

Genetically Designed Peptide-Based Molecular Materials

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ABSTRACT With recent developments of nanoscale engineering in the physical and chemical sciences and advances in molecular biology, molecular biomimetics is combining genetic tools and evolutionary approaches with synthetic nanoscale constructs to create a new hybrid methodology: genetically designed peptide-based molecular materials. Following the fundamental principles of genome-based design, molecular recognition, and self-assembly in nature, we can now use recombinant DNA technologies to design single or multifunctional peptides and peptide-based molecular constructs that can interact with solids and synthetic systems. These solid-binding peptides have made significant impact as inorganic synthesizers, nanoparticle linkers, and molecular assemblers, or simply as molecular building blocks, in a wide range of fields from chemistry to materials science to medicine. As part of the programmatic theme, "Nanoscience: Challenges for the Future", the current developments, challenges, and future prospects of the field were presented during a symposium at the 237th ACS National Meeting held in March 2009. This Nano Focus article presents a synopsis of the work discussed there.

In materials science and engineering, for the last 25 years, "biomimetics" has meant mimicking biology through creating nano- and microstructures with complexity and architecture similar to those in biology, such as hard tissues with examples of sea shells, bones, spicules, nanoparticles, and thin films, with the desire that the functions would also be the same.^{1,2} Although there has been enormous progress in traditional structural biomimetics, the successes have been limited mostly in developing model micrometer-scale and surface structures and in a limited diversity of functional materials systems.^{3–5} In biology, among the major building blocks, proteins are central to the assembly of biological materials that have highly controlled nanostructures and functions.^{6–9} Under the genetic control of organisms, biological hard tissues are assembled in aqueous environments in mild physiological conditions using biomacromolecules: primarily proteins but also carbohydrates and lipids.^{10–13} Proteins are actively involved in the following functions:^{14–18} transport of raw materials; enzymatic reactions for inorganic synthesis; controlled nucleation, growth, and morphogenesis. In addition, they consistently and uniformly self- and co-assemble subunits into

short- and long-range ordered structures. Therefore, as the first step in molecular biomimetics, peptides having shorter sequences compared to proteins are selected through combinatorial mutagenesis as the first-generation peptides based on the fast evolution carried out for a specific material interaction.¹⁹ These genetically engineered peptides for inorganic solids (GEPs)¹⁹ are now becoming ubiquitous in peptide-based hybrid systems.^{20–25} Here, we describe the major steps in the selection and design of solid-binding peptides, their binding and assembly characteristics studied experimentally and computationally, evolutionary approaches for next-generation peptides *via* bioinformatics toward tailored multifunctional molecules, genetic approaches in creating fusion molecular constructs, and practical implementation in nanotechnology, biotechnology, materials science and engineering, and medicine, illustrated with examples presented at the symposium as well as from our own work (Figure 1).

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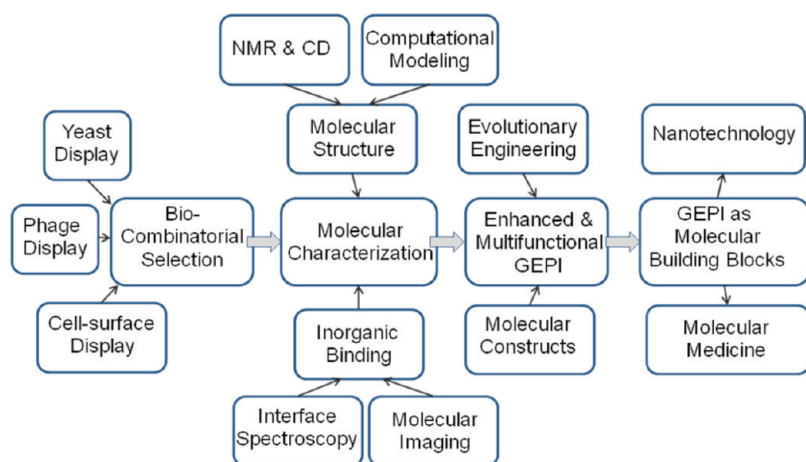


Figure 1. Flowchart of biocombinatorial selection of solid-binding peptides, their molecular structure and binding characterization, tailoring for enhanced functionality and utility.

Solid-Binding Peptides. There are several ways to obtain inorganic solid surface-specific proteins. The traditional approach, extraction from hard tissues, was heavily used during the 1990s and involves complex and time-consuming procedures including isolation, purification, and sequence and structure analysis of proteins.^{26–41} Another method is to use existing proteins that are known to bind inorganic surfaces, for example, amelogenin,^{13–15,41–43} a major protein in enamel, sillicatein (extracted from skeletons of diatoms),^{16,27,29} and magnetite-binding peptides from magnetotactic bacteria.^{34–36} Although there have been significant successes, generally they have had limited applicability. This is mainly because of the large sizes of natural proteins (usually more than 100 amino acids long), the requirement of specific physiological conditions, and the presence of a cohort of proteins that operate simultaneously, such as during biomineralization processes.^{13,43} Usually, these proteins bind nonspecifically to solids, and the primary mechanism is likely to be chemisorption or physisorption.^{44,45}

Another approach is first-principles design of proteins through molecular-recognition principles, that is, molecular complementarity between the protein (molecular architecture) and solid-surface crystallography (atomic lattice).^{46,47} Clearly, the molecular recognition of solids by proteins is far from understood; therefore, this approach is not yet a realistic one. A more rational

approach to obtain surface-specific proteins would be molecular design of recombinant proteins *via* genetic engineering techniques. In the absence of the knowledge of precise surface topography of a given solid material, the complementary molecule that would fit tightly with high binding energy (large K_d) could be selected using site-directed mutagenesis of the existing proteins or genetic selection of polypeptide motif using *in vivo* and *in vitro* peptide libraries. This latter approach has been successful during the past decade identifying numerous peptide sequences with affinity to many practical solid material systems.^{48–57}

Selection of Solid-Binding Peptides Using Peptide Display Libraries. Solid-binding peptides are selected through affinity-based biopanning protocols including phage display^{48,53} and cell-surface display⁴⁹ techniques. Biopanning steps consist of contacting the peptide library with the material of interest (in the form of either powder or solid substrate), then washing out weak or nonbinders (chemically or physically), and repeating the process to enrich for tight binders to select a subset of the original library exhibiting the ability to interact strongly with the desired surface.¹⁹ During the biopanning step, a minimum of 3–5 cycles of enrichment is usually performed. Generally, in early rounds, low-affinity binders can be accessed if the selection is performed under mild conditions. In later rounds, as the conditions get harsher, tight binders are also

recovered. Because the chimera is encoded within the phage genome or on a plasmid carried by the cell, the identity of the selected sequences (e.g., their amino acid compositions) can be deduced by DNA sequencing.⁵⁸ Many groups,^{19–25,59–63} including ours, have selected peptides for a variety of materials including noble metals (Au, Pt, and Pd), structural metals (Ag, Fe, and Ti), oxides and semiconductors (Cu₂O, GaAs, CdS, ZnS, TiO₂, and ZnO), minerals (mica, hydroxyapatite, calcite, and sapphire), or biocompatible substrates (silica, titania, and alumina). Usually, commercially available phage libraries, such as M13,⁴⁸ or cell surface⁵¹ libraries (e.g., Flitrx) have been used, although some groups have developed their own library systems.

Molecular Recognition of Solids by Peptides.

In the design and assembly of functional inorganic solids with addressable structures using peptides as synthesizers, catalyzers, couplers, molecular templates, and scaffolds, it is desirable to understand the nature of peptide recognition and binding onto solid materials.¹⁹ The knowledge of the chemical and physical structure of the molecular interface would allow the manipulation of the peptide molecular architecture and its function.⁶⁴ Clearly, the goal is to control the solid/biological interface, including thermodynamics, structure, and function, similar to the biological protein's control over the mineral (silica, magnetite, calcite, and hydroxyapatite) in the formation of a myriad of functional hard tissues in biological systems, such as bones, teeth, spicules, spines, shells, nanoparticles, and thin films.^{1,2,10,17} Although considerable research has been directed toward a general understanding of proteins binding to solids, it is not yet clear how proteins recognize an inorganic surface and how this could be manipulated to control the behavior of the solid. This problem is similar to protein–protein recognition in biology^{65–68} in the current hybrid systems, the problem reduces to one of peptide/solid interface. Here, the peptide is relatively small, *ca.* 10 amino acids long (1 kD), and the inorganic solid is relatively flat but with atomic and molecular features with a variety of surface lattices.⁶⁵ In general, the specificity

of a protein for a surface may originate from both chemical (e.g., hydrogen bonding, polarity, and charge effects) and physical (conformation, size, and morphology) recognition mechanisms.^{69–71} For a given system, all of these mechanisms may be significant, to varying degrees depending on the peptide sequence, chemistry, and topography of the solid surface, and the conditions of the solvent (water). The molecular architecture (conformation) of the peptide on the specific solid leads to its specific interaction with the surface since amino acid sequence, not the content of the amino acid, plays the major role in peptide molecular recognition of solid surfaces.⁶⁵ Despite considerable computational and experimental work in this area, we are far from a clear understanding of the mechanism of how peptides recognize solids.^{72–76} The understanding of the peptide–solid interactions that lead to binding and assembly can only be accomplished using GEPIs with well-known affinity and selectivity to materials of known surface structures.⁶⁵ Nonetheless, the prospect of utilizing the peptide sequence to control solid behavior, that is, genetically engineering novel functional materials systems, has great appeal.^{19,77} As we demonstrate here, significant progress has already been achieved, from nanoparticle synthesis to assembly of complex materials in peptide-based inorganic systems.

Quantitative Molecular Binding and Assembly of Peptides on Solids. As in any molecular system, it is essential to have a knowledge base regarding the binding, kinetics, and assembly of peptides on solids, simply for practical implementation of GEPIs.^{19,58,77} The simplest techniques used for rapid monitoring of peptide adsorption and binding are fluorescence microscopy (FM) and enzyme-linked immunosorbent assay (ELISA); these are now both routine tools for affinity and selectivity tests and are an essential part of the screening protocol in many laboratories.⁷⁷ Neither FM nor ELISA, however, is quantitative. Detailed processes of adsorption of peptides on solids could be readily obtained using quartz crystal microbalance (QCM)^{78,79} and surface plasmon

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resonance (SPR) spectroscopy.^{79–81} These techniques provide molecular binding kinetic parameters under various protein concentrations, solution properties (e.g., pH and salinity), and solid surface conditions. Other more conventional spectroscopic techniques, such as X-ray photoelectron spectroscopy (XPS), time-of-flight secondary ion mass spectroscopy (TOF-SIMS),⁸² Fourier transform infrared spectroscopy (FTIR), and others, may also provide a fingerprint of peptide adsorption, with different degrees of success.⁸³ Although difficult to carry out (because of signal from the solid overwhelming that of the biomolecule), the application of solid- and liquid-state nuclear magnetic resonance (NMR) spectroscopy provides quantitative information on molecular conformations of peptides, essential knowledge toward the understanding of the mechanism of polypeptide binding onto solids.⁸⁴ Circular dichroism (CD)⁸⁵ and attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR)⁸⁶ are also among the techniques providing information on the peptide structure in solution as well as on the surface. Most GEPIs have short sequences that allow them to adopt many different possible conformations in solution. As the peptide binds to the surface, it is likely to go through various stages of binding processes. These dynamic conformation changes, in addition to surface diffusion and assembly processes, can be observed at molecular scales using techniques such as atomic force microscopy (AFM),⁸⁷ coupled with QCM and SPR. Such obser-

vations are providing better insight into the phenomena of specific recognition of solids by peptides, beyond that which can be explained with simple Langmuir models, to models that take into account not only peptide–solid interactions but also inter- and intramolecular interactions, as well.^{85,87}

Finally, molecular modeling of peptide/solid interface interactions will lead to rapid evaluations of various types of hybrid interfaces.⁸⁸ These molecular dynamics studies, which make use of computational chemistry, biology, and physics, are still in their infancy but are expected to provide protocols in the near future through the implementation of model experimental systems coupled with theoretical approaches.^{72–76} A detailed understanding of the peptide recognition and assembly processes will inevitably lead to better insights into design of peptides for tailored binding.

Evolutionary Engineering of Next-Generation Peptides with Enhanced Binding and Functional Characteristics. In nature, cycles of evolution and mutation may lead to improved progeny. The biological hard tissues, which provide inspiration to researchers in biomimetics, are the result of millions of years of evolution.¹⁰ Although combinatorial genetic techniques permit the identification of peptides recognizing specific inorganic materials, molecular libraries may be limited in size to cover the evolutionary process toward finding the best sequences. In the evolutionary engineering of solid-binding peptides, one may utilize the biocombinatorially selected peptides as the first-generation peptides, and then introduce cycles, mutations, and genetic design approaches to obtain the next generation(s) of peptides. Here, one may utilize knowledge-based approaches introduced by various tools such as bioinformatics,⁸⁹ site-directed mutations, conformational constraints, and multimerizations.^{90,91} Peptide affinities can be tuned with material specificity and other functionalities (*i.e.*, inorganic synthesis) for desired application areas. On the basis of the known sequences of inorganic binding peptides and their relative solid-binding affinities, recent developments in bioinformatics provide a means to design

peptides with selective binding to materials. In this approach, we combine sequence alignment techniques and produce unique, material-specific scoring matrices.⁸⁹ These computational methods developed using bioinformatics allow design of peptides with enhanced and multifunctionalities with inorganic material specificities.

Multifunctional GEPI-Based Fusion

Proteins. GEPIs selected, engineered, and tailored can be combined to create multifunctional molecular constructs bringing together different nanostructures. Here, GEPI-connected materials might consist of different nanoparticles (e.g., metal and metal oxides) or material and biological molecules (e.g., cancer-probing).^{92,93} Bifunctional peptides can be synthesized chemically or genetically. In genetic approaches, cloning and expression can be used to produce desired peptides as part of larger functional proteins such as enzymes. While the chemical synthesis methods are appropriate for small peptides (up to ~50–70 amino acids), recombinant DNA methods^{94–96} have advantages in producing larger peptides, introducing conformational constraints, and spatial and orientation control.

Implementations of GEPI in

Nanotechnology. The ability of GEPIs to recognize inorganic surfaces provides a unique capability in the self- and directed-assembly of nanodimensional objects and molecules.^{90,91} One of the

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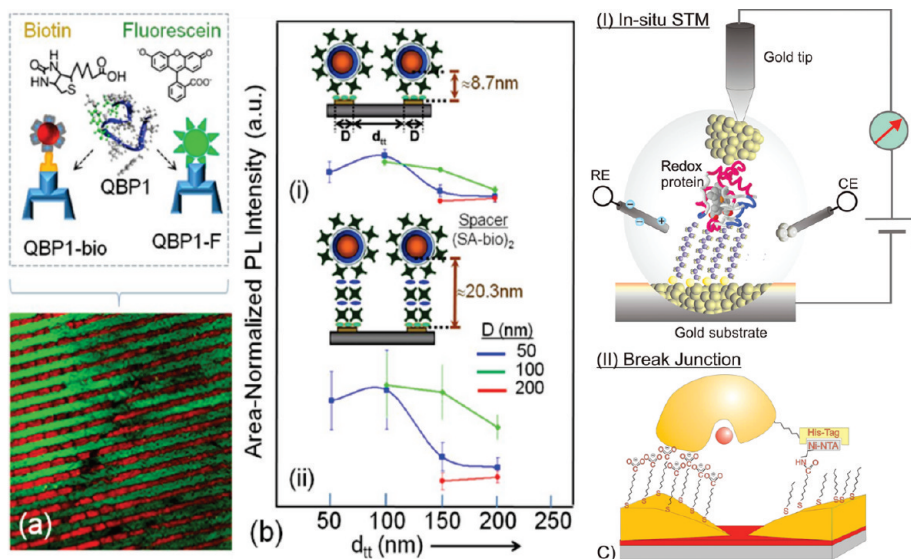


Figure 2. (a) Directed-assembly of QBP1-F (i) on a quartz substrate prepatterned using QBP1-bio/SA-QD.⁸⁹ (ii) Digitized overlay image was recorded by using QD605 (for the QD) and FITC (for fluorescein) filters. The original micropattern was made using soft lithography. (b) QD nanoarrays with surface-plasmon-enhanced photoluminescence. Area-normalized PL peak intensity from QDs in a particular pattern at different QD–metal distances of 8.7 and 20.3 nm. Schematic illustrations show the structure of hybrid nanoassemblies.⁸⁹ Reproduced from ref 90. Copyright 2009 IOP Publishing (<http://www.iop.org/EJ/journal/Nano>). (c) Examples of a possible experimental setup for determining electron transport through an enzyme using thiols as linker molecules, with potential replacement by a GEPI. Image courtesy of Andreas Offenhäuser, Institute of Bio- and Nanosystems, Jülich, Germany.

key areas for application of inorganic solid-binding peptides is in nanotechnology, especially as linkers, assemblers, and bridging molecules.^{90,91,97} Overcoming the limitations imposed by thiol- and silane-based chemical linkers,^{98,99} by far the most direct application of GEPI is surface functionalization of nanoparticles. In this case, materials commonly used to synthesize nanoparticles, including metals such as gold or silver, oxides such as silica or alumina, or semiconductors such as ZnO or ZnS, could be functionalized with solid-specific peptides, such as gold-, silver-, silica-, alumina-, ZnS-, and ZnO-binding peptides.^{90,91,97}

Another application is in targeted assembly of nanostructures on patterned complex solid surfaces. In this case, the particle is either functionalized with the GEPI conjugated with the molecule of interest (e.g., QBP1-fluorescein) or a biotinylated GEPI is used.⁹⁰ The latter provides a means for directed-assembly of streptavidin-functionalized quantum dots (SA-QDs) on specific regions of the substrate (Figure 2a). Further improvement in this system is the use of a bifunctional GEPI, known as

AuBP1-QBP1.⁹¹ Here, one end of the peptide is specific to one material (e.g., Au) and the other end to another material (e.g., silica), enabling the immobilization of gold nanoparticles on silica surface, or *vice versa*. Using this approach, we developed a protein-enabled strategy to fabricate QD nanoarrays and observed up to a 15-fold increase in surface-plasmon-enhanced fluorescence.⁹¹ This approach permits comprehensive control both laterally (*via* lithographically defined gold nanoarrays) and vertically (*via* the QD–metal distance) of the collectively behaving assemblies of QDs and gold nanoarrays by way of biomolecular recognition. Specifically, we demonstrated the spectral tuning of plasmon resonant gold nanoarrays and self-assembly of gold-binding peptide-functionalized QDs on them in a stepwise fashion with a concomitant incremental increase in separation from the metal surface through biotin-streptavidin spacer units (Figure 2b).⁹¹

Another exciting area for the utility of GEPI goes beyond metal recognition and molecular binding for the assembly of functional nanostruc-

tures; these inorganic-binding peptides may also be used as electron (or proton) transporting molecular bridges. For example, a large area of bionanoelectronics is concerned with the integration of biological cells and biomolecules with electronics.^{100,101} Here, the goal is to develop a broad range of functional devices toward establishing a communication interface between biological materials and electronic components and, therefore, to study biomolecular and cellular functions. Once accomplished, this would allow proteins and cells as nano- and microcomponents in higher-level functional devices for recognition or sensing, such as diagnostics and biosensors (Figure 2c). The GEPIs with the appropriate electron and proton transport properties could be designed *de novo* by incorporating, in their material-specific sequences, amino acids with π -conjugated electrons to produce semiconducting behavior.¹⁰¹ The peptides could be those that bind to gold, platinum, or palladium (AuBP, PtBP, and PdBP, respectively),¹⁹ which may also be genetically fused to the enzymes of interest. The use of GEPI would overcome the limitations imposed by both the use of thiol-based chemistries and the use of gold as the electrode material.

While solid-binding peptides are used as molecular linkers to immobile nanoparticles, quantum dots, and biomacromolecules on solid surfaces and substrates, there is another significant, but only recently unexplored, area, which is that GEPIs could be used as molecular erectors for targeted immobilization of functional inorganic nanoparticles on biomolecular substrates, such as designer proteins,¹⁰² virus capsids,¹⁰³ and DNA lattices.¹⁰⁴ All of these biomolecules provide precise means to immobilize nanoparticles on spatial positions on molecular structures which themselves self-assemble into organized architectures, thereby, providing addressable molecular platforms. In each of these cases, the functionalization of GEPIs could be performed either by chemical linking or by genetic fusion using recombinant DNA approaches. For

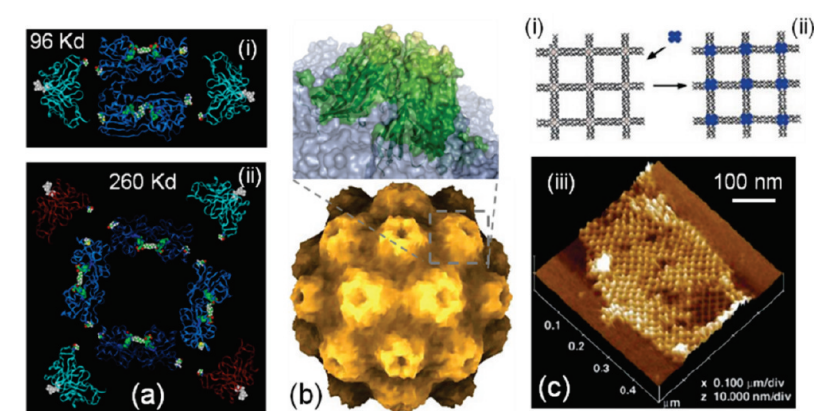


Figure 3. Examples of protein, virus, and DNA molecular templates for potential GEPI genetic conjugation for enhanced functionality for (a) multifunctional self-assembled antibodies for molecular probing⁹² or (b) highly enriched microenvironment offered by turnip yellow mosaic virus-coated surface.¹⁰⁵ (c) A 4 × 4 DNA cross tile for potential GEPI conjugation toward directed assembly of functional nanoinorganics.¹⁰⁶ Panel (a) courtesy of Carston Wagner, University of Minnesota. Panel (b) courtesy of Qian Wang, University of South Carolina. Panel (c) reproduced from ref 106. Copyright 2003 AAAS (<http://www.sciencemag.org/>).

example, in protein nanorings that are pseudo-2D molecular substrate, the designed protein could provide a precise template for the conjugation of the GEPI.⁹¹ The protein has various sizes, shapes, and functional positions for numerous attachment options (Figure 3a). In the second example (e.g., plant viruses, such as turnip yellow mosaic virus (Figure 3b)), the protein shell comes in a variety of sizes, shapes, symmetry,

and organization, all providing genetic functionalization of the protein capsid for specific utility.^{103,105} Finally, DNA, beyond its use as genetic duplication and storage in biology, is also useful as an engineering material for construction of molecular tiles with nanometer-scale feature resolution. Organized in mostly two-dimensional symmetrical, self-assembling nanostructures, DNA tiles (Figure 3c) offer great potential for

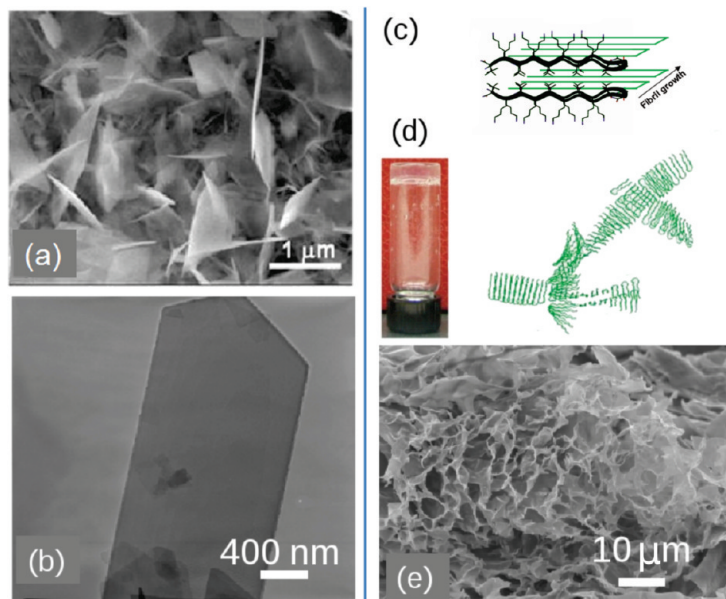


Figure 4. Examples of applications of GEPI in regenerative medicine. (a) Scanning electron and (b) transmission electron microscopy of crystalline hydroxyapatite particles formed in the presence of HA-binding peptide, HABP1.⁶³ Peptide-amphiphile-based hydrogel offers prospects in injectable molecular scaffolding for hard tissue engineering. (c) Molecular structure, (d) demonstration of a stable gel, and (e) scanning electron microscopy image of the gel. Panels (c) and (d) reproduced from ref 64. Copyright 2009 American Chemical Society. Panel (e) courtesy of Joel Schneider, University of Delaware.

nanofabrication of materials and objects with ever smaller features.^{104,106,107}

GEPI Applications in Regenerative Medicine.

In reconstructive and regenerative medicine, a major ongoing challenge is the successful repair or replacement of hard tissue, such as enamel, dentin, cementum, or bone.^{108–112} In a recent study, combinatorially selected peptides with high binding affinity to hydroxyapatite (HA) were shown to regulate calcium phosphate mineral formation in an enzyme (alkaline phosphate)-mediated reaction.⁶³ Specifically, we demonstrated that a strong HA-binding peptide, HABP1, accelerates and regulates formation of crystalline calcium phosphate in a mineralization solution, while a non-binding or a control peptide does not. The HA-mediated biomineralization results in elongated, thin, and plate-like particles (Figure 4a,b).⁶² A variety of GEPIs that can control mineral formation, morphology, and crystallography can have major impact, especially if many such peptides can be selected or designed with desired induced functions in the repair or regeneration of specific hard tissues.

In clinical applications, injectable molecular scaffolds are desirable as they can be placed at the defect site with three-dimensional matrix formations.^{113–116} These have advantages compared to those that are prepared *ex situ* and introduced into the defect even if they present similar mechanical and physicochemical properties with the living hard tissues. Peptide hydrogels are becoming more significant since they facilitate formation of scaffold materials that can be used in the absence of chemical cross-linking agents or assembling reactions.¹⁰⁹ These synthetic molecules may have adverse effects to the surrounding tissues. Peptide hydrogels also mechanically resemble the native extracellular matrix (ECM). As an example, a 20 amino acid residue peptide hydrogel, MAX8, has been shown to self-assemble into a three-dimensional hydrogel network (Figure 4c–e).¹¹⁴ By molecularly integrating GEPIs with these in-

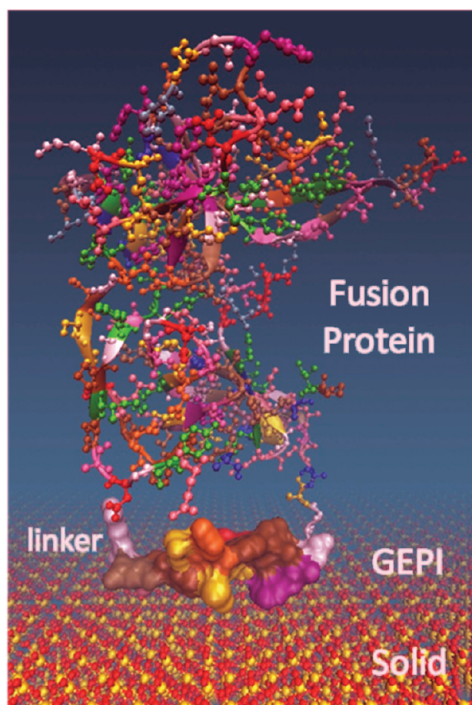


Figure 5. Model of mutant pIII protein of M13 phage, representing a functional protein (e.g., an enzyme or a probe molecule) containing quartz-binding peptide binding to quartz (100) surface. The GEPI and the protein attached with a simple GGG linker and represent a genetic fusion bifunctionalized as both a solid binder and a functional protein. The hybrid system offers a wealth of fundamental scientific challenges as well as opportunities for implementations for novel practical systems.

jectable hydrogels, they would be endowed with an inherent functionality, such as controlled mineralization. These mineralizable fibrillar gels may be highly effective hybrid molecular constructs, exceptional candidates for tissue engineering. In regenerative medicine, both cell-to-cell and cell-to-material interactions are considered.^{111,112} Understanding the mechanism of cell-to-material interactions, facilitated by GEPIs, may assist in the control of various biological processes such as vascularization.^{107,108,113} Cell-to-cell interactions can also be assisted *via* these peptides toward controlled cellular self-assembly, which may be adapted in developing cocultures models.^{109,110} Therefore, HA-binding peptides that are easily incorporated into peptide-based hydrogels and control biomineralization offer exciting prospects in the coming years in hard tissue regeneration and also con-

trol integration of soft (cartilage) and hard (bone) tissues.

Future Prospects: Fundamental Questions and Practical Implementations of GEPI.

The ability to create designed interfaces using solid-binding peptides between the biological and materials worlds opens both exciting fundamental scientific questions as well as practical applications of these molecular materials that can be genetically controlled and manipulated (Figure 5). On the one hand, the understanding of the molecular recognition of inorganic solid substrates with selected/ designed peptides is the cornerstone of the peptide/protein-based materials technologies of the future.¹⁹ These technologies will inevitably form the basis of proteomics,¹¹⁷ pharmacogenomics,¹¹⁸ protein biosensors,¹¹⁹ tissue engineering,¹⁰⁹ industrial enzymes,¹²⁰ and nanoparticle-based nanotechnologies,^{121–123} with major impact in medicine (e.g., nanoparticle-based cancer probing) and other areas. Com-

putational approaches^{124–126} toward understanding peptide–solid interactions, such as molecular dynamics, whole-atom, or *ab initio* approaches, as well as peptide kinetics and assembly on solid surfaces, such as kinetic Monte Carlo techniques, all require quantitative experimental observations at high spatial resolutions and under various experimental conditions. These approaches also require the knowledge of the molecular architecture of the peptides that depend on their specific amino acid sequences, their stability, and conformational energetics at the solid surface as well as in water.^{65,87} The required knowledge base also includes restructuring of the water at the solid surface as well as surrounding the peptide. The prospect of new peptides, beyond first-generation species selected through biocombinatorial techniques, with enhanced binding, assembly, linking, and other functionalities (e.g., electron transport), offers new challenges in

molecular design using computational biological (e.g., bioinformatics) as well as genetic manipulations.

As in any self-assembling system, such as metallic atoms on semiconducting substrates during the 1970s and 1980s leading to vacuum-based technologies toward practical microelectronics and magnetics,^{127–129} and synthetic linker molecules, such as thiols and silanes during the 1980s and 1990s leading to self-assembled monolayer based systems in nonwater solvents,^{130,131} the GEPIs^{19,58,77} also offer major challenges in the understanding of fundamental aspects of binding to and assembly on solids, with enormous opportunities in using these peptides in the development of a new generation of peptide-based molecular materials and systems, based in water, both in practical nanotechnology and molecular medicine during this decade and beyond. The coming years will no doubt bring challenges as well as opportunities in peptide-based materials and systems.

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