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Review

Molecular biomimetics: Utilizing nature's molecular ways in practical engineering ☆

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Abstract

In nature, proteins are the machinery that accomplish many functions through their specific recognition and interactions in biological systems from single-celled to multicellular organisms. Biomolecule–material interaction is accomplished via molecular specificity, leading to the formation of controlled structures and functions at all scales of dimensional hierarchy. Through evolution, molecular recognition and, consequently, functions developed through successive cycles of mutation and selection. Using biology as a guide, we can now understand, engineer and control peptide–material interactions and exploit these to tailor novel materials and systems for practical applications. We adapted combinatorial biology protocols to display peptide libraries, either on the cell surface or on phages, to select short peptides specific to a variety of practical materials systems. Following the selection step, we determined the kinetics and stability of peptide binding experimentally to understand the bound peptide structure via modeling and its assembly via atomic force microscopy. The peptides were further engineered to have multiple repeats or their amino acid sequences varied to tailor their function. Both nanoparticles and flat inorganic substrates containing multimaterials patterned at the nano- and microscales were used for self-directed immobilization of molecular constructs. The molecular biomimetic approach opens up new avenues for the design and utilization of multifunctional molecular systems with wide ranging applications, from tissue engineering, drug delivery and biosensors, to nanotechnology and bioremediation. Here we give examples of protein-mediated functional materials in biology, peptide selection and engineering with affinity to inorganics, demonstrate potential utilizations in materials science, engineering and medicine, and describe future prospects.

Keywords: Molecular biomimetics; Inorganic-binding peptides; Multifunctional proteins; Hybrid materials and systems; Bionanotechnology

Contents

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1. Introduction – lessons from nature and molecular biomimetics

Nature has evolved mechanisms of simplicity and elegance to synthesize soft and hard tissues exhibiting remarkable functional properties [1–4]. Nature achieves these feats of engineering by making use of molecular building blocks and by controlling materials assembly in a hierarchical manner from the nano- to the macroscale [5–7]. With a growing understanding of the processes involved came the realization that biological principles may have applications for solving problems in human-made systems. There is indeed a rich and long history of gaining inspiration from nature's biological structures to design practical materials and systems. Biomimeticists have traditionally focused on emulating or duplicating biosystems using mostly synthetic components and conventional approaches [1–3]. By merging recent advances in molecular biology [8,9] with state-of-the-art engineering and physical sciences [10–12], the new goal in the emerging field of molecular biomimetics is to shift biomimetic materials science away from imitating to engineering materials as nature does to perform artificial functions from the molecular scale up [7]. The new research is focused on combining proven biomolecular tools with synthetic nanoscale constructs to make molecular biomimetics a full-fledged methodology.

Nature provides abundant examples of multifunctional materials, devices and systems that scientists could investigate to understand the bases of synthesis, formation and function, and engineers could then emulate their practical utility in everyday applications. In Fig. 1, we present the four examples from our previous research where proteins control engineered material systems formation in which both components, proteins and inorganics, are essential for their synthesis, assembly and function [13–17]. For example, in magnetotactic bacteria (Fig. 1A), a biocompass is made of aligned magnetosomes that are composed of protein-based membrane compartments that control Fe^{2+}, Fe^{3+} and O^{2-} ion transport, synthesis, nucleation and morphogenesis of the magnetite (Fe_3O_4) nanoparticles. Our second example is from an Antartic sponge; although residing 200 m under the ocean, *Rosella racovitzea* has a symbiotic relation with green algae that live within its barrel-shaped body [13]. This is possible because of the silica-based spicules that collect and transmit light effectively across the outer wall of the sponge (Fig. 1B). Both the spicular tip (a lens) and the shaft (optical fiber) are molecular composites of silica and bound proteins that provide the structural, architectural and functional properties to the spicular system. The third is a classic biomimetic example: mother-of-pearl, the natural armor of mollusks' shells. The interior of the shell is constituted of nacre, a layered and segmented hybrid composite of aragonite (orthorhombic $CaCO_3$) and a biopolymer mixture, i.e. nanostructurally integrated proteins and polysaccharides (e.g. chitin) with a 95/5 inorganic/organic volume ratio (Fig. 1C). In spite of what appears to be rudimentary components, both the architecture of the soft and hard phases, i.e. the "bricks and mortar", and their chemical and mechanical coupling result in this unique biocomposite with the highest specific toughness and fracture strength of all known ceramic-based materials [14,15]. The fourth example is enamel; it is the crown of the tooth, the hardest material in the body, providing protective cover to the dental tissues of mammalians [16]. On the underneath, the enamel is integrated to dentin, a softer and, therefore, tougher bone-like tissue that provides an energy-absorbing cushion during cutting and chewing. The unique woven architecture of enamel provides the essential network resistance to the mixed stresses during mastication, thereby preventing premature fracture or failure (Fig. 1D).

The examples above and countless others have unique architecture and functions, providing biodesign lessons to engineers and technologists. In addition to an inorganic material, each biosystem involves many proteins that may come into play spatially and temporally in a complex bioscheme during the transport of species, synthesis, fabrication, system integration and networking. Understanding the roles of proteins during biofabrication would provide means to develop protocols for regeneration or emulation of these tissues, as well as to develop novel hybrid materials and systems with unique physical properties [17]. For example, in enamel, more than 40 different proteins are known to take part in its formation; and in nacre, perhaps 10–20 different ones do the same. The complexity of understanding the biochemical and biophysical nature of each of the proteins, their multifaceted interactions and their roles in the biofabrication and functional performance of the tissue or organ is enormous, and requires a gargantuan task for immediate practical utilization in materials science. While this major goal is being undertaken in proteomics and genomics, simple polypeptides with specific functions could be incorporated into mainstream materials science and engineering in more practical ways. Molecular biomimetics, through genetic selection of inorganic-binding peptides and their tailoring through post-selection engineering would be one way to achieve the immediate utilization of nature's molecular ways to make practical materials with novel applications [17].

2. Genetically engineering proteins for inorganics (GEPI)

Proteins offer three unique advantages in developing future materials and systems: molecular recognition,

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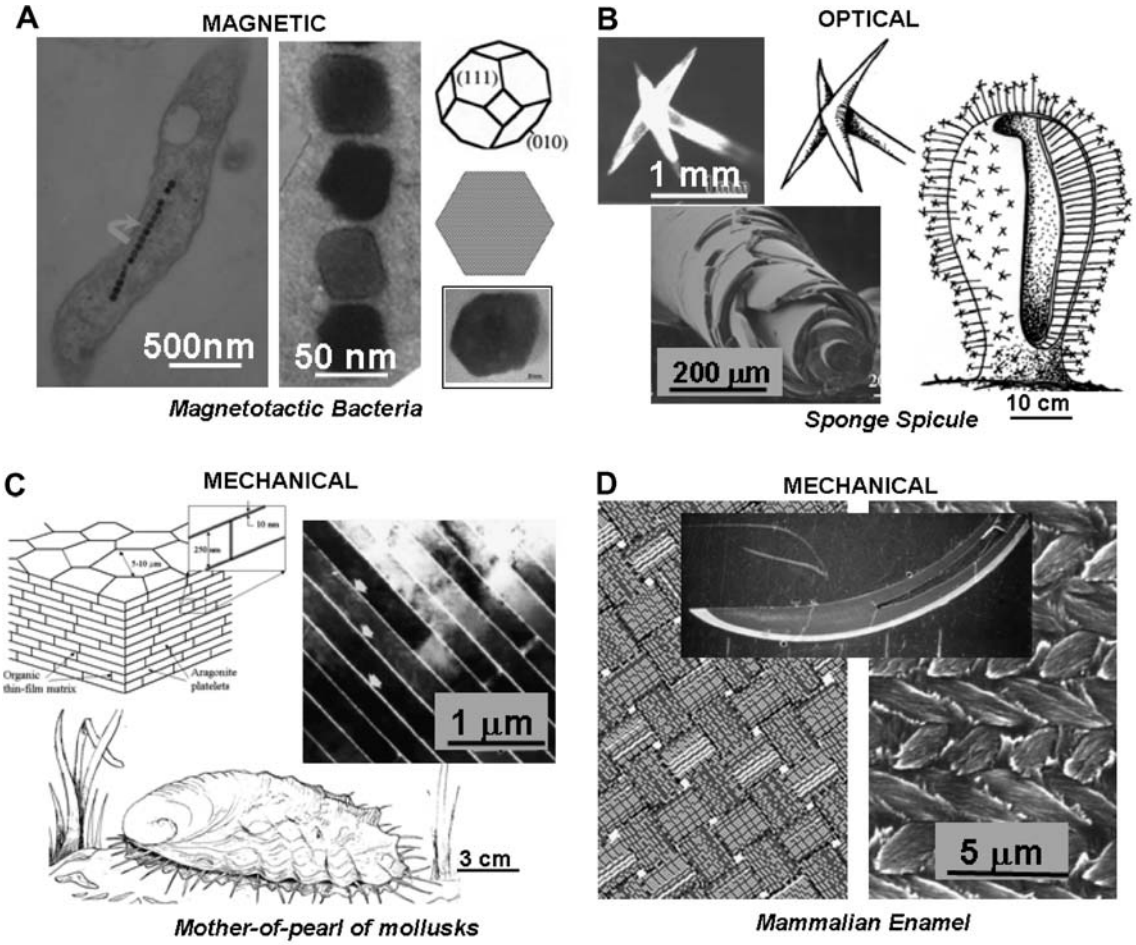

Fig. 1. Examples of functional biological materials systems: (A) Magnetotactic bacteria, e.g. *Aquaspirillum magnetotacticum*, have aligned magnetite cubo-octahedral-shaped particles that are ordered single crystals. (B) The spicules of *Rosella racovitzea* have star-shaped tips that act as gatherers of light, which is pumped through the silica-based biological optical fiber to the interior of the sponge. (C) Nacre, mother-of-pearl, is a segmented laminated composite of calcium carbonate and biomolecules with excellent mechanical properties that provide an armor to mollusks such as the red abalone, *Haliotis rufescens*, shown here. (D) Mammalian enamel, such as from the mouse, is ~100% hydroxyapatite that has a hierarchically ordered woven structure to enable mastication under complex mechanical stresses (the right is an SEM image of the fractured surface and the left is a schematics of the woven architecture) [17].

self-assembly and genetic manipulation [17]. These concepts are depicted in Fig. 2 with examples from our current research. Although the fundamental mechanism of the recognition of a material surface by a short peptide is far from clear, quantitative binding experiments and modeling give some clues of how this might be possible. For example, as shown in Fig. 2A, a molecular dynamics model of constraint platinum-binding septapeptides (CPTSTGQAC, Cs providing the constrained conformation to the peptide through disulfide bridging) reveals that this GEPI has sub-nanometer-scale protrusions (called polypods) that match with the ideal metal surface, possibly interacting via the polar groups [18]. It is conceivable, then, that molecular recognition leads to nucleation, growth and morphogenesis of inorganics under favorable synthesis conditions, and crystal-specific display of peptides. Once a peptide recognizes a material, it could also further self-arrange on the surface to form supramolecular architectures. One such example is shown in Fig. 2B, where a three-repeat gold-binding peptide forms a self-assembled molecular organization with sixfold symmetry on the surface of Au(1 1 1) [17].

The third advantage is that the new approach is a genome-based manufacturing technology, i.e. the proteins and peptides coded by the genes (of bacteria, phage, and yeast) provide means to genetically modify them and, therefore, precisely engineer their practical functions. Here, we present the plasmid presentation of five repeats of a GBP being genetically fused to alkaline phosphatase to create a bi-functional molecule [19]. Developing under this framework would provide a multidisciplinary platform towards realizing hybrid building blocks in which the polypeptides are tailored genetically while the synthetic component is designed for its specific chemical and physical functions for a wide range of applications from materials science to medicine.

Combinatorial biology-based selection techniques have been a major tool for a myriad of biotechnological applica-

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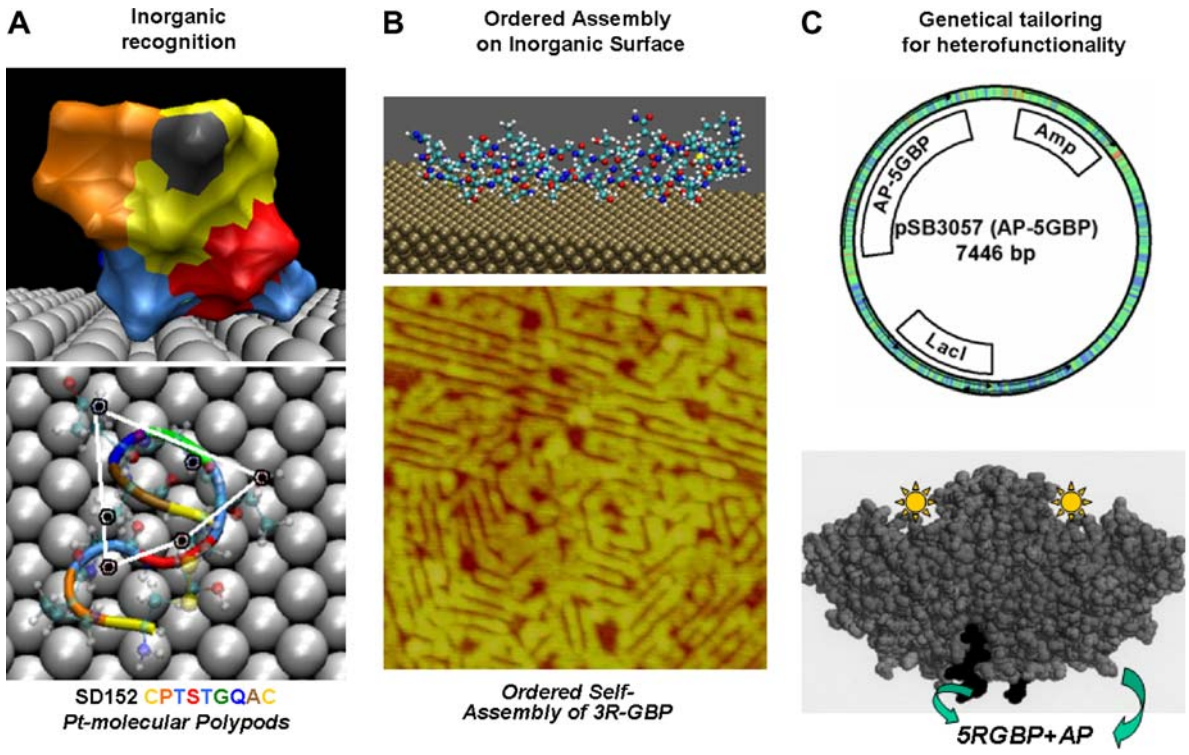

Fig. 2. The demonstration of the three pillars of molecular biomimetics – molecular recognition, self-assembly and genetic manipulation: (A) Recognition of platinum, a noble metal, by a phage-display selected Pt-binding septapeptide that forms polypod molecular architecture. (B) Genetically designed three-repeat gold-binding peptide that recognizes the Au(1 1 1) surface and assembles into a two-dimensional ordered supramolecular structure. (C) Plasmid construct used to genetically fuse five-repeat gold-binding peptide to an enzyme, alkaline phosphatase, resulting in a bi-functional molecule.

tions, including characterization of receptor-antibody binding sites, the study of protein–ligand interactions, and the isolation and directed evolution of enzymes and peptides for improved catalysis or altered binding characteristics [20]. Among in vivo combinatorial selection techniques, phage and cell surface display methods have used extensively. In phage and cell surface display techniques (PD and CSD, respectively), random sequences of amino acids, encoded within a phage genome or on a plasmid, are exposed to the desired environment within the context of a protein that naturally localizes on the surface of the virus or cell, respectively. Outer membrane proteins, lipoproteins, fimbria and flagellar proteins have all been used for bacterial cell surface display, while the coat proteins of bacteriophages M13, fd and f1 have been exploited to expose random peptides on virus surfaces [20–23]. A common feature of these systems is that the genetic information encoding the displayed molecule is physically linked to the product by the displaying organism.

We [7,17,24,25] and others [26–29] have adapted combinatorial biology technologies and selected GEPIs for metals, oxides, minerals and semiconductors. In our group, using pentavalent M13 phage display (Fig. 3A) and multivalent FliTrX bacterial flagellar display (Fig. 3D), we have so far identified more than 1000 peptides binding to a variety of inorganics. Here, randomized oligonucleotides, displayed on the coat proteins of bacteriophages or on the cell surface, are inserted into either phage genome or plasmids, respectively (Fig. 3B). The molecular library is then exposed to the material of interest. Next, a chemical-based elution protocol is carried out for the selection of the tight binders followed by several washing and elution cycles (Fig. 3C). Once the tight binders are eluted from the surfaces, their DNA is extracted and sequenced. Some examples of the sequences identified by our group, including noble metals (Pt, Pd, Ag, Au), metal oxides (ZnO, Al_2O_3, SiO_2), semiconductors (GaN, Cu_2O, TiO_2, ITO, sulfides, selenides) and other functional materials (hydroxyapatite, mica, graphite, calcite), are given in Fig. 4 [7,17,24,25].

Usually there are up to 50 or more peptides selected for any given inorganic material with various degrees of binding strengths. These peptides can be referred as the first set of selected peptide sequences from an initial random library screening (Fig. 5). Although a convergence towards a strong consensus in the amino acid residues of the selected peptides (high affinity and high specificity) is possible in protein–protein interactions, in our experience this may be difficult in identifying a material-specific motif with desirable characteristics. In natural evolution, progeny with improved features are obtained following recurring cycles of mutations and selection. Similarly, the information obtained from screening an initial library can be used for the construction of a second-generation combinatorial library in which specific amino acids contributing to ligand binding are held invariant while neighboring residues are randomized (Fig. 5) [17]. These libraries could be subjected

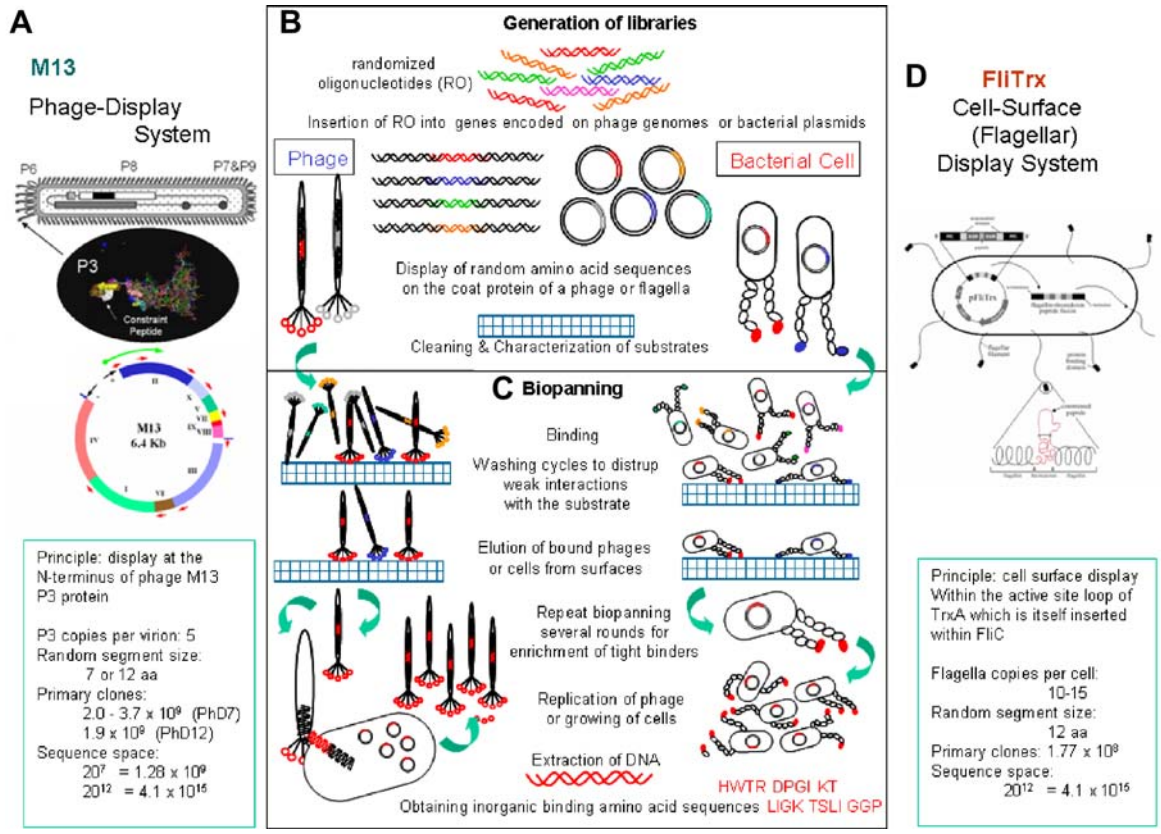

Fig. 3. A schematic illustration of the combinatorial display protocols adapted from molecular biology for selecting material-specific peptides: (A) M13 phage-display library. (B) Basic steps in preparing a random phage or flagella library. (C) Biopanning procedure using random libraries. (D) FliTrX flagella library.

GEPI – Genetically-Engineered Polypeptides for Inorganics: The Molecular Toolbox

Phage Display Selected

Pt-Binders:	TiO_2-Binders:	Al_2O_3-Binders:	SiO_2-Binders:
PtBP1:DRTSTWR	SK12: PWSFQTP	(001)	(100)
PtBP2:TSPGQKQ	SK28: FEVGPLH	AO1 :RTTHQAY	DS202: RLNPPSQMDPPF
PtBP3: IGSSLKP	SK 31: QHGMTRQ	AO17:ELRPTVA	DS189:QTWPPPLWFSTS
Pd-Binders:	**HA-Binders:**	AO23:HLHEPWL	DS 30:LTPHQTTMAHFL
PdBP1:SAGRLSA	HABP 42: LDTPSPH	(100)	(001)
PdBP2:TLPNHTV	HABP 18: PPTRHLL	AO7: SYQFSHH	DS250:APRDNFNTVNLL
PdBP3:HTSKLGI	HABP 17: RTPDNTS	AO6: ETQNRPM	DS256:MPAKEWLPKHNN
Mica-Binders:	**GaN-Binders:**	A04: QPYNKLT	DS 262:SVSVGMKPSPRP
MBP 25: SAPTLRQ	GNBP132: TAAFERNMKPLL		
MBP 89: IQSGHPQ	GNBP133: GALGAKMLHRPS		
MBP 30: RVHEHPH	GNBP136 HSSPHFSRHGLL		

Cell Surface Display Selected

Au Binders (identified by S. Brown):	ZnO Binders:	Cu_2O Binders:
GBP1:MHGKTQATSGTIQS	CN122:LGSWGELLWQRQ	CN225: RHTDGLRRIAAR
GBP2:ALVPTAHRLDGNM	CN173:YRDLLRSYRKRW	CN85: RTRRQGGDVSRD
GBP3:LGQSGASLQCSEKLTNG	CN177:HYANSIWALASQ	CN44: NTVWRLNSSCGM

Fig. 4. Molecular toolbox: examples of inorganic-binding peptides selected by our group via phage, cell surface or flagella display.

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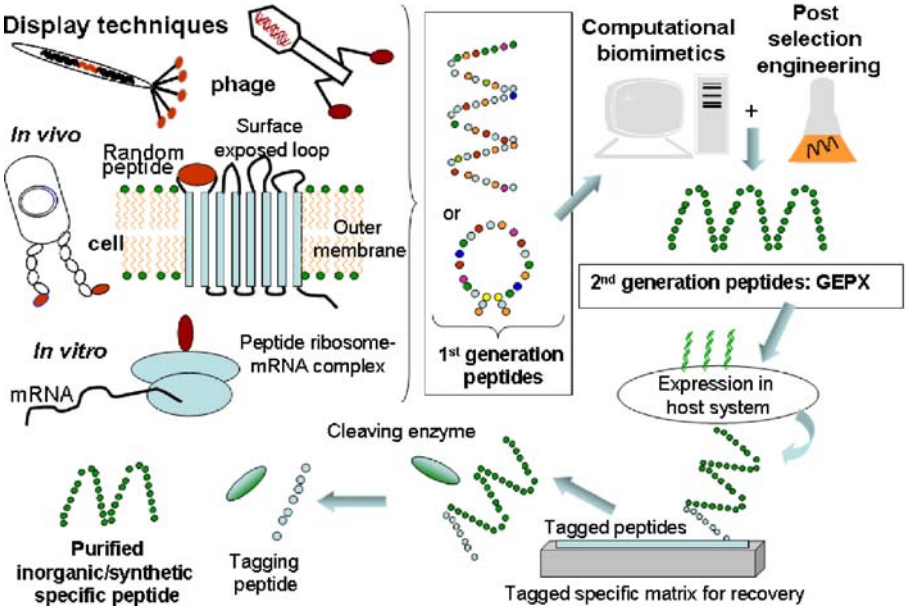

Fig. 5. A schematic illustrating the genetic routes to tailor and express second, and higher, generation inorganic-binding peptides for improved functionality.

to a new screen to isolate higher affinity binders and/or sequences exhibiting a high degree of specificity for one material without interacting with other closely related compounds.

As an alternative to increased binding affinity, one could use molecular biology approaches to create multiple repeats of a binding motif, thereby generating a set of binders exhibiting a tailored K_d for a particular material. Through this strategy we have engineered gold-binding peptide (GBP) [24]. In GBP, the second generation library was constructed by maintaining a known gold-binding sequence (KTQATS) as well as a motif encountered in several gold-binding peptides (SKTS), randomizing intervening amino acids and multimerizing these sequences. Another example is Arg–X–X–Arg (where X is any amino acid), where the tetrapeptide is implicated in metal oxide binding, with Arg–Arg and Arg–Lys pairs allowing for discrimination between Cu_2O and ZnO [25]. To understand the core amino acids crucial to the binding process, one could utilize an alanine scan using site-directed mutagenesis, where each of the amino acid residues in the selected sequences is replaced by alanine one by one. For directed evolution of inorganic-binding polypeptides, one can keep the core amino acids but change the noncontributing ones with the residues to improve both affinity and specificity. Starting from the first-generation GEPIs, the binding affinity could be assessed, initially qualitatively, using immunofluorescence microscopy. Then quantitative binding and kinetics can be obtained using techniques such as quartz crystal microbalance and surface plasmon resonance spectroscopy [30–32]. The assembled molecular structures can also be visualized using atomic force microscopy (Fig. 2B). Furthermore, peptide conformational structures can be modeled by molecular dynamics (Fig. 2A) or quantified experimentally using nuclear magnetic resonance spectroscopy [17]. Although many sequences specific to different inorganics have been identified by many groups [26–29] up to now via application of display technologies, there is still a limited number of quantitative binding characterizations providing the essential data for the evaluation of polypeptide-inorganic surface affinity and selectivity [30–32]. Clearly, this information is essential in the robust design and realization of protein/inorganic hybrid materials.

3. Post-selection engineering

As our understanding of inorganic binding grows through a synergistic combination of experimental and computational approaches, one would expect to identify particular arrangements of residues necessary for binding in a directed manner. This knowledge could be combined with bioinformatics approaches to computationally design GEPIs that have tailored binding and functional properties (Fig. 5). For instance, we are developing a novel bioinformatics protocol to identify sequence patterns that confer inorganic-binding specificity. Briefly, when one compares all the binders isolated using PD or CSD for a given material with those for different materials, it is possible to assign sequence similarity scores using genetic algorithm procedures. In essence, we can create a BLOSUM-like matrix (typically used for comparing the protein sequences of different organisms), which is optimized so that peptides with similar binding properties for a particular material have a very high score and those with dissimilar binding have a low score. One can then generate random sequences and perform similarity comparisons to known binders, with the assumption that peptides that have a significant match to a known binder are likely to bind with high affinity to

that surface and combine results with the de novo structure prediction strategies. The resulting sequences would be experimentally tested, allowing fine-tuning of in silico predictions [33].

The genetic engineering-based approaches, e.g. recombinant DNA technology, can be utilized in many different ways. For example, tuned-up GEPIs can be developed for the desired affinity and specificity by computational design and post-selection engineering following the combinatorial selection (Fig. 5). Also, desired peptides can also be generated in an in vivo environment. The engineered peptides can be expressed in *Escherichia coli*, or other hosts, with additional modifications such as introduction of cleavable hexahistidine tails to simplify fusion peptide purification via Ni-NTA affinity chromatography. The GEPIs can then be produced in desired amounts following the removal of purification tags to be utilized as tools for many applications (Fig. 5).

4. Current multidisciplinary applications of engineered polypeptides

Controlled binding and assembly of proteins on inorganic substrates are at the core of bionanotechnology and biological materials engineering [33–35]. GEPI provides the molecular means to anchor, couple, brace, display and assemble functional molecules, nanoparticles and structures [17]. The examples in Fig. 6 provide a summary

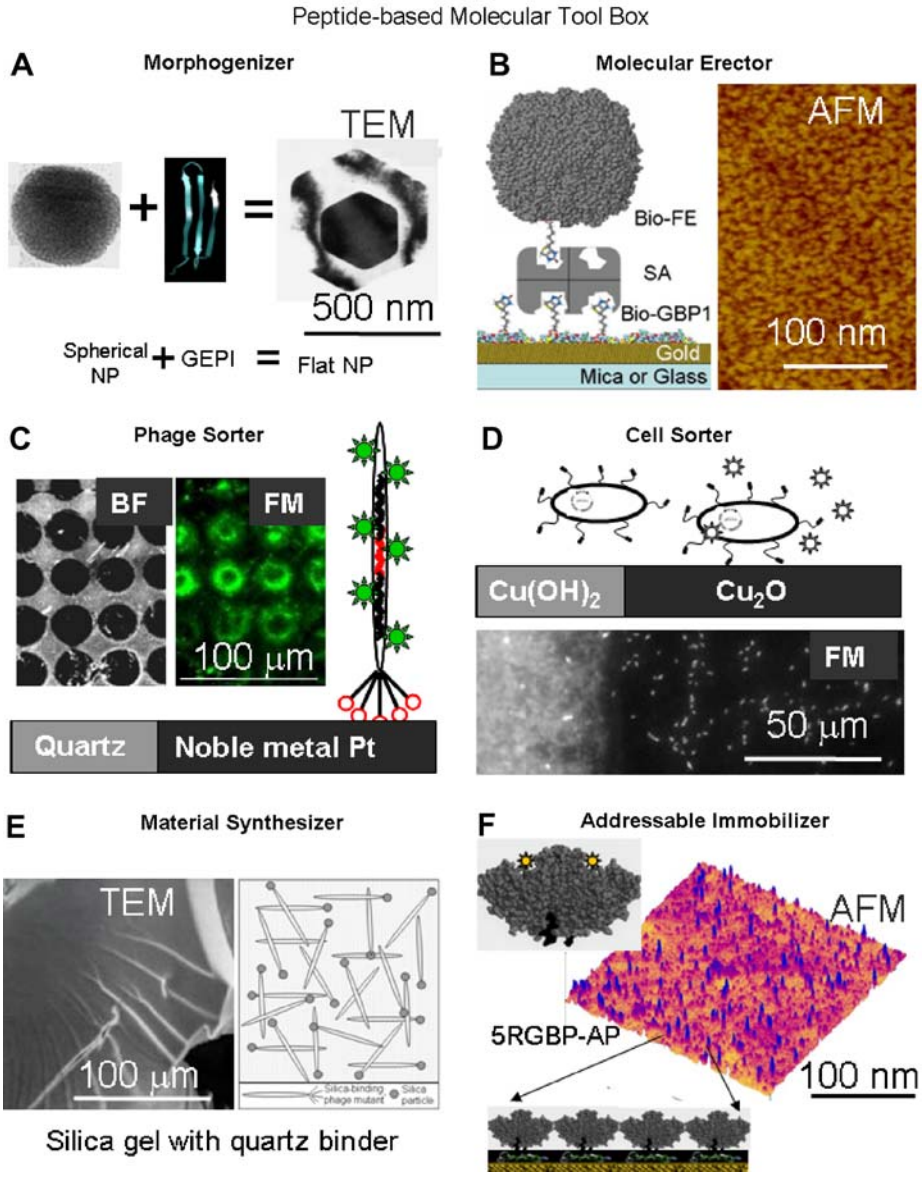

Fig. 6. Some examples of diverse applications of GEPI: (A) Morphogenesis of inorganic nanoparticles using a GEPI; flat gold particles form in the presence of GBP1 during synthesis. (B) Immobilization of target protein (FE, ferritin) using biotinylated GBP1 that assembles on Au(111). (C) Competitive assembly of Pt-binding phage mutant on micropatterned platinum compared to surface silica (substrate is Si-wafer). (D) Cell sorting using mutant cells with cuprous oxide-binding peptides displayed on their flagella. (E) Formation of silica gel using tetraethylorthoslicate and quartz-binding phage mutant. (F) Directed immobilization of GBP1-AP construct on a gold substrate with retained phosphotase activity.

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of potential uses from our current work. Here the engineered peptides are used as molecular manipulators for a wide range of applications. The peptides are made available from our molecular toolbox, a protein data bank containing fully characterized GEPIs. Furthermore, genetic fusion of GEPIs into functional proteins, for example, enables them to be used as more practical ligands for many bio- and bionanotechnological applications by directly utilizing multifunctional protein-based constructs.

Similar to morphogenesis in hard tissues (such as mollusk shells, bones, spicules and dental tissues) provided by inorganic-binding proteins, GEPIs could be used to control the geometrical shapes and sizes of inorganic nanoparticles (Fig. 6A). Here, we demonstrate that GBP affects the Au particle morphology through controlling crystal growth. Nanogold (monosize, 120 Å diameter) particles can be formed at ambient conditions using the well-known Faraday's technique by reducing $AuCl_3$ by $Na_3C_6H_5O_7$ (or other reducing agents) [7]. Reducing the gold concentration and temperature allows particle formation at a slower rate, giving the protein time to interact with surfaces during the growth and providing conditions to examine the effect of gold binding during colloidal gold formation. We have tested more than 50 mutants in our study for their influence on the rate of crystallization of nanogold particles, and our sequence analysis shows that two separate mutants that accelerated the crystal growth also changed the particle morphology from cubo-octahedral (the usual shape of the gold particles under equilibrium growth conditions) to flat, triangular or pseudo-hexagonal particles [24]. This new observation is interesting in demonstrating the effect of gold-binding peptides in crystal growth rather than traditionally-assumed templating effect.

Target DNA and functional proteins adsorbed specifically onto probe substrates are used to build microarrays suitable for modern functional genomics, pharmogenetics and proteomics [33–35]. Gold-binding polypeptides, selected by cell surface display, are one of the first examples of engineered polypeptides for inorganic surfaces. They were screened via random peptide libraries expressed on the outer surface of *E. coli* as part of the maltodextrin porin, LamB protein. As we have discussed here and elsewhere, among the identified peptides, GBP1 (MHGKTQATSGTIQS) has been well characterized by our group. In Fig. 6B, a biotinylated form of GBP is utilized as a molecular erector for ferritin attachment to the gold surface. Streptavidin linkage in ferritin provides a specific linkage for biotin, and consequently ferritin adsorption on the gold surface is achieved by GBP binding on the surface [17].

The utilization of the ability of GEPI to selectively bind to a specific inorganic would allow development of new platforms for virus, phage and cell sorting using micro-patterned substrates (Fig. 6C and D, respectively). In Fig. 6C, we observe the phage sorting on a platinum-patterned silica surface through a specific platinum-binding peptide displayed on M13 phage. To prepare the substrate, we used an electrochemical approach in which platinum macrodots were printed on a silica (glass) substrate [36]. Relatively flat and circular regions of nominally 50 μm diameter containing metallic platinum regions were verified via scannong electron microscopy (SEM) and the chemical distribution of Si, O and Pt elemental maps were obtained using energy dispersive X-ray spectroscopy (not shown here). A fluorescently tagged phage mutant displaying the specific platinum-binding peptide was exposed to the patterned substrate in a buffer solution, resulting in self-directed phage binding onto the Pt dots preferably over the silica regions [36]. Similarly, in Fig. 6D, selective adsorption of fluorescently labeled *E. coli* can be sorted by its binding to the cuprous oxide regions rather than on cupric hydroxide. Here, the cell flagella express a specific dodecapeptide that binds to cuprous oxide (Cu_2O) with high affinity and chemically distinguishes it from $Cu(OH)_2$ [25].

Our next example uses a mutant phage incorporating an inorganic binder. Here the GEPI is utilized for material-specific synthesis and the three-dimensional construction of the resultant material while being an integral component of it. A silica-based composite material is developed consisting of a silica-specific phage mutant that forms a three-dimensional network with silica as the filler (Fig. 6E). In nature, biosilica exhibits diverse shapes and structures. The proteins directing silica synthesis in biological systems have been studied extensively. For example, silaffins, extracted from the cell walls of a diatom, *Cylindrotheca*, or silicatein, extracted from the spounge spicules of *Terhya aurantia*, are well known examples [37,39]. Following nature's examples, in our research we identified quartz-binding peptides using a dodecapeptide phage display library selected using a single-crystal substrate. Here, we used the strong quartz-binding peptide (DS 202: RLNPPSQMDPPF) displayed on phage to test their effect on silica synthesis. Samples (containing 10^{13} pfu) were incubated in freshly prepared tetramethylorthosilicate (TMOS) solution for 3–4 min at room temperature. We next centrifuged the solution and, after discarding the supernant, removed the precipitated samples using a syringe. The samples were either freeze-dried or air-dried before testing for the presence of silica. The microstructure and the elemental composition of the silica formed were examined using SEM and transmission electron microscopy, and energy-dispersive X-ray spectroscopy (not shown). The results demonstrate that the selective peptides can be utilized for the biofabrication of the inorganic material in an aqueous environment [39].

Our final example concerns with the use of inorganic-binding peptides for self-oriented immobilization of enzymes. Although many methods have been used to immobilize enzymes, there has always been a compromise between trying to maintain the high activity of the enzyme and having the advantages of immobilization. The existing molecular systems that have been the hallmark for self-assembly in chemistry are mostly thiol- and silane-based. Although these linkers have been used successfully so far, their utility can be limited because of their non-specific interactions. The proteins immobilized through these link-

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ers might be positioned on the surface in random orientations, resulting in a loss of their biological activity. As demonstrated in Fig. 6F, the inorganic-binding peptides can be utilized as potential linkers, as not only is each specific to an inorganic surface, but they also allow genetic conjugation to create bi- or multifunctional constructs. The example here uses a five-repeat GBP genetically fused to an enzyme, alkaline phosphatase (AP). The resulting bi-functional enzyme is then self-immobilized, homogeneously covering the gold substrate (Fig. 6F) [19]. The AP is an essential hydrolase enzyme for regulating (preventing or enhancing) biomineralization of hydroxyapatite via control of the extracellular phosphate concentration by catalyzing, for example, pyrophosphate degradation. Here, the bi-functional hybrid molecular construct keeps both its enzymatic function and its inorganic-binding activity simultaneously. The approach is a general one, and can be used for directed immobilization of a variety of enzymes and other functional proteins and biomacromolecules with the retained activity on desired substrates.

5. Future prospects and potentials of molecular biomimetics

The utilization of genetically engineered polypeptides as building blocks and molecular tools in designing, synthesizing and assembling practical systems in technology and medicine necessitates the amalgamation of new concepts from major science and technology fields (Fig. 7) [7]. The specific interaction between the inorganic surfaces and the polypeptides presented by GEPIs could have a significant impact on bio- and bionanotechnological applications, offering several novel immediate practical advantages. The attachment of biomolecules, in particular proteins, onto solid supports is fundamental in the development of advanced biosensors [40] for the detection of a variety of agents, and uses such as drug screening, bioseparation [41], many diagnostics applications in medicine [42] and cancer therapeutics. Protein adsorption and macromolecular interactions at solid surfaces play key roles in the performance of implants and hard-tissue engineering. Proteins and DNA adsorbed specifically onto probe substrates are used to build micro- to nano-arrays suitable for genomics, pharmacogenetics and proteomics applications [43–45]. Finally, engineered polypeptides can be hybridized with functional synthetic molecules and nanoparticles, and thus be used as heterofunctional building blocks in nanoscale electronics, magnetics and photonics. In these fields, the major challenge to obtaining the desired effects, i.e. controlling particle separations, organizations and distributions, can be overcome by utilizing the peptides for multifunctionality via the genetic engineering tools.

The future use of biological materials and systems will depend on how readily the overlap of the physical and biological sciences is established [46–50]. Nature has many examples that offer lessons for solving challenging practical engineering problems. Not only does biology offers design lessons, but it also provides practical molecular tools to synthesize hybrid systems [49,50]. By making useful materials using genetically engineered peptides, the multidisciplinary field of molecular biomimetics could provide a new platform for achieving the goal of efficient utilization of biological principles by simultaneous integration of science, engineering and technology [7,17]. The coming years will inevitably show the impact of this new field in a range of diverse areas from materials to medicine, as depicted in Fig. 7.

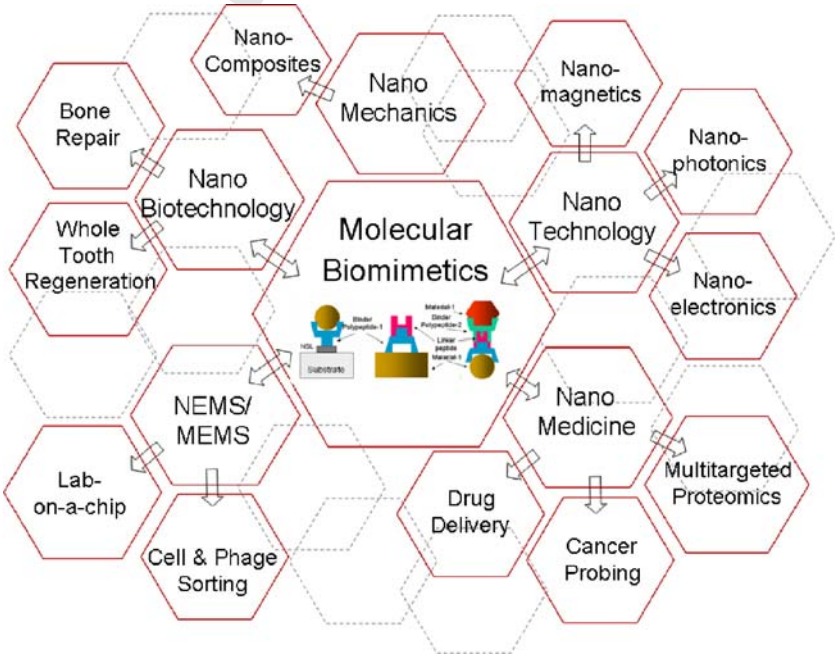

Fig. 7. Research in molecular biomimetics is multidisciplinary and provides molecular tools for applications in diverse fields of engineering and medicine.

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