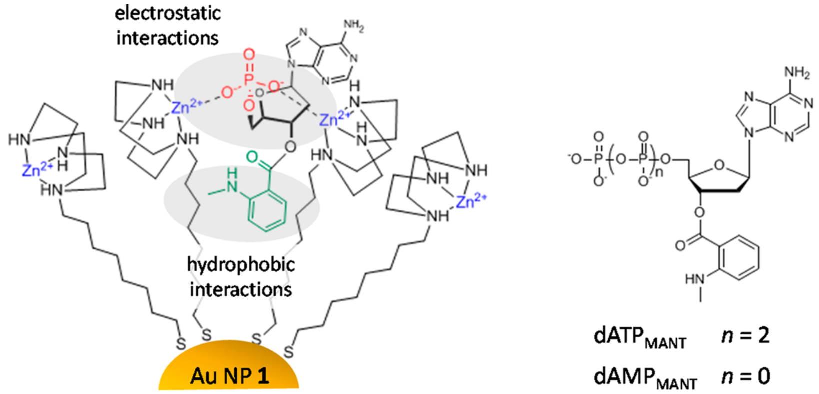

Figure 2. Negatively charged small biomolecules, such as Asp/Glu-rich peptides and nucleotides, have a high affinity for Au NP **1**. Binding is driven by a combination of hydrophobic and electrostatic interactions.

ionic strength, temperature, etc.) in which such aggregates can exist. For that reason, it has remained relatively unclear how and at which stage a self-sufficient organic structure could have emerged.

Here, we propose a hybrid inorganic/organic structure as an intermediate step for the transition from inorganic to organic sustained chemical processes. The main reason is the high stability of these structures as compared to the assemblies discussed above. The anchoring of organic molecules on an inorganic support through bonds with stabilities equal (or close) to covalent bonds makes these hybrid structures very stable even at very low concentrations and under a large variety of conditions. It is the precise scope of this Account to demonstrate that a monolayer of organic molecules surrounding an inorganic particle can be considered as a primitive form of organized organic matter. It will be shown that such a monolayer can indeed exert the exact same functions (concentration, selection, catalysis) that are typically attributed to inorganic surfaces. In addition, these simple systems are able to develop rudimentary signaling pathways and have the ability to evolve as a function of stimuli arriving from the surrounding medium. The important aspect is that all these functions derive exclusively from the organic monolayer, whereas the role of the inorganic core has been reduced to that of an inert support providing stability to the system. This suggests that the transition from inorganic to organic matter could have occurred already in a very early stage.

Over the past years, we have extensively exploited Au NP **1** for the development of innovative sensing and catalytic systems. Au NP **1** is a gold nanoparticle ($d \approx 1.8 \pm 0.4$ nm) covered with a monolayer of hydrophobic C9-thiols terminating with a 1,4,7-triazacyclononane (TACN)·Zn(II) headgroup (Figure 1). It was the participation in two COST-networks related to the Emergence and Evolution of Complex Chemical Systems that led to the awareness that this system, and its properties could also be of value within a discussion on the origin-of-life.[16] For that purpose, we have on this occasion revisited the original results from this new perspective. Based on that analysis, we argue that Au NP **1** is an attractive model system for studying and understanding how the role of inorganic surfaces in controlling chemical processes in the early stages of life may have been taken over by organic molecules.

In particular, we will focus on the ability of Au NP **1** to concentrate small peptides and nucleotides on the surface and will show that Zn(II)-metal ions complexed in the monolayer play an important regulatory role in this process. The same Zn(II)-complexes also render Au NP **1** an efficient catalytic system for the transphosphorylation of an RNA model compound. In an alternative manner, chemical reactions can

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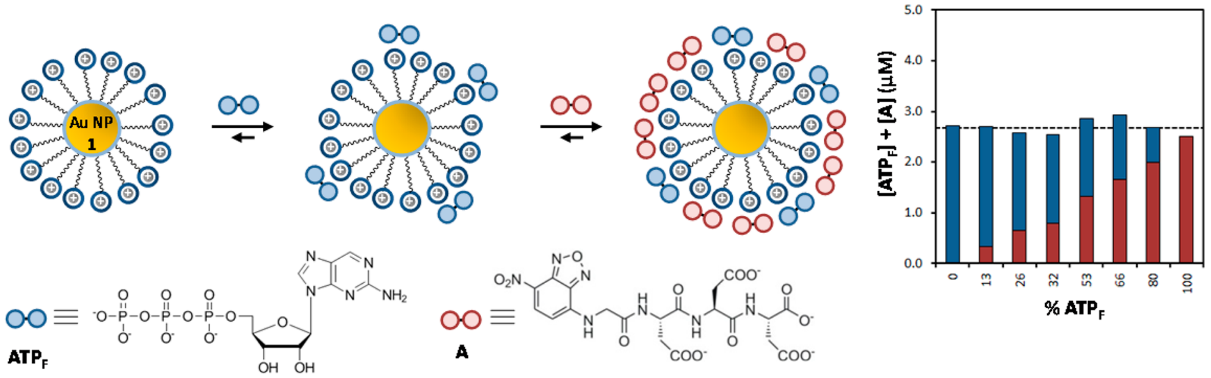

Figure 3. Coassembly of ATP$_F$ and peptide **A** on Au NP **1** leads to a heterogeneous surface composition. This experiment shows that the monolayer can serve to simultaneously attract different molecules causing an enhancement of their effective concentration.

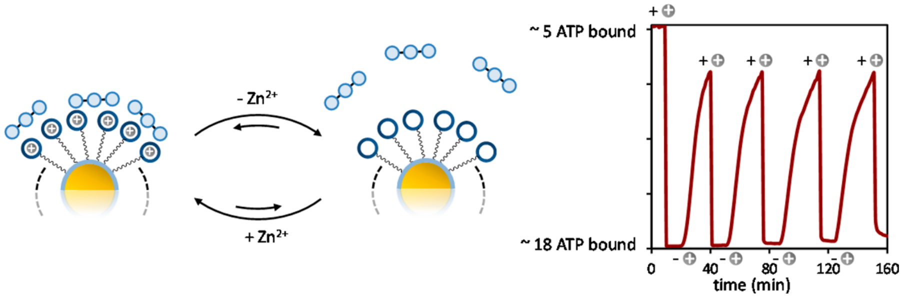

Figure 4. Zn(II)-metal ions in Au NP **1** are regulatory elements for the surface concentration of ATP$_F$ (for the structure, see Figure 3). Removal of Zn(II) from the monolayer upon the addition of a strong Zn(II)-chelator results in a lower surface capacity and consequently a release of ATP$_F$. The renewed addition of Zn(II) reverses this process.

be accelerated by coassembling substrate and catalyst on the monolayer surface causing a strong increase in effective concentration. Finally, the ability of this system to express rudimentary signaling pathways and adaptive behavior is discussed.

2. ORGANIZATION

2.1. Self-Assembly

Negatively charged small biomolecules, such as Asp/Glu-rich oligopeptides and nucleotides, have a high affinity for Au NP **1** and bind to the surface of Au NP **1** under saturation conditions even at low micromolar concentrations in aqueous buffer at physiologically relevant pH values.[17] Binding is driven by electrostatic interactions between the oppositely charged species and the affinity strongly depends on the number of negative charges present in the probes. However, detailed studies revealed that also hydrophobic interactions between the probe and the apolar part of the monolayer strongly contribute to binding (Figure 2).[18]

The surface saturation concentration (SSC) defines the maximum number of small molecules that can be accommodated simultaneously by Au NP **1**. This value emerges in a straightforward manner from fluorescence titration experiments in which increasing amounts of a fluorescent probes are added to a constant amount of Au NP **1** (typically $[\text{TACN}\cdot\text{Zn(II)}] \approx 10 \pm 1$ μM). Although the SSC depends on the size of the probe and the experimental conditions (headgroup concentration), typically a value between 2 and 4 μM has been determined. Considering that the surface of Au NP is covered with roughly 80 thiols, this implies that 16–32 probes can be simultaneously bound to the surface.

The fact that binding occurs under saturation conditions has two important implications, which will be discussed next. First, it gives the possibility to saturate the surface with two (or even more) different probes leading toward a heterogeneous clustering of small molecules around Au NP **1** (Figure 3).[17] The second feature is that the self-assembly process leads to a significant increase in the local concentration of the small molecules. Based on dynamic light scattering measurements, we estimated that the bound probes are roughly within a distance of 4 nm from the monolayer surface, which corresponds to a volume of 3.3 zL for each nanoparticle.[19] For a 100 nM solution of Au NP **1**, this implies an increase in the effective concentration of more than 3 orders of magnitude. This is much larger than the 140–180 times concentration increase reported for the adsorption of amino acids on mineral clays.[20] For the binding of nucleic acids to mineral clays, on the other hand, concentration increases up to 1200 were determined under optimal conditions (pH = 7). Indeed, for those interactions a very strong pH dependence was reported with the factor dropping to 150 times when the pH was raised by just 1 unit. It appears evident that the increased local concentration can have a tremendous accelerating effect on reactions when these are of second- (or higher) order (see subsection 3.2).

2.2. Regulation

It is well-known that Au NPs having cationic headgroups strongly interact with negatively charged macromolecules, such as proteins and DNA.[21,22] In the large majority of cases, the positive charge originates from the presence of quaternary ammonium groups in the monolayer. In Au NP **1**, however, the positive charge originates from Zn(II)-metal ions that are complexed by the TACN ligands. Compared to other systems,

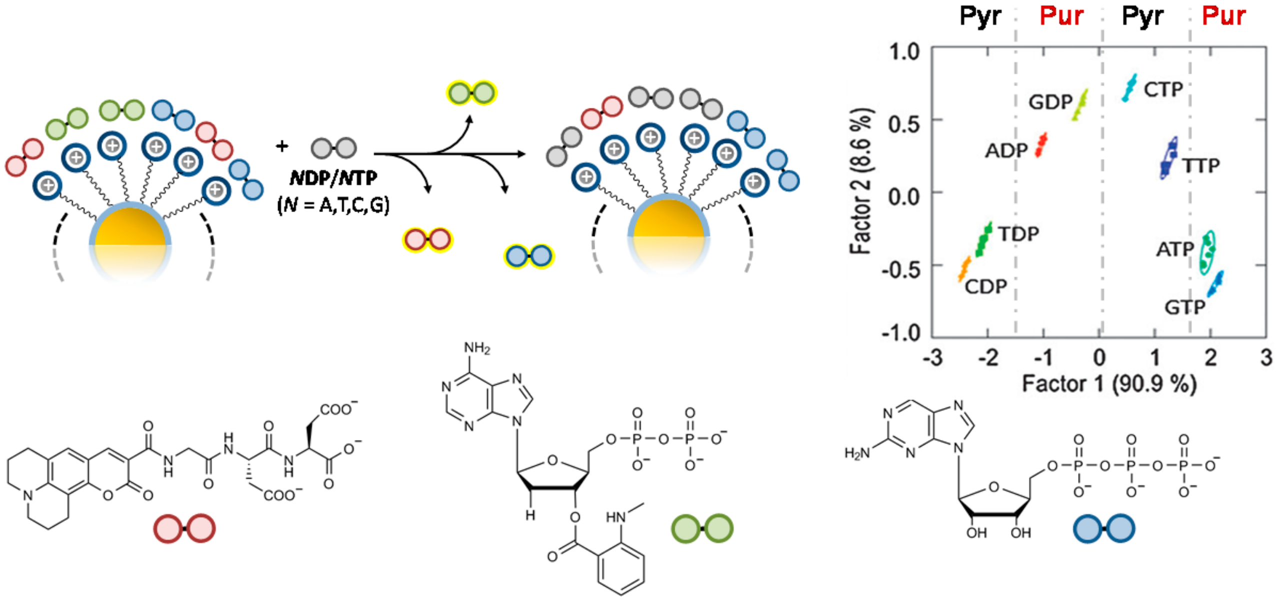

Figure 5. Multi-indicator displacement assay used for nucleotide sensing. The addition of di- or trinucleotides to Au NP **1** with three different fluorescent probes assembled on the surface causes their displacement.

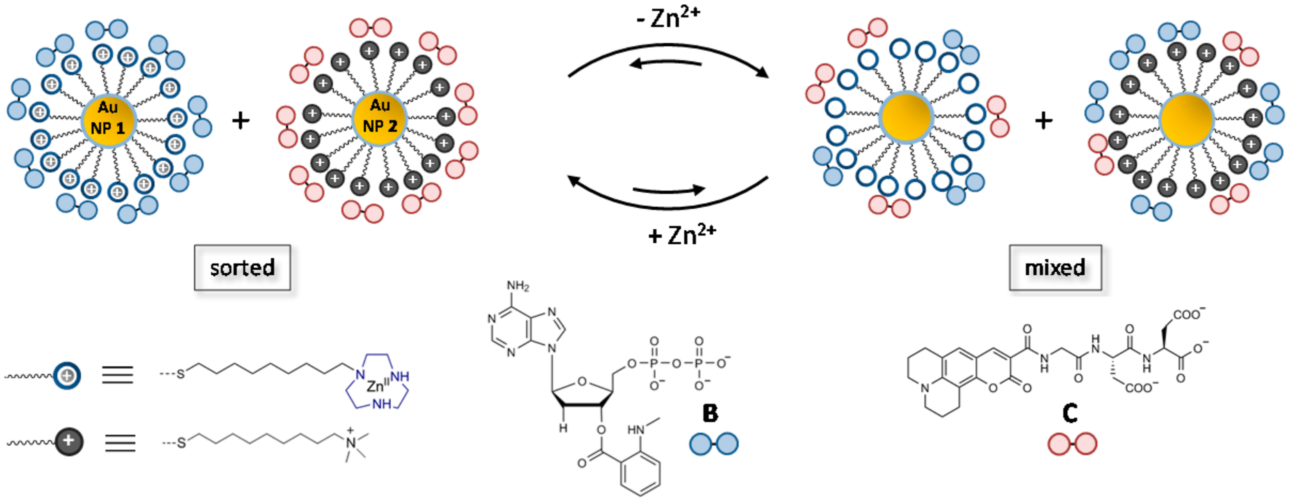

Figure 6. Addition of nucleotide **B** and peptide **C** to a mixture of Au NP **1** and Au NP **2** results in self-sorting. The strong selective interaction between the phosphate probe **B** and Au NP **1** causes the localization of **B** on Au NP **1**, leaving **C** to interact with Au NP **2**. The selectivity is lost upon the removal of Zn(II) by an external chelator resulting in a scrambling of the probes.

this gives the possibility to actively control the self-assembly process by using the Zn(II)-metal ions as regulatory elements.

The importance of the Zn(II)-metal ions emerged when we compared the self-assembly of ATP_F on the surface of Au NP **1** in the presence and absence of Zn(II) as a function of pH (Figure 4).[23] Whereas in the presence of Zn(II) a nearly constant SSC (2.3 ± 0.2 μM) was determined over the entire pH range, in the absence of Zn(II) the SSC dropped gradually upon increasing the pH, reaching a negligible value of 0.2 at pH 8.0. These results demonstrate two things: First, also in the absence of Zn(II), Au NP **1** is able to strongly bind oliganions as long as the pH is sufficiently low to protonate the secondary amines. Second, and more important, it shows that the Zn(II) ions act as "buffering agents" for the self-assembly process conferring a stability of the ensemble over a much larger pH-range. Evidently, the robustness of a system with such a buffering capacity would have a much stronger change of survival in a prebiotic scenario. It is reminded that the binding of nucleic acids and amino acids to mineral clays showed a very strong pH-dependence (see subsection 2.1).

The buffering capacity of Zn(II) could be exploited to regulate in a fairly precise manner the number of ATP_F-molecules bound to Au NP **1**. By dosing the amount of Zn(II) removed from Au NP **1** using a strong Zn(II)-chelator the number of surface-bound probe molecules could be regulated between approximately 18 (max. SSC) and 5 (min. SCC at pH 7.0). This process was found to be completely reversible, as the saturation of the depleted monolayer with newly added Zn(II) restored the original SSC.

2.3. Selectivity and Differentiation

Although appearing as a system deprived of any structural features that would permit selective interactions, Au NP **1** is actually able to discriminate between all 8 di- and trideoxyribonucleotides (*X*DP and *X*TP, with X = A, T, C or G).[24] This is a direct result of the fact that binding of small

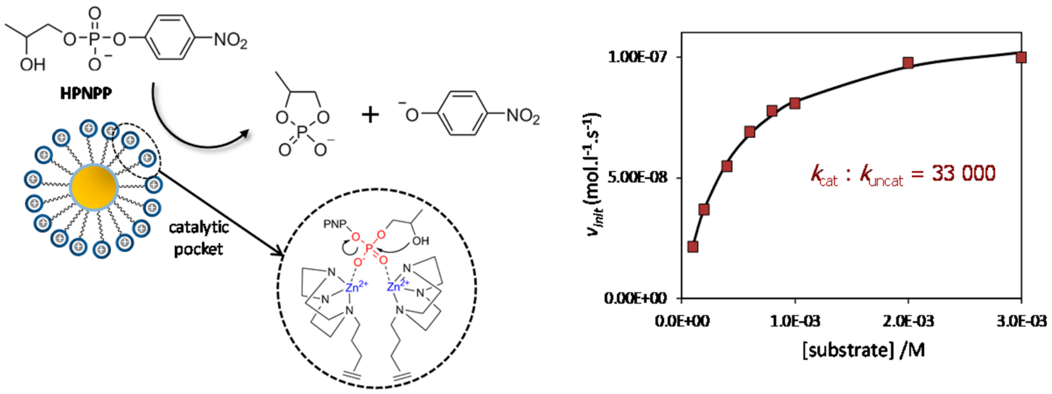

Figure 7. Transphosphorylation of 2-hydroxypropyl-*p*-nitrophenyl phosphate (HPNPP) catalyzed by Au NP **1** displays Michaelis–Menten saturation kinetics. Two neighboring TACN·Zn(II) complexes in the monolayer create a catalytic pocket in which the two metal ions cooperatively act on the substrate.

molecules to Au NP **1** is driven by a subtle interplay of electrostatic and hydrophobic interactions.[18] This discriminatory behavior was demonstrated through a newly designed multi-indicator displacement assay relying on the displacement of three fluorescent probes from Au NP **1** by nucleotides (Figure 5). Each nucleotide competes in a different manner with the probes resulting in the generation of a characteristic fingerprint output signal for each nucleotide. Principle component analysis (PCA) clearly illustrated the discriminatory behavior of Au NP **1** with respect to the nucleotides. As a general trend, it was found that purine nucleotides had a higher affinity for Au NP **1** compared to pyrimidine nucleotides and that trinucleotides had a higher affinity compared to dinucleotides.

A key feature of high-level organizations, as in cells, is the coexistence of many different compartments each of which with a chemical composition adapted to the function that needs to be performed. The clustering of molecules around a (nano)-particle, be it covered with a monolayer or not, defines the topological localization of a population of molecules, which can be considered as a first very rudimentary step toward the organization of organic matter. In a conceptual study, we have shown that a primitive form of self-organization takes place in a mixture of two different Au NPs and two different small molecules (a nucleotide and a peptide) leading toward two topologically distinct populations of molecules (Figure 6).[25]

This study relied on two features of Au NP **1** that are directly attributable to the presence of Zn(II) in the monolayer: *selectivity* and *affinity*. Competition experiments between phosphate probe **B** and carboxylate probe **C** revealed the selective binding of **B** to Au NP **1** in case both probes were present simultaneously. Such a selectivity was hardly observed when Au NP **2** with quaternary ammonium head groups was used. The increase in affinity both for phosphates and carboxylates originating from the presence of Zn(II) in Au NP **1** (as compared to Au NP **2**) emerged from binding studies in solutions with a high ionic strength.

As a consequence of these two properties, spontaneous self-sorting occurred in a mixture containing Au NP **1** and **2** and both probes **B** and **C**. That is, the selective high affinity interaction between Au NP **1** and **B** caused the exclusive localization of probe **B** on Au NP **1**, leaving probe **C** to interact exclusively with Au NP **2**. It was shown that the system could be reversibly switched between a self-sorted and mixed state through the removal of Zn(II) from Au NP **1** by a chelator and the renewed addition of Zn(II).

This study demonstrates several important features. First, Au NP **1** is able to capture selectively small molecules from a mixture driven by the selective interaction between the Zn(II) metal ions and the phosphate groups in **B**. Such selective interactions are at the basis of the differentiation and chemical evolution processes that will be discussed in section 4. Second, it shows that different populations of small molecules can coexist. Clearly, in this case, formation of the second population (probe **C** on Au NP **2**) is a passive process driven by the high selectivity of **B** for Au NP **1**. However, one can imagine that the concomitant presence of different organic monolayers (or coronas) containing, for example, containing different metal complexes or other (hydrophobic) recognition units, would result in the separation of mixtures of small molecules leading toward coexisting populations of molecules, leading toward a primitive form of differentiation. Third, simple chemical processes, like in this case the addition or removal of Zn(II) from the monolayer, can induce mass transport between different populations.

3. CHEMICAL TRANSFORMATION

A fundamental role of inorganic surfaces in the early stages of life is the catalysis of chemical transformation of organic molecules leading toward a greater structural variety. In the hypothesis that Au NPs are a good model for describing the successive phase of chemical organization in the early stages of life, this implies that the organic monolayer must be able to exert catalytic activity. In this section, we will illustrate two ways in which Au NPs can be involved in accelerating chemical reactions. Importantly, it will emerge that the multivalent nature of the monolayer plays an important role in determining the catalytic efficiency of the system. Elsewhere, we have extensively reviewed the catalytic properties of monolayer-protected gold nanoparticles in a variety of reactions.[26]

3.1. Catalysis in the Monolayer

Au NP **1** and analogues were found to be excellent catalysts for the transphosphorylation of 2-hydroxypropyl-p-nitrophenyl phosphate (HPNPP), which is a model compound used for mimicking RNA-hydrolysis (Figure 7).[27,28] Rate accelerations up to 4 × 10^4 were observed compared to the background reaction, ranking these systems among the best-performing Zn(II)-based synthetic catalysts for this reaction.[29−31] The

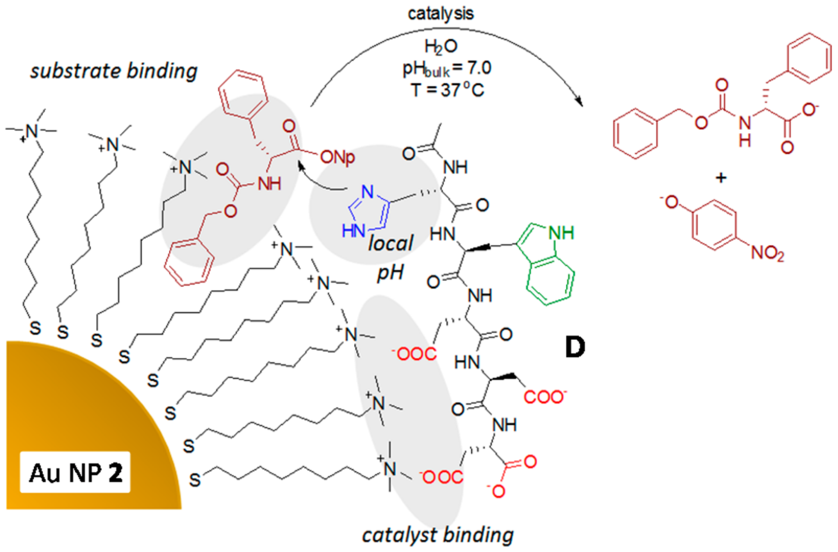

Figure 8. Coassembly of catalytic peptide **D** and the *p*-nitrophenyl ester of N-Cbz phenylalanine on the surface of Au NP **2** (see Figure 6) results in a rate enhancement for the cleavage of the ester by 2 orders of magnitude. The main reason for the rate enhancement is the increase in effective concentration of substrate and catalysts with additional effects caused by a higher local pH.

important role of the Au NP in organizing and orienting individual TACN·Zn(II) complexes emerged from the fact that a 600-fold lower second-order rate constant was observed for the monomeric catalytic headgroup.[27]

Within the context of this Account, several features related to the catalytic activity of Au NP **1** are of importance. First, the catalytic activity originates from metal ions (here Zn(II)) that are now embedded in the monolayer rather than the inorganic surface. Thus, this system represents a transitory phase in which catalysis has shifted from a heterogeneous phase to a hybrid heterohomogeneous phase. Second, like enzymes, these systems display Michaelis−Menten-like saturation behavior, implying that the catalytic activity can be described in terms of a dissociation constant (K_M) and a first-order rate constant (k_{cat}).[27] Third, detailed studies have shown that the catalytic efficacy of Au NP **1** results from the formation of catalytic pockets by two neighboring TACN·Zn(II) complexes in the monolayer.[28] Evidence for this came from the observation of a sigmoidal profile for the initial rate as a function of the amount of Zn(II) added. These experiments indicated that catalytic activity is only present in case the amount of TACN·Zn(II) complexes on the surface is sufficiently high to form neighboring complexes. This was confirmed by detailed studies on mixed monolayer studies composed of TACN·Zn(II) and triethylene-glycol-terminating thiols. These systems showed a significant drop in catalytic activity (k_{cat}) for systems with a low content of TACN·Zn(II) (<40%).[28] As such, these catalytic pockets resemble the active sites of metallonucleases in which multiple metal ions cooperatively cause the hydrolytic cleavage of the phosphodiester bonds in DNA or RNA. Clearly, having just TACN·Zn(II) complexes, Au NP **1** has a much lower complexity compared to such active sites, but it is not hard to image that the clustering of different organic molecules on a surface (with the ability to complex different metal ions) could lead to a variety of potential catalytic sites. In addition, it was recently shown by Scrimin et al. that local medium effects caused by the presence of other functionalities can further enhance the reactivity of these systems just like what happens in the active site of enzymes.[32]

3.2. Catalysis on the Monolayer

In section 2, we have shown that Au NP **1** has a strong capacity to concentrate small molecules on the monolayer surface and have speculated that this could intrinsically favor chemical reactions. Chmieleweski et al. have indeed reported that cationic Au NPs can promote the association and ligation of peptide fragments driven by the complementary electrostatic interactions between the peptide fragments and the monolayer.[33] We have recently shown that the self-assembly of histidine-containing peptide **D** on the surface of Au NP **2** triggers their esterolytic activity resulting in a more than 100-fold rate acceleration in the cleavage of the *p*-nitrophenyl ester of N-Cbz phenylalanine (Figure 8).[34] Self-assembly is a prerequisite for catalysis, as the peptides are not catalytically active at all in the absence of Au NPs. Detailed studies showed that colocalization of substrate and catalyst on the multivalent surface was the main reason for observing catalytic activity. The catalysis was further enhanced by a local pH at the surface that was 0.7 units higher than the pH of the bulk solvent, caused by the cationic quaternary ammonium groups. This increases the concentration of free-base imidazole which acts as the nucleophile during catalysis.

4. COMMUNICATION AND ADAPTATION

An essential feature of all living systems is the presence of signaling pathways that permit communication with the external world and the possibility to adapt to changes therein. In this section, we show that even a simple organized system as the one discussed here is able to develop a primitive response mechanism that conceptually bears resemblance to known signaling transduction pathways occurring in Nature. Finally, it is shown that the surface composition of small molecules on Au NP **1** may spontaneously adapt to the presence of external stimuli resulting in differentiation of the surface composition.

4.1. Signal Transduction

The affinity between Au NP **1** and peptides or nucleotides strongly increases as a function of the number of negative charges present in the probes. Recently, we have shown that this property can be used to install a simple signal transduction

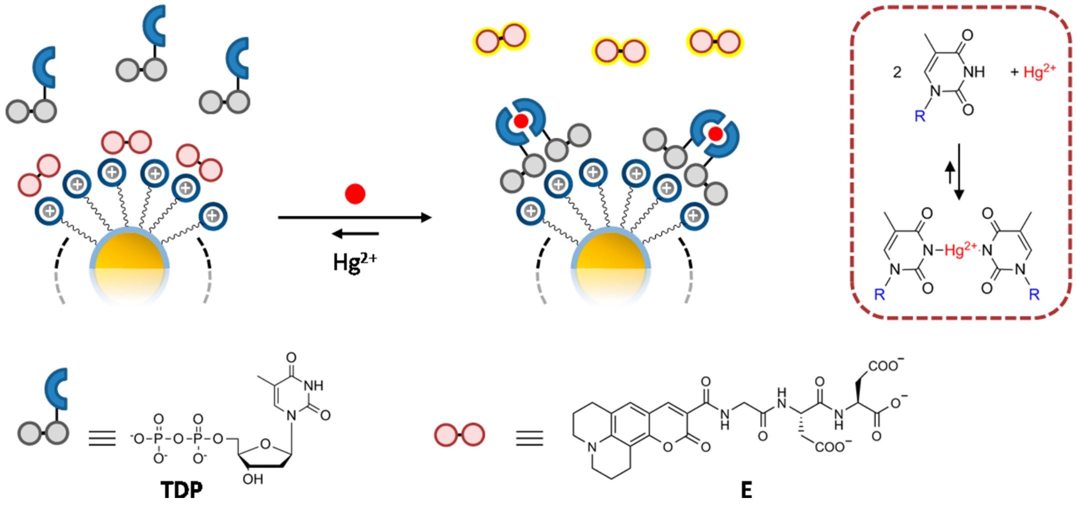

Figure 9. Installment of a rudimentary signaling pathway on the surface of Au NP **1**. Complex formation between TDP and Hg(II) leads to the formation of a ternary complex TDP·Hg(II)·TDP with a high affinity for Au NP **1** able to display fluorescent probe **E**.

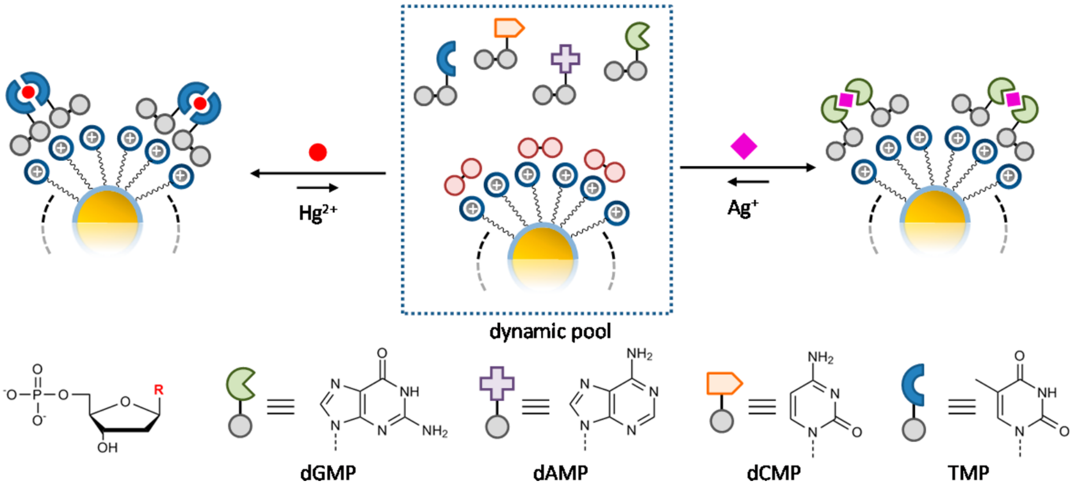

Figure 10. Chemical evolution of a dynamic system composed of Au NP **1** and the four nucleotides TMP, dAMP, dCMP, and dGMP is dependent on the added trigger. Whereas the addition of Hg(II) leads to the selection of TMP, addition of Ag(I) to the same system leads toward the selection of dGMP. This shows the potential of this system to develop into different directions depending on the external environment. It is pointed out that the self-selection experiments did not provide information on the exact chemical nature of the complexes formed between nucleotides and metal ions.

pathway exploiting ternary complex formation between Hg(II) and two nucleobases thymine of the type T·Hg(II)·T (Figure 9).[35] Multivalency is exploited when thymine nucleotides (T*X*P with *X* = M, D, T) are used, because in that case complex formation with Hg(II) results in the clustering of negative charges in the complexes and, thus, an increased affinity for Au NP **1**. This concept was demonstrated experimentally by observing an increase in fluorescence intensity originating from displaced probe **E** upon the addition of Hg(II) even at submicromolar concentrations of the analyte. An important feature of the system is that formation of the ternary complex between thymine and Hg(II) only indirectly leads to an output signal. Signal generation requires displacement of probe **E** from the Au NP through competitive binding of the ternary complex. It is the strength of this interaction that determines the efficacy at which ternary complex formation is transduced into a signal. It was indeed shown that the strength of the fluorescence output signal (for the same concentration of Hg(II)) was dependent on the type of thymine nucleotide T*X*P used (*X* = M, D, T).

4.2. Self-Selection

The Hg(II)-induced assembly of TXP on Au NP **1** is a result of the selective interaction between Hg(II) and the thymine nucleobase. We wondered whether this selectivity would be high enough for Hg(II) to self-select the thymine nucleotide from a mixture containing also guanine, adenine, and cytosine nucleotides (Figure 10). This would demonstrate the capacity of the system to install a self-selection mechanism, which could be considered a primitive form of adaptation.[36] Self-selection experiments were performed by adding Hg(II) to a mixture of Au NP **1**, probe **E** and a mixture of the four monophosphate nucleotides dGMP, dAMP, dCMP, and TMP.[37] The adsorption of nucleotides on Au NP **1** was monitored by sampling the composition of the dialysate obtained after ultrafiltration of the solution, which indeed revealed a selective depletion of TMP in the dialysate.

Importantly, a completely different result was obtained when the same experiments were repeated using Ag(I) instead of Hg(II). In this case, both LC/MS and fluorescence measurements indicated that the addition of Ag(I) to the identical starting mixture resulted in the self-selection of dGMP. This demonstrates the ability of the system to develop into different directions depending on the stimulus that arrives from the external environment. It can be envisioned that as a consequence of such local differences the hybrid inorganic–organic structures would start to differentiate and acquire different properties and functions.

5. CONCLUSIONS AND PERSPECTIVES

Were monolayer-protected gold nanoparticles involved in the origin of life ? Considering the unlikelihood that gold nanoparticles were present in the primordial soup, the answer is a definite no. Also the TACN-functionalized C9-thiol does not represent a valid candidate for being an early stage-of-life molecule. However, the key point that we want to make here is that all properties and functions of Au NP **1** that we have discussed in this Account originate from an organic monolayer of small molecules surrounding the inorganic gold core. In particular, processes such as self-assembly, concentration increase, and the catalytic transformation of bound molecules are precisely those attributed to inorganic surfaces in the early stages-of-life. The important point is that, in our model system, the role of the inorganic material (the gold nucleus) has been reduced to that of supporting and stabilizing the organic fraction. The importance of this role should not be underestimated though. The strong Au–S bond ensures a stability of the system even at concentrations at which, for example, a micelle, which is a conceptually related structure but lacking the inorganic core, could never exist. Thus, the gold core ensures the formation of a stable multivalent structure, which is essential for the functions described here. For many different materials, including those likely to have been present in the early stages of life, strong interactions with organic molecules having appropriate chelating groups have been described and, indeed, such interactions are considered essential to the functioning of the system. However, whereas in many origin-of-life hypotheses the role of the inorganic surface remains dominant in terms of controlling chemical processes, the results obtained from studying Au NP **1** indicate that that is not necessary. A corona of small molecules surrounding the inorganic surface could be already at an early stage becoming the dominant force in directing chemical processes by complexation of metal ions, recruiting new molecules, and catalyzing chemical transformations.

Abundant literature has appeared in the past decades on hybrid organic–inorganic structures. In addition to various metal particles covered with organic molecules,[38] examples include inorganic–organic mesoporous silicates,[39] metal–organic materials (MOMs),[40] and antifouling coatings.[41] Their application in fields such as molecular recognition, sensing, and catalysis makes it evident that an organic corona has the potential to develop a much richer chemistry than the inorganic support itself. Whereas at an early stage the inorganic material would be an essential support for guaranteeing the essential stability, the increase the interconnected organic matter surrounding such a support would at some point be sufficient enough to make the organic matter autosustainable.

In our opinion, monolayer-protected gold nanoparticles are an attractive model system to study the possible role of hybrid inorganic–organic structures in the early stages of life. This originates from the ease of preparation and functionalization, the high stability of these systems under a wide variety of conditions, and, most importantly, a relatively well-ordered monolayer. In particular, the latter aspect permits a clear manifestation of the effects originating from multivalency, which may be less evident in other systems. In our imagination, the earliest manifestations of hybrid inorganic–organic clusters would most likely have appeared as a less organized corona of organic molecules attached to an inorganic surface, be it two- or three-dimensional. It is pointed out that all studies described in this Account are performed with very simple structures. Just two types of Au NPs have been used in combination with a small series of nucleotides and peptides. This illustrates the robustness of the system and its properties. Within the context of the origin-of-life question, it is of interest to note that small nucleotides and peptides play a fundamental role both in the recognition and catalytic transformation processes. The results clearly demonstrate the effectiveness of such molecules in participating in recognition processes either through electrostatic interactions or the formation of coordination bonds.

We see the following interesting questions ahead of us. The first is whether the demonstrated properties can be transferred to an entirely organic structure, that is, lacking an inorganic core and whether such a process can be accompanied by a surface amplification mechanism. The second one is whether monolayer surfaces such as in Au NP **1** are capable of chiral recognition and whether chiral amplification mechanisms can be installed leading toward an enantio-enrichment of the entire system.

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Notes

The author declares no competing financial interest.

Biography

Leonard J. Prins (1974, Netherlands) is associate professor in the Department of Chemical Sciences at the University of Padova. He obtained his Ph.D. degree from the University of Twente, Netherlands with prof. David Reinhoudt in 2001. After postdoctoral research with prof. Peter Dervan at Caltech, Pasadena, CA, and Prof. Giulia Licini at the University of Padova, Italy, he started his independent career in 2004.

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