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Peptide-based nanomaterials: Self-assembly, properties and applications

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ABSTRACT

Peptide-based materials that have diverse structures and functionalities are an important type of biomaterials. In former times, peptide-based nanomaterials with excellent stability were constructed through self-assembly. Compared with individual peptides, peptide-based self-assembly nanomaterials that form well-ordered superstructures possess many advantages such as good thermo- and mechanical stability, semiconductivity, piezoelectricity and optical properties. Moreover, due to their excellent biocompatibility and biological activity, peptide-based self-assembly nanomaterials have been vastly used in different fields. In this review, we provide the advances of peptide-based self-assembly nanostructures, focusing on the driving forces that dominate peptide self-assembly and assembly mechanisms of peptides. After that, we outline the synthesis and properties of peptide-based nanomaterials, followed by the applications of functional peptide nanomaterials. Finally, we provide perspectives on the challenges and future of peptide-based nanomaterials.

1. Introduction

Molecular self-assembly represents the spontaneous association of individual molecules under thermodynamic conditions into a well-defined and fairly stable supramolecule through non-covalent interactions, and it is ubiquitous in nature [1]. Molecular interactions maintain molecules at a stable, low-energy state [2].

Peptides that consist of amino acids can self-assemble into diverse nanostructures, which usually show good biocompatibility and biological activity [3,4]. Owing to their inherent advantages, functional peptide nanomaterials are considered a kind of versatile materials that have broad application prospects in the field of materials science. In recent decades, many scientists have performed extensive studies of peptide self-assembly and gained a certain understanding of it. Moreover, well-ordered nanostructured supramolecules are extremely attractive "bottom-up" biomaterials, which can be used in the fields of nanotechnology and nanomedicine [5,6]. The research of biomimetics and biologically inspired nanomaterials is currently an important field and is rapidly escalated [7]. The peptide-based nanomaterial is attractive due to several reasons:

I. Peptides synthesized through solid-phase methods could be modified at the molecular level [8], yielding peptide-based nanomaterials with customized properties.
II. Additional functionalization of peptide-based nanomaterials could be performed by introducing exterior substances, such as enzymes, to the peptide nanostructure [9].
III. The self-assembly process could be well-designed by tailoring the secondary structures of peptide building blocks, such as α-helices and β-sheets [10].

In recent decades, the development of peptide-based nanomaterials has progressed rapidly. Some reviews from different perspectives have summarized the recent advances in peptide-based nanomaterials. For example, Levin et al. summarized recent conceptual and experimental advances in self-assembling artificial peptidic materials [11].

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Apostolopoulos et al. discussed the current state-of-the-art short peptide-based therapeutical developments [12].

In this review, we list the recent advances of peptide-based nanomaterials, from the aspects of peptide self-assembly mechanism, factors influencing peptide self-assembly, and the applications of functional peptide nanomaterials. Furthermore, the synthetic approaches and properties of diphenylalanine peptides are classified and discussed. Finally, we discuss the challenges and provide outlooks for future research focuses and trends of the peptide-based nanomaterials.

2. Peptide self-assembly mechanism

2.1. Mechanism of peptide self-assembly

Peptide dissolved in a solvent can adopt a special conformation, which usually determines whether the self-assembly occurs or not. Secondary structures that prefer peptide self-assembly include α-helices, β-sheets, and β-hairpins. α-helix is the main secondary structural motif in proteins [13–15]. Due to its inherent thermodynamic instability, linear peptides with α-helix structures would lose their helical conformation in solution when separated from their original environments [16]. Therefore, the stabilization of α-helix is important to trigger peptide self-assembly [17–19]. Approaches for α-helix stabilization include side chain cross-coupling, hydrogen-bond surrogates [16], metal coordination [20], and salt bridge formation [21]. A 17-peptide segment designed by Mihara et al. was stabilized into an α-helix structure by two sets of E-K salt bridges, and further self-assemble into stable nanostructures [22]. Short α-helical peptides show the ease of chemical synthesis and modification but lack stability in solution. Therefore, the de novo design of peptide assemblies based on ultrashort α-helical peptides remains a challenge. Recently, Gazit et al. reported functional super-helical assemblies formed by α-helical heptad peptides. They incorporated a non-coded α-aminoisobutyric acid into the sequence to stabilize the helical conformation of the heptad peptide. To drive the directional self-assembly, they anchored two phenylalanines at the first and fourth positions of the peptides, and the intermolecular aromatic interactions provided by the side chains of phenylalanines dominate the dimeric interface of the conformers [23].Compared to linear short helical peptides, constrained peptides with crosslinkers represent a class of more intriguing ultrashort helical peptide building blocks for peptide assembly due to their hyperstability and low molecular free energy. Based on a peptide scaffold with a thioether-containing side chain staple, Li et al. designed the coiled coil nanofibers from peptides that contain five amino acids [24,25]. Lee et al. showed that peptide self-assembly mediated by β-sheet could stabilize α-helix artfully, thus making the peptide self-assemble to nanostructures in aqueous [26]. The β-sheet is also a critical secondary structural motif in peptide molecules. There are many studies on the self-assembly of peptides based on β-sheets. Lego peptides are a typical representative of peptides that contain hydrophilic and hydrophobic surfaces [27–29]. Due to its molecular structure, Lego peptide can form β-sheet structures in aqueous solution by hydrogen bonding. In water, β-sheet formation and hydrophobic collapse of the aliphatic tail induce molecules to assemble into supramolecular one-dimensional nanostructures, commonly cylindrical or ribbon-shaped nanofibers [30]. RADA16-I peptide designed by Yokoi et al. composed of alanine, aspartic acid and arginine. In aqueous solution, the hydrophobic alanine residues gathered together to lower the energy of the system, while the aspartic acid and arginine residues attracted to each other through electrostatic interaction and arranged in the outer layer of the assembly. Alanine residues can slide laterally to reduce their contact with water molecules, and finally make the hydrophobic surface of the peptide chain completely fit to form a regular β-sheet structure and self-assemble to form nanofibers [31]. In addition to forming nanofibers, peptides can also self-assemble to form nanotubes, vesicles and other assemblies by β-sheet secondary structure [32–34]. The assembly of peptide nanotubes provides an ideal model for a highly ordered, uniformly conformed antiparallel β-sheet system [35,36]. β-hairpin is the derivative of β-turn, which requires the peptide chain segment containing an amino acid sequence that can be bent. Schneider et al. designed MAX1-7 peptides that can form β-hairpin structure [37]. These peptides are typically composed of an alternating sequence of hydrophilic lysine residues and hydrophobic valine amino. By increasing the pH values of the solution or increasing the ion concentration of the solution to shield the electrostatic repulsion, the peptides can form β-hairpin structures with lysine residues as the inner surface while valine residues as the outer surface, and further utilize its hydrophobic effect to self-assemble to form nanofibers [37–39].

Compared to individual peptides, peptide assemblies can act as nanoscale scaffolds [40]. Diffusivity is the key difference between individual peptides and peptide assemblies. Diffusion of monomeric peptides is faster than peptide assemblies. A way to control the peptide assemblies is by controlling the diffusive kinetics of peptide monomers [41]. Based on this feature of peptide assemblies, the concept of enzyme-instructed self-assembly (EISA) is proposed, which means yielding peptide assemblies through bond formation [42] or bond cleavage [43] in an aqueous solution. Biologically important molecules' formation and transformation are generally catalyzed by enzymes under physiological conditions. Moreover, the expression levels of a series of enzymes correlate with diseases. EISA may occur in the location of disease or within the abnormal cells. Therefore, it is feasible to use EISA to trigger the self-assembly of nanomaterials in situ and to diagnose and treat diseases [44]. Peptide assemblies generated by EISA in the cellular environment could mimic the bio-macromolecular condensates. Enzymatic substrate, the precursor for instructed assembly, which generated via integrating a short peptide with naproxen (a nonsteroidal anti-inflammatory drug (NSAID) and a ligand of cyclooxygenase-2 (COX-2)) [45]. As context-dependent signaling for the death and morphogenesis of cells, the dynamic continuum of non-covalent filaments is formed by the instructional assembly (iA) of supramolecular phosphoglycopeptide (sPGP). iA, a multifaceted signal, controls the behaviors of cells according to local enzyme activity [46].

In many cellular processes, molecular self-assembly regulated by enzymes plays a key role, which inspires the development of small molecule enzymatic hydrogelation [47]. There are three essential steps in the enzymatic hydrogelation of small molecules: The enzyme converts the precursor into a hydrogenator through bond cleavage firstly. Hydrogenator self-assemble into nanofibers then entangle to perform as the matrix for the hydrogel [43]. Besides, the self-assembly of small molecules to form supramolecular hydrogels also has three characteristics: The molecular arrangement within the nanofibers shows obvious orderliness although the nanofibers are randomly entangled; The molecular order within the nanofibers can be polished by the relatively simple structural modification of the small molecules; Small molecules are more easily converted into hydrogelators [48]. Introducing o-[bis (dimethylamino)phosphono] tyrosine protection strategy in the self-assembly motif, the programmed precursor resists hydrolysis by phosphatase inside and outside the cell, because the exposure of the enzymatic cleavage site occurs selectively in the acidic lysosome environment. The acid phosphatase in the lysosome instructs the self-assembly of the hydrogel spatiotemporally in the lysosome [49].

2.2. Interactions responsible for peptide self-assembly

2.2.1. Non-covalent interactions of peptide self-assembly

Non-covalent interactions are widespread in nature, and help form complex, advanced bio-molecular structures, for example, the DNA double helix, secondary or higher-order protein structures, and the phospholipid bilayer structure of cell membranes [3]. Non-covalent bonds are weaker compared to covalent bonds and reversible. They could aid peptide monomers in forming stable structures, although individual non-covalent bond presents weak bond energy [50]. Peptide self-assembly is a spontaneous process driven by thermodynamics and

kinetics. The intermolecular non-covalent interactions, including π-π stacking, hydrophobic, electrostatic, van der Waals, and hydrogen-bonding, could maintain the structural integrity and stability of self-assembly systems (Fig. 1.) [51,52]. The final nanostructures' thermodynamic stability and minimum energy state are determined by the synergistic effect of non-covalent interactions [53–55]. Herein, we focus on the following non-covalent interaction types to understand peptides' self-assembly.

2.2.1.1. Hydrogen-bonding. Hydrogen-bonding interactions are one of the principal forces determining the self-assembly processes and the structure of peptide assemblies [56]. The strength of hydrogen bonds is 10–40 kJ mol^{-1} at 298 K or about 5–10 kara per bond, making their energies between those of the covalent bond and those of the van der Waals interactions [50]. They can occur between atoms, molecules, or ions and exist in gaseous, liquid, solid, or supercritical phases. Besides, they can exist in non-polar environments. Peptides have abundant hydrogen bond-forming sites [56]. Hydrogen bonds are essential for forming and stabilizing peptides' secondary structure and have selectivity and high directionality that could induce the peptides' assembly into distinct nanostructures. Therefore, they are a particularly important driving force for peptide assembly [57].

2.2.1.2. π-π interactions. π-π stacking, another kind of weak non-covalent interaction, is also common in peptide self-assembly. It exists mainly in the peptide nanostructures that assemble by peptides contain aromatic amino acids, such as phenylalanine, tyrosine, and tryptophan. Due to the limited solubility of molecules containing aromatic groups, π-π interactions are very stable in water. Moreover, π-π interactions can induce directional growth [58].

2.2.1.3. Hydrophobic interactions. Many studies have shown the importance of hydrophobic interactions for the rational design of water-soluble amphiphilic polypeptide molecules. Amphipathic molecules tend to aggregate their hydrophobic tails in the interior of the aggregates through hydrophobic interactions, while the hydrophilic heads are exposed on the periphery of the aggregates and in contact with water. In terms of inducing self-assembly, the hydrophobic interactions are stable due to favorable entropy rather than favorable enthalpy. As long as entropy is favorable, it may even be unfavorable [59]. Despite the bonding energy is weak, hydrophobic interactions play an important role in peptide self-assembly. The aromatic residues of the peptide building blocks may function through hydrophobic interactions or π-π interactions: it has been found that the organization pattern of aromatic residues in hydrophobic interactions is usually disordered, whereas in π-π interactions the organization pattern of aromatic residues is ordered [51].

2.2.1.4. Electrostatic interactions. Another type of non-covalent interaction employed in self-assembly is the interaction between charges [60]. In contrast to the critical roles of hydrophobic interactions and hydrogen bonding, electrostatic interactions are commonly used to induce the structural specificity of charged peptides [61]. Electrostatic interaction is non-directional and has weak bond energy, including electrostatic attraction and electrostatic repulsion, as well as intramolecular and intermolecular electrostatic interaction of points. The pH and ionic strength are two important factors in electrostatic interaction. The electrostatic interaction greatly influences the self-assembly behavior of peptides containing acidic or basic amino acids, so the electrostatic interaction can be controlled by changing the pH or ionic strength of the solution to influence the self-assembly process of peptides [62].

2.2.2. Dynamic covalent bonding in peptide self-assembly

Peptide self-assembly may involve non-covalent and dynamic covalent interactions [63]. Reversible covalent chemistries, such as disulfide bond formed by cysteine residues and imine bond formed by the reaction of aldehyde and amine groups, have been widely investigated as a combination of non-covalent interactions in aid of peptide self-assembly. Recently, Zhang et al. reported an interesting helical fibril structure assembled from C_3-peptides bearing glycine–cysteine (Gly–Cys) dipeptide pendants. The oxidation of the thiol groups forms disulfide bonds between adjacent building blocks, which can stabilize the left-handedness of the long helical fibers and enhance the overall stability of the nanostructures [64]. Mechanically interlocked molecules as prototypes of molecular machines have gathered much attention from synthetic chemists. Recently, Link et al. achieved the synthesis of a kind of mechanically interlocked peptides, enabling by the self-assembly of fully peptidic, cysteine-decorated building blocks in water, which generate a diversity of disulfide-bonded dynamic interlocked molecular libraries [65].Besides the disulfide chemistry, the peptides decorating with aryl aldehyde and acyl hydrazide functionalities were used to construct peptide quaternary assemblies. A mixture of peptides with complementary functionalities could react in mild conditions to form peptide-peptide intermolecular macrostructures with tunable ring sizes. More interestingly, sophisticated ladder structures could be formed by controlling the proportions of reacting peptides. This study represents a canonical method to create complex abiotic quaternary structures [66].

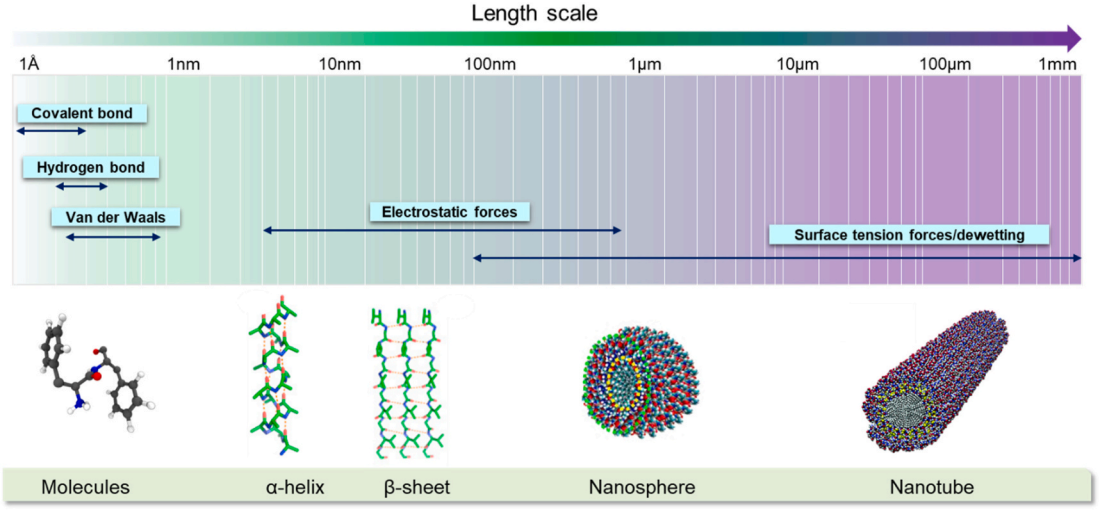

Fig. 1. The patterns of forces involved in self-assembly and its generated structures [52].

3. Factors influencing peptide self-assembling

The study of external factors that influence peptide self-assembly is essential for the rational design of desired peptide-based nanostructures. Factors affecting peptide self-assembly can be categorized into intrinsic and external factors (Fig. 2). Intrinsic factors refer to the structure of the peptide, including the sequence of the peptide, the number of amino acids, and the properties of the amino acid side chains. External factors include pH, temperature, solvent, ultrasound, and others. The peptide sequence can be elaborated to achieve controllable self-assembly by adjusting the factors influencing peptide self-assembly.

3.1. Intrinsic factors

The internal factors that affect the peptide self-assembly mainly include the sequence of amino acids, the number of amino acids, and the hydrophilicity and hydrophobicity of amino acids [67]. The common peptide self-assembled structures include nanofibers, nanobelts, nanotubes, etc. The main reason for different self-assembly morphology is that the electrostatic, hydrophilic, or hydrophobic interactions providing by the side chains of different amino acid residues are varied [68–71]. The nature of amino acid side chains plays a vital role in the process of peptide self-assembly. For example, hydrophobic amino acids lead to significant changes in the mechanical properties of the forming materials and the self-assembly speed [70,72]. Therefore, rational selection and design of peptide sequences are exclusively crucial for studying peptide self-assembly.

A huge of studies have demonstrated the diphenylalanine and its analogs could self-assemble into well-ordered nanotubes. Gazit et al. revealed that diphenylglycine could form spherical nanometric assemblies [73]. The properties of diphenylglycine are similar to diphenylalanine. TEM revealed that diphenylglycine peptides form spherical nanometric structures while diphenylalanine peptides form nanotubes under the same conditions. The side chain of phenylglycine is more rigid than that of phenylalanine due to the side chain of phenylglycine lacks a methylene group. The enhancement of the lateral growth ability makes it similar to that in the long axis direction, so that the original tubular structure becomes a spherical structure [74].

In peptides that possess very similar overall hydrophobicity and charges, the arrangement order of amino acids could influence the self-assembly ability and morphology [75]. Therefore, a rational design of the amino acid sequence is of great significance for the formation of desired morphology to achieve controllable self-assembly [71]. Lee et al. investigated the influence of the order of amino acid sequences on the peptide self-assembly morphology [69]. They compared the self-assembly behavior of Ac-$(FKFE)_2$-NH_2 peptide with other related amino acid sequences: Ac-$(FK)_2(FE)_2$-NH_2, Ac-KEFFFFKE-NH_2, Ac-$(KFFE)_2$-NH_2, and Ac-FFKEKEFF-NH_2. Under acidic conditions, the Ac-$(FKFE)_2$-NH_2 and Ac-$(FK)_2(FE)_2$-NH_2 peptides self-assemble into β-sheet nanoribbons at concentrations of 1.0 mM and 0.2 mM, respectively. The Ac-KEFFFFKE-NH_2, Ac-$(KFFE)_2$-NH_2, and Ac-FFKEKEFF-NH_2 failed to self-assemble into well-ordered structures at 0.2 mM, although the Ac-FFKEKEFF-NH_2 peptide could form micelle-like aggregates at higher concentrations. These findings evidence that amino acid sequence patterns have a great influence on the ability and morphology of self-assembly, even when the overall hydrophobicity and charges of the peptides are very close.

The hydrophilic and hydrophobic properties of the amino acids themselves and the sequences of the amino acids in the polypeptide chain have an important impact on the self-assembly behavior of the polypeptide. It can change the nanostructure morphology formed by peptide self-assembly. Meng et al. studied the effect of systematic changes in the type and number of hydrophilic and hydrophobic amino acids on the self-assembly of the amphiphilic peptide [75]. The hydrophobicity of the peptide increased by replacing a more lipophilic amino acid such as Glycine. In consequence, the self-assembled nanostructures transformed from vesicles to tubes and ribbons. Based on these results and others, it is apparent that the nanostructure's morphologies were closely related to the peptide sequences. It is thus possible to tune the morphology of the self-assembled nanostructures by changing the peptide sequences. Besides, it provides a valuable means for designing new peptide nanomaterials [76–78].

Wang et al. observed the dynamic self-assembly of A_6K and A_9K peptides [79]. At neutral pH, A_6K initially self-assembles into small spherical deposits and fuse into large peptide nano-aggregates as a building block for short nanofibers. In contrast, the self-assembly kinetics of A_9K is faster. Small nanoaggregates were initially formed, then the nanorods with diameters around 3–4 nm and a length of less than 100 nm were formed [77]. The differences observed during the self-assembly could be ascribed to the increase in the length of the

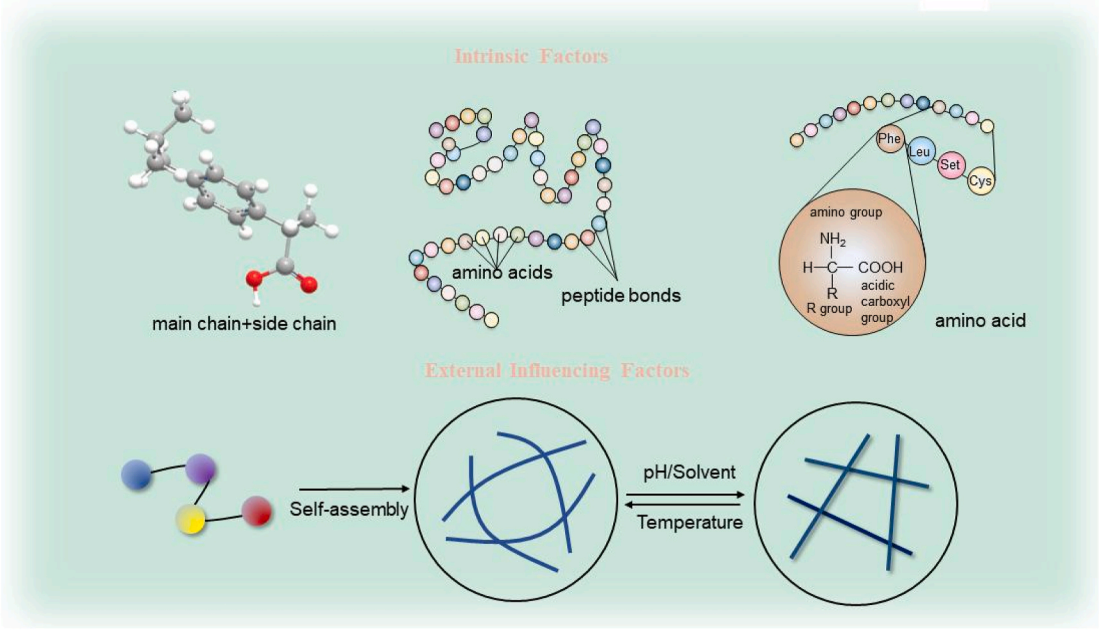

Fig. 2. Factors of influencing self-assembly.

hydrophobic peptide tail, which increases entropy gain and electrostatic interactions while decreases the critical aggregation concentrations.

3.2. External influencing factors

The peptide self-assembly is affected by not only the nature and sequences of amino acids but also various external environmental factors. Herein, we mainly introduce the effects of temperature, pH, solvent, and ultrasound on peptide self-assembly.

3.2.1. Temperature

Hydrophobic interactions and hydrogen bonding interactions can be affected by changes in temperature. When the temperature increases, the hydrogen bonding effect is weakened, while the hydrophobic effect is enhanced. In different systems, hydrophobic interactions and hydrogen bonding contribute differently to the self-assembly of peptides, so temperature changes have different effects on the self-assembly behavior in different systems [80].

When the temperature rises from 25 °C to 110 °C and drops back to 25 °C, the secondary structure of L-EAK16 shows no change. The D-EAK16 exhibits a β-sheet conformation at 25 °C. When the temperature rises to 110 °C, it changes into an α-helix. When the temperature drops back to 25 °C, the secondary structure remains an α-helical conformation, indicating that the secondary structure conversions are irreversible. DAR16-IV peptide powder dissolved in water has an α-helical structure, while a stable β-sheet structure was observed after being aged at 4 °C for several days. When the temperature rises to 50 °C, the β-sheet conformation directly transforms into a stable α-helical conformation without going through an irregular coiled state, and the kinetic process is irreversible. However, after storing at 23 °C for several weeks, it can return to a β-sheet structure [81].

3.2.2. pH

Under different pH conditions, the amino acid side chains of peptides present different charge propensities [82]. Varying the pH could change the protonation degree of amino acids. Consequently, it can impact the electrostatic and hydrophobic interactions of peptides, enabling the transformation of peptide assemblies from a particular morphology to others [83]. Zhao et al. discovered that RATEA16 exhibits different self-assembly behaviors in different pH solutions [84]. Under acidic conditions (pH 3.5), there is a strong electrostatic repulsion within and between the peptide molecules, which prevents the peptide from forming long nanofibers. Under alkaline conditions (pH 12.5), peptide molecules usually present neutral electricity, making it difficult to form β-sheets. The charges on the surface of peptides are shielded due to the formation of ion pairs by the charges within and between molecules. The strong electrostatic attraction causes the hydrophilic amino acids to gather together, and the hydrophobic Ala layer is exposed to water, then the solubility is reduced, resulting in precipitation [85].

Stupp et al. studied the self-assembling morphology of $C_{16}H_{31}O$-VEVEGRGD under different pH conditions [86]. At low pH, multilayered nanobelts are formed due to the low protonation degree of $C_{16}H_{31}O$-V-EVEGRGD. At high pH, the protonation degree was increased, and the multilayered nanobelts broke into single bilayer nanobelts due to the electrostatic repulsion.

3.2.3. Solvent

The solvent has a significant effect on the morphology of the self-assembly. It can cause a huge change in morphology and directly induce the chiral inversion of the nanofiber structure [87].

Huang et al. studied the self-assembly morphology of diphenylalanine peptide (L-Phe-L-Phe, FF) in different solvents [88]. Results showed that the self-assembly of diphenylalanine formed into hollow tubular structures with size in nanometers. Similar structures were also reported in previous work [89,90]. Interestingly, microtubes and fibers were formed when acetonitrile was mixed into the aqueous phase. In addition, the microtubes will disappear when the proportion of acetonitrile increased. It shows that small size, highly uniform peptide nanofibers can be obtained from pure acetonitrile solvent.

Yang et al. synthesized four dipeptides that are derived from D- and L-alanines with long alkyl chains [91]. They studied the self-assembly behavior of these dipeptides in water and tetrahydrofuran (THF). Field-emission scanning electron microscopy images showed that dipeptides organized into twisted nanoribbons and the terminal alanine chirality controlled the handedness of the nanoribbons. More interestingly, the handedness of the nanoribbons formed in the two solvents is opposite.

4. Self-assembly of FF peptide: synthesis and properties

Many studies of peptide self-assembly systems have been reported so far. In this review, a representative diphenylalanine peptide that can self-assemble into nanotubes was selected for introducing its synthetic approaches and properties. As for other systems, such as the self-assembly of cyclic peptides, the readers could reference other reviews [92,93].

4.1. Synthesis of Peptide Nanomaterials

Diphenylalanine is the smallest aromatic dipeptide derived from β-amyloid (Aβ) self-assembled peptides, and can self-assemble into nanoarchitectures [74]. Different methods have been developed to promote the self-assembly of FF and its analogs. Fig. 3 illustrates the proposed models of FF self-assembly through diverse methodologies [94–97].

4.1.1. Solvent control

Since Reches et al. discovered FF nanotubes through the self-assembly of FF dipeptides in solution, the FF-based self-assembly has aroused huge interests from researchers [74]. The homo-aromatic dipeptide motif could form tubular, spherical, fibrillar structures with nanoscale sizes. They performed the unidirectional growth of ADNT induced by evaporation under mild conditions to form nanoforests. The controlled pattern of this alignment tube was achieved by spreading monomer building blocks dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFP) on the siliconized glass. During the rapid evaporation of the HFP solvent in the direction of the growth axis, the geometrically restricted accumulation of the aromatic part derived by the gas-liquid-solid system may promote the orderly organization of the structure [94].

4.1.2. Chemical- and physical vapor deposition

Reches et al. found that diphenylalanine peptides could self-assemble into well-ordered, hollow and long peptide nanotubes [98]. Through physical and chemical vapor deposition techniques, ordered arrays of nanostructures can be formed, such as nanoforests, where the gas-liquid-solid mechanism controlled the unidirectional growth of nanotubes and nanowires. Shklovsky et al. developed new peptide nanotubes (PNTs) by physical vapor deposition process that combines the peptide building blocks' "bottom-up" self-assembly process with the "top-down" common sputtering technique [95]. By adopting the novel vapor deposition process, new nanotechnology for PNT patterning can be developed [95]. From the typical top and side views of the scanning electron microscope (SEM) images of the deposited PNT, it can be known that the orientation of the nanotubes is usually evenly distributed. The diameter of FF PNT ranges from 50 nm to 300 nm. By adjusting the deposition parameters, the average length, thickness and surface density of nanotubes could be controlled. This method allows the use of biological elements to coat large, dense and uniform areas. The obtained PNT possesses unique optical and electrochemical properties [99].

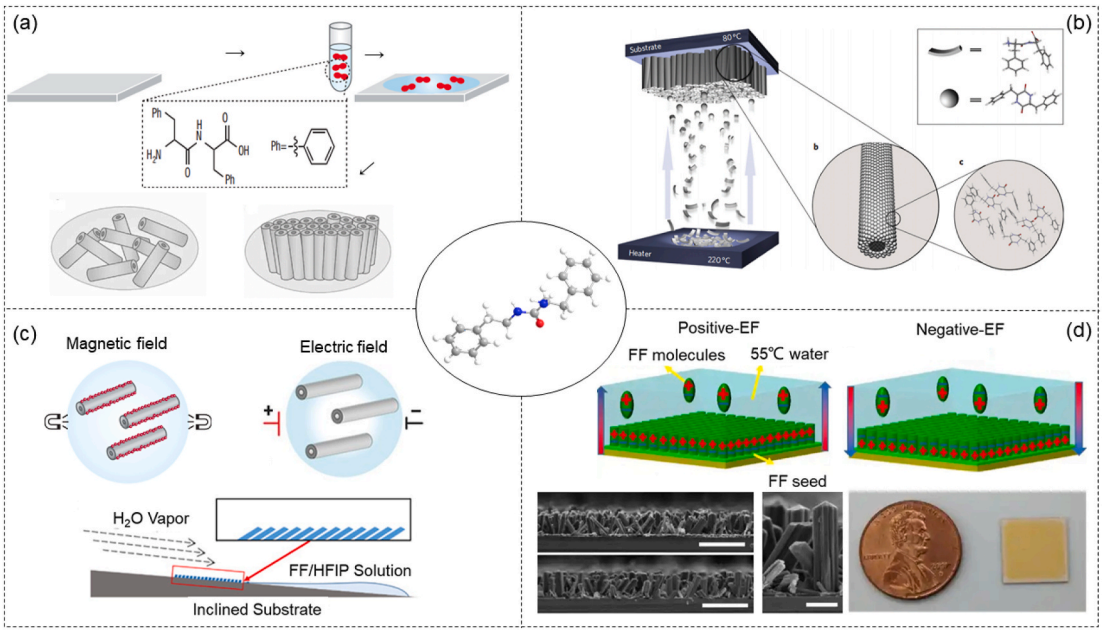

Fig. 3. Synthesis of Peptide Nanomaterials (a) The dipeptide monomer dissolved in an organic solvent is applied to siliconized glass, resulting in the formation of a vertically arranged array of peptide nanotubes [94].(b) Schematic of the vapor deposition technique [95]. (c) Control the alignment of FF nanotubes through external fields or different crystallization modes [94,96]. (d) Growth and control of vertical FF peptide microrod array [97].

4.1.3. Magnetic field control

A study by Abramovich et al. showed that a nanoforest could be formed through the axial unidirectional growth of a dense array of peptide nanotubes, and the nanotubes were horizontally aligned [94,96]. These highly ordered peptide nanotubes possess excellent mechanical and chemical stability and can be modified with functional groups. Their controllable arrangement allows them to be applied in multi-array sensitive sensors, nanomechanical and nanofluidic devices [94,95,100–102].

Previous studies have shown that magnetic fields can arrange β-amyloid fibers for X-ray fiber diffraction [103,104]. Hill et al. magnetically calibrated the FF tube in an aqueous solution of hexafluoroisopropanol and used atomic force microscopy (AFM) to image the residue [105]. Different from the previous experiment, in this experiment, the FF tube is only subjected to the magnetic field, and there are no other additional conditions. The arrangement that occurred in the experiment can be ascribed to the influence of the magnetic moment caused by the antimagnetic anisotropy of the aromatic ring of phenylalanine. The aromatic ring plays a key role in the fiber-forming process, and drives the orderly accumulation of aromatic rings through π-π interaction [106,107]. According to the nanotube orientation in the magnetic field, the orientation of the aromatic ring can be acknowledged and compared with the model structure. Magnetic calibration is a simple method for preparing ordered FF tube arrays and is a highly relevant method for constructing functional nanoscale materials for largescale applications [103,104,108–110].

4.1.4. Electrical field control

FF nanotube is a potential biomaterial for a piezoelectrical nanogenerator. Nguyen et al. demonstrated the growth of FF peptide microrods with fully controlled polarization [97]. The FF peptide microrods grew in an FF-concentrated solution [111]. The substrate coated with a seed film was applied to an electric field. During the FF peptide self-assembly, electrical dipoles of FF molecules were along the applied electric field [112]. As reported, the orientation of the depositing FF molecules will determine the polarization of the microrods. Hence, the polarization direction of the microrods was the same as the direction of the applied electric field.

4.2. Properties of peptide nanomaterials

4.2.1. Thermostability and mechanical stability

Some of the desired properties of peptide nanomaterials for flexible devices include thermostability and mechanical stability. Understanding the properties of nanomaterials is crucial to investigate their applications.

Previous studies observed the thermostability of peptide nanotubes under aqueous and dry conditions [113]. In a solution above the boiling point of water temperatures, peptide nanotubes evidence excellent stability. Thermogravimetric analysis shows the durability of peptide nanotubes at high temperatures. It also demonstrated that at a temperature up to 150 °C, the peptide nanotubes remain stable and show the same morphology as the untreated tube.

Sedman et al. used AFM to observe the structural stability of nanotubes after drying and heating [114]. When FF nanotubes were heated at 150 °C for a long time, their structural integrity was lost. The morphology and size of the nanotubes remain unchanged when the temperature is below 100 °C. However, at 100 °C, the nanotubes were degraded due to the release of phenylalanine. The AFM image revealed that as the temperature increases, the nanotubes deform and a groove appears at the top of the cross-section. In addition, with the loss of the smooth outer wall morphology of the nanotubes, the morphology along the nanotube axis has undergone considerable changes. When the temperature further increases to 150 °C, the nanotubes lose spatial volume and form a structure similar to a flat ribbon. When the temperature is up to 150 °C, a stable AFM image cannot be generated.

AFM was used to perform indentation experiments to study the mechanical stability of peptide nanotubes [115,116]. Peptide nanotubes were deposited on the surface of a mica plate and imaged by an AFM [117]. The results show that the average stiffness of these peptide nanotubes is 160 N/m and the Young's modulus is about 19 GPa, which is higher than other biological nanostructures.

Inorganic nanomaterials can be combined with polymer resins to produce new composite materials with better thermostability and mechanical stability [113,117]. In addition, the mechanical stability of composite materials has been significantly improved. Epoxy resins are widely used in composite materials systems, but epoxy resins are brittle

due to the limit of plastic deformation [118]. It is particularly important to improve its mechanical stability and heat resistance. Compared with other non-covalent self-assembly organic nanostructures, the self-assembly diphenylalanine peptide nanostructures show significant thermal resistance and good mechanical stability [113,117,119]. Studies have shown that the use of peptide nanotubes as nanofillers in an epoxy matrix improves shear strength by approximately 70% and peel strength by 450% compared to unmodified epoxy, while the thermal and chemical durability of epoxy resins are retained [120].

The supramolecular stacking motifs are determined by the kinetics and thermodynamics of the crystallization process. They code the optoelectronic properties of the peptide assembly [51]. The conductivity and photoluminescence of self-assembled phenylalanine-tryptophan (FW) nanostructures are better than FF nanotubes [121], due to their much smaller bandgap [122]. These compact packing patterns inspired Tao et al. to research the stability and mechanism of the cyclo-glycine-tryptophan (cyclo-GW) crystals(Fig. 4a and b.) [123–125]. They demonstrated the crystal packing and excellent thermostability and mechanical stability of cyclo-GW. As a dimer, cyclo-GW exhibits a narrower energy gap structure than the monomer, so it has long-term stable visible photoluminescence performance.

4.2.2. Semiconductivity and conductivity

The use of organic materials in nano-industries has attracted massive attention in recent years [4]. One of the most studied bio-organic molecules is peptides [126,127]. Studies have shown that some natural proteins have inherent semiconductivity [128]. Self-assembly structures composed of short peptides may also possess semiconducting properties [129]. Conventional semiconductive materials bear inherent limitations. The increasingly developed peptide nanostructures may serve as candidates for both bioinspired and durable nanoscale semiconductors. Besides, its semiconducting properties can be easily tuned, doped and functionalized [130,131].

Pioneering work in peptide self-assembled semiconductors was performed by Gazit et al., who first proposed the concept of peptide self-assembled semiconductors. Aromatic short peptide molecules were reported sequentially self-assembling into oligomeric quantum dots and then semiconducting nanotubes [132].

Short aromatic dipeptides of diphenylalanine and phenylalanine-tryptophan (FW) can form peptide nanodots (PNDs) with unique optical properties and crystal structures [132–134]. Tryptophan served as an effective electron mediator for solid-state electron transport, and used a conductive probe atomic force microscope to detect the ability of tryptophan to strengthen electron transport through a network of PNDs [135]. According to the results, although the FF and FW PND have similar surface morphologies, the efficiency of electron transport measured by FW PND at 1V is about five times that of FF PND. The conductivity measured by the FW network is nearly three times higher than the conductivity measured by the FF network.

Peptide-based nanostructures are generally synthesized in an aqueous solution, thus affected by water. Using the Self-Consistent Charge Density Functional-based Tight-Binding method augmented with Dispersion interactions (SCC-DFTB-D), the electronic properties of L-diphenylalanine nanotubes were studied [136]. Interaction between water molecules and nanostructures and their existence in the central hydrophilic channel are also discussed. The results show that the interaction between the nanotubes and water causes the conduction and valence bands to split and lead to greater dispersion, which may be related to the alignment of the dipole moment of the water molecules and the greater dipole moment of the entire structure. The presence of water molecules increases the probability of transitioning electrons, thereby increasing the conductivity of the nanotubes.

4.2.3. Piezoelectricity

Many natural biomaterials, such as peptides, possess weak piezoelectricity due to the existence of polar bonds and natural asymmetry [137]. These organic materials are important building blocks for modern nanotechnology. Diphenylalanine has a great prospect due to its unique piezoelectricity and the excellent mechanical properties of its derivative structures. The studies on FF peptides exert a profound step toward developing them into a biocompatible material platform [138].

FF peptides possess many intriguing properties, including strong piezoelectricity, which have huge potentiality as a smart material (Fig. 4c.) [139]. However, the antiparallel polarization and weak piezoelectric coefficients of FF peptide limited its applications. Nguyen et al. demonstrated the power generation of a peptide-based power

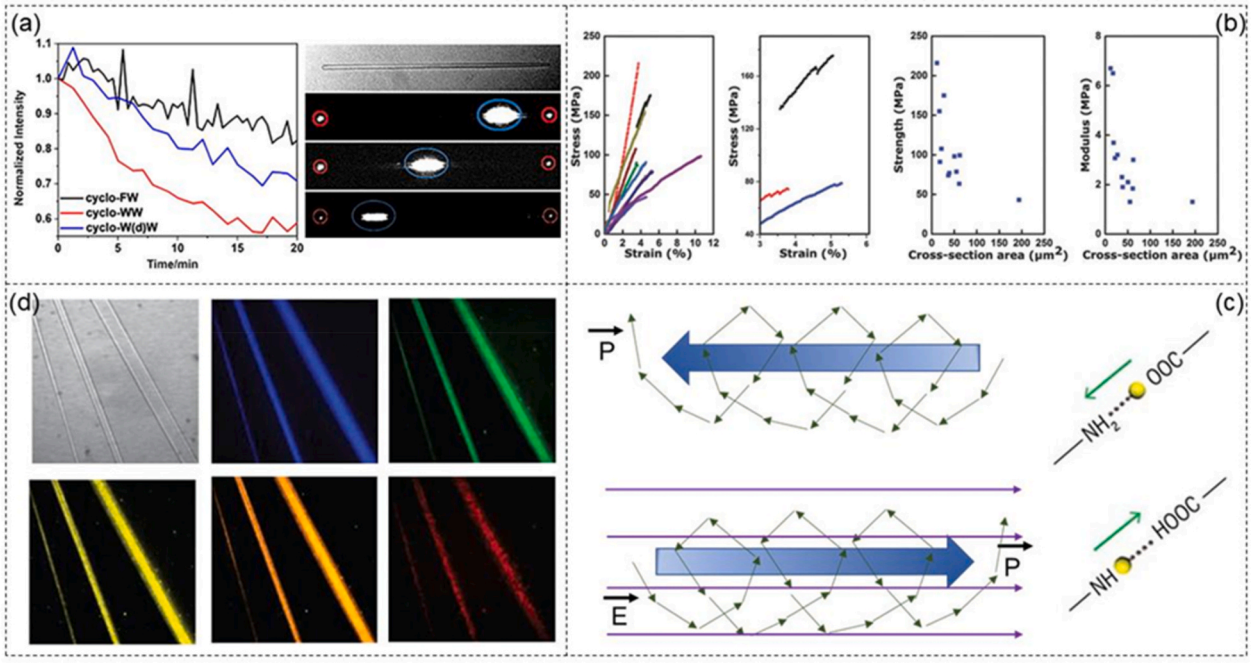

Fig. 4. Properties of Peptide Nanomaterials. (a)Photostability and optical waveguiding of cyclo-FW crystals [124]. [][][](b) Mechanical measurements of Boc-FF crystal [125]. (c) Emission wavelengths in the visible region of PNA [139]. [][][](d) Mechanism of the origin of the SP and the predictable FE [148].

generator. During the peptide self-assembly process, the control of polarization through applying an electric field also be shown. In this work, a method of growth through the engineered FF seed film has been proposed. During the seed film formation they controlled the water diffusion, then the polarizations were uniform with the application of an electric field. With controlled polarization and improved piezoelectric strength, the vertical FF peptide microrods are used to fabricate a power generator, the outputs of which were shown to exceed other bionic generators [140].

Studies have shown that self-assembly diphenylalanine peptide nanotubes exhibit exceptionally strong shear piezoelectric activity, indicating that the polarization is along the axis of the tube [141]. Polarization components of PNT include both out-of-plane and in-plane are measured. It can be seen that in PNTs, the only polarization component is along the tube axis. To further prove the piezoelectric property of the signal, the experiment gauged the AC voltage dependences of deformation of the two tubes in opposite directions. The results showed that even at a high AC voltage of 16 V there is no non-linearity or irreversibility. That is, the observed piezoelectric response is very stable, and PNT can be driven at high excitation levels. The effective piezoelectric generated by PNT is at least 60 p.m./V. In addition, PNTs exhibit linear deformation over a wide range of driving voltages without irreversible degradation. One notable feature is that the dependence of the observed piezoelectric response on the tube diameter. For thick enough walls, the piezoelectric response will only depend on the piezoelectric properties of the underlying PNT material, not on the geometric constraints. The bioinspired PNTs with strong and robust piezoelectricity make them potential candidates for nano-piezoelectrics.

However, due to the limitation of the vertical nanotubes' geometry and the extremely high coercive electric field, the polarization cannot be fully achieved, and attempts to switch polarization in this material have not been successful before. Yet the applications of electronics and optics containing switch polarization and create artificial polarization patterns are unexplored [142]. In Bdikin's work, they observed the process of polarization switching and polarization pattern of FF-NTs annealed at 150 °C by using piezo-response force microscopy [143]. The annealed tube exhibits a radial polarization switch with a threshold voltage of approximately 30V and a polarization saturation of approximately 100V, as evidenced by the piezoelectric response hysteresis loop acquisition. The relatively stable hysteresis loops and polarization patterns observed by PFM prove that the molecular dipoles are partially reoriented in the radial direction. The experimental results are supplemented by strict molecular calculations, which prove the electric field induced the deformation of the aromatic ring and provide a solid background about the corresponding polarization conversion.

In Vasilev's work, the piezoelectric properties of microtubes assembled from linear dipeptide diphenylalanine were studied, and the piezoelectric coefficient matrix was derived based on the hexagonal symmetry of the FF structure [144]. The self-assembly structure of FF peptide is used to explain the strong piezoelectric anisotropy of the piezoelectric coefficient [145]. Remarkably, the surface of the peptide is easily functionalized, and it can anchor various biomolecules by harnessing free amino and carboxyl groups on the surface of the peptide as binding sites [146]. The temperature dependence of the piezoelectric coefficient of d15 in the range of 20–120 °C was studied experimentally. When the microtube is heated to 70–80 °C, the varistor monotonously decreases and is completely reversible. After an instantaneous temperature rise to 120 °C, the piezoelectric response irreversibly decreased from about 50 p.m./V to 32–35 p.m./V and remained constant within the temperature range studied. The results show the importance of temperature treatment.

4.2.4. Optical properties

During the self-assembly process, π-electrons of the aromatic system delocalized and the free proton of hydrogen bonds transferred. The peptide supramolecular semiconductor can continuously emit photons along the axis under excitation, making it an optical waveguide(Fig. 4d.) [147,148]. The peptide-based quantum-confined nanostructure leads to structure-related optical properties due to the forced coulomb interaction between highly restricted holes and electrons, thereby forming excitons with specific absorption and luminescence properties [149]. Studies have shown that aromatic rings' interacting can be expressed through spatial conjugation, and hydrogen atoms can shuttle between the donor and acceptor groups in the hydrogen bond [150].The resulting changes in the electronic structure can reduce the energy band gap and promote the photoluminescence redshift to the visible light region. It was proposed that the limitation of molecular rotation and vibration in the crystal structure hinders the transfer of energy between molecules, which allows photons to be continuously emitted, thereby enabling the device to be used in optoelectronic applications [123].

The photoluminescence (PL) observations in the blue and ultraviolet regions originating from excitons in peptide nanotubes have been reported [151]. Experiments also showed a remarkable difference between PNT and FF monomers. The PL of a phenylalanine residue is at 284 nm. At the same excitation wavelength, the FF PNT revealed a sharp peak at 305 nm. These findings provide new ideas for integrating PNT into a new generation of optical equipment.

Extensive researches have been conducted on quantum confinement materials in the field of photoluminescence [152]. However, due to inherent limitations such as low biocompatibility and difficulty in modulation, the application of traditional inorganic quantum-limited photoluminescent materials in bioimaging and biomechanical interfaces is facing severe limitations [153]. Tao et al. proposed an aromatic ring dipeptide that dimerizes into quantum dots as a building block for further self-assembly into quantum-confined supramolecular structures with different morphologies and photoluminescent properties [154]. Experimental results show that the optical properties and morphology of aromatic ring dipeptide self-assembly can be tuned. The addition or loss of water molecules will cause the red or blue shift of the UV photoluminescence. The density functional theory calculation confirmed that the adding water molecules to PNTs will cause the valence band peak to split, which corresponds to the observed movement and the split of the UV-PL peak [155].

Peptide nanoparticles with fluorescence properties spark scientists' interest in optical imaging due to their promising biodegradability. But their restricted inherent optical properties limit their applicability as high-efficiency imaging probes. To date, it is still unclear whether fluorescent peptide nanoparticles with tunable optical properties could be synthesized by self-assembly. Recently, tryptophan–phenylalanine (Trp-Phe) nanoparticles were shown to transfer the inherent fluorescence signal of peptides from ultraviolet to the visible light range [121]. By optimizing the synthesis parameters, the dipeptide nanoparticles (DNPs) that showed visible fluorescence properties, photostable, biocompatible was produced.

5. Application of peptide nanomaterials

5.1. Supercapacitor

The PNT has been demonstrated to possess diverse favorable physical properties such as piezoelectricity, thermostability, and electrochemical properties. The superb electrochemical properties of PNTs make them potential electrode materials for supercapacitors (SC). However, SCs bear the problem of low energy density. The most direct way to solve this problem is to develop electrode materials with larger specific surface areas.

Carbon materials have been widely used as electrode materials for supercapacitors, but it has low specific capacitance due to poor wettability. When the carbon electrode was modified with vertically arranged PNT, its capacitance increased more than an order of magnitude [156]. It is worth noting that even after 10,000 cycles, the PNT electrode was not significantly damaged. Based on previous work, Beker et al.

examined the electrochemical performance of carbon electrodes modified with different densities and heights PNT coatings [102]. The data showed that the PNT modified carbon electrode increases the available surface area of the electrode, thereby increasing its capacitance. The wet surface area in nano-scale hydrophilic channel of the peptide nanotube is the critical factor affecting its capacitance.

Metal oxide, an electrochemically active material, can accelerate the redox reaction on the electrode and increase the energy and capacitance of the electrode. Therefore, by combining peptide-based nanostructures with metal oxides, a new type of electrode for high-performance supercapacitors can be produced. The peptide would dissolve slightly in the electrolyte, resulting in a rapid decrease in the capacitance of the device in the cyclic stability test. Depositing a layer of TiO_2 film on the surface of the peptide can improve the performance of the capacitor. Hu et al. studied the formation of TiO_2 on the surface of self-assembly FF nanotubes and probed its application in supercapacitors (Fig. 5a.) [157]. At a current density of 0.1 A/g, the TiO_2 modified peptide electrode has a mass-specific capacitance of 125 F/g and an area capacitance of 8.6 mF/cm^2. After 5000 cycles, the capacitance retention reached more than 95%, showing excellent stability and capacity as a supercapacitor.

Hu et al. designed cyclic pentapeptides of Ac-$CAAAS_5$(X)-NH_2 (BDCPs) that varied in terms of in-tether chiral center substituents as model peptides. They demonstrated that chirality-induced helical BDCPs assemble into different nanostructures when the aromatic substituent provided π-π intermolecular interactions as a driving force [19]. On this basis, Hu et al. investigated the energy storage properties of peptide assemblies as active materials for supercapacitors. The electrochemical properties of four groups of peptide molecules were systematically compared, the results showed that the energy storage capacity of peptide materials could be controlled by peptide sequences. Via cyclic voltammetry, constant current charge and discharge, and other electrochemical measurement methods, they proved that chirality-induced helical peptide materials have good cycle stability, rate and specific capacitance properties [158].

Xiong et al. proposed a new core-shell nanobrick structure, peptide-Co_9S_8, which has high prospects in the application of wearable supercapacitors [159]. A self-powered system that integrates facile peptide--Co_9S_8//AC supercapacitors and triboelectric nanogenerators was designed in order to further probe the application of peptide-Co_9S_8//AC supercapacitors in wearable devices(Fig. 5b.). Compared with TENG-, the integrated TENG/SC system provides better power supply performance for wearable electronic devices. TENG can convert environmental mechanical energy into electricity, depending on the coupling effects of triboelectrification and electrostatic induction. TENG has obtained extensive attention in many research fields due to its advantages, such as low costs, high conversion efficiency, and environmental friendliness [160,161]. They are ideal materials for integration with peptide Co_9S_8//AC supercapacitors, due to its excellent stability and flexibility. When TENG continuously charged for 2.7 h, the polypeptide-Co_9S_8//AC supercapacitor can supply power to the red LED for 21 min, which demonstrated the high efficiency of the self-powered function of the TENG/SC integrated system. In addition, no obvious self-discharge was observed for a good while. All these characteristics show that the TENG/SC system is very suitable for wearable devices.

Nguyen et al. reported a polypeptide-based battery (Fig. 5c.), in which polypeptide cathodes and anodes contain redox-active side groups to determine their redox activities and behaviors in the full polypeptide batteries [162]. To clarify the energy-storage characteristics of the battery, they assembled each peptide into a lithium metal half-cell. Then a metal-free, polypeptide-based battery was constructed. In addition, they determined the degradation products to demonstrate the recyclability of the battery. Through the ring-opening polymerization of highly reactive cyclic N-carboxylic acid anhydride, the viologen and biTEMPO polypeptide were synthesized as the anode and cathode of the battery, respectively. The polypeptide-based battery could reach a maximum charge capacity of 37.8 mAh g^{-1}.

5.2. Biosensing

The conformation of peptide changes under external stimulation, its

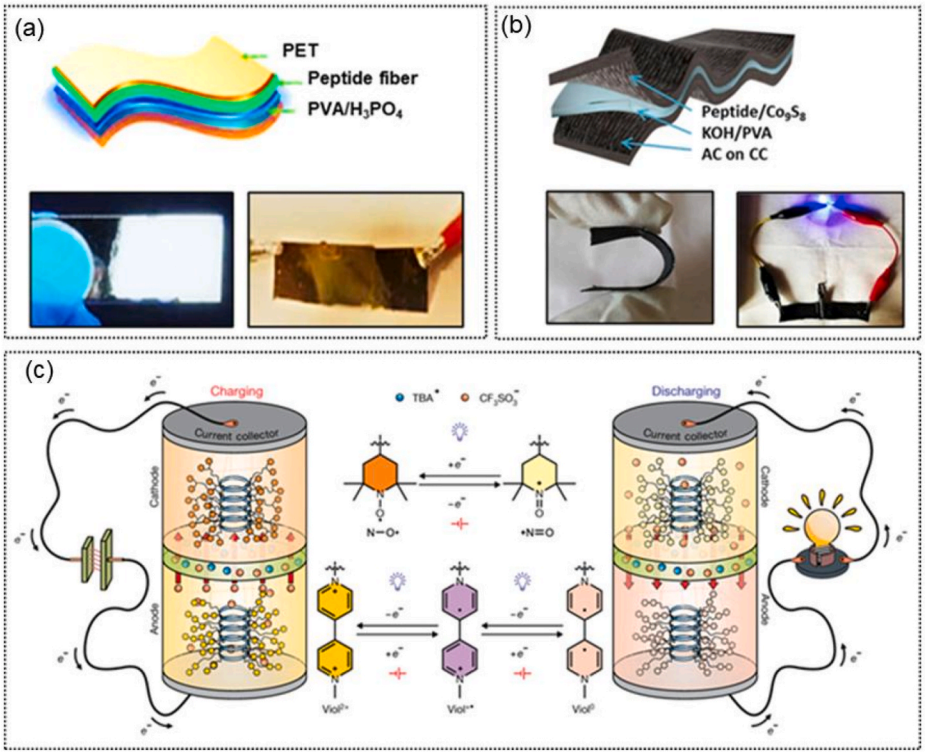

Fig. 5. (a) Schematic illustration for fabrication of the peptide@TiO_2 capacitor device [157]. (b) Preparation for peptide-Co_9S_8 core-shell nanostructures and TENG/SC system [159]. (c)Schematics of the polypeptide-based organic battery [162].

recognition function also changes accordingly. Therefore, the peptide self-assembly system can be designed to have a molecular recognition function and play an important role in biosensing [163]. PNTs are considered as promising multifunctional molecular bricks for rising nano-scale devices due to their electrical properties. Based on the specific interaction between PNTs and biomolecules, PNTs can be used for biosensing.

PNT could bind virus-antibody without destroying the recognition function, which makes PNT based sensors sensitive and versatile. The sensor consists of two electrodes separated by a micrometric gap (Fig. 6a.) [164]. The capacitance variations of the electrodes can reflect the binding event between the virus and its antibodies. The composition of polymers and semiconductors could be characterized by the capacitance probe in nanoscale.

Yemini et al. designed and constructed a highly sensitive amperease biosensor based on immobilized self-assembly peptide nanotubes (Fig. 6b.) [165]. The ethanol dehydrogenase (ADH) and glucose oxidase (GOx) were used as model enzyme systems to verify the superiority of the sensor. By comparing the responses of the peptide nanotube electrode and the bare electrode to hydrogen peroxide, the response current of the modified electrode is significantly higher than that of the bare electrode. After continuously adding 0.2 mM glucose to the GOx modified peptide nanotube electrode, the current at the anode of the peptide nanotube-based electrode immediately increased and reached a stable state within a few seconds.

Abramovich et al. introduced the electrochemical characteristics of FF NT-based sensors and compared them with CNT-based sensors [100]. Firstly, they separately deposited FF peptide nanotubes or carbon nanotubes on the electrode surface. In the presence of carbon nanotubes, the oxidation and reduction peaks are very close, which means a reversible electron transfer reaction has occurred. However, the peaks are higher while peptide nanotubes exist, which means the electrode surface increases. When the two nanostructures were deposited on the same electrode, this combination showed the best results.

Preparation of electrochemical peptide-based biosensor for matrix metalloproteinase 2 (MMP-2) detection based on bimetallic Pt/Pd NPs has also been reported [166]. The analytical performance of the biosensor was significantly improved, due to the excellent catalytic capacity of Pt/Pd/mhCeO$_2$NS (Fig. 6c.). It is an effective strategy to accurately determine MMP-2 using Pt/Pd/mhCeO$_2$NS as nanocarriers and transducing the peptide-based cleavage events into an electrochemical signal through targeting MMP-2.

In addition, combining PNTs with other biological materials can form innovative hybrid materials. Peptide nanotubes have been used to prepare nanometer-sized peptide-polymer hybrid nanotubes [33]. Cyclic peptides composed of D-and L-alternating amino acids can be modified by certain chemical groups at different side chain positions. The initiator of polymer hybrid nanotubes is the polymeric coating of the polypeptide core, and the covalently bound polymer shell is used. By self-assembly of dipeptide monomers in chitosan aqueous solution, a new composite material of peptide nanotube and chitosan (PNT-CS) can be prepared. The PNT-CS can be further used as an electrochemical cell for detecting cancer cells [167].Peptides could be used as recognition elements in biosensing due to the characteristics of peptides such as easy access, easy modification, versatility and so on. A new molecular probe composed of a photoacoustic dye, an antibacterial agent, and an enzyme-responsive peptide as a linker was developed. It enables the real-time and accurate detection of bacterial infection due to the

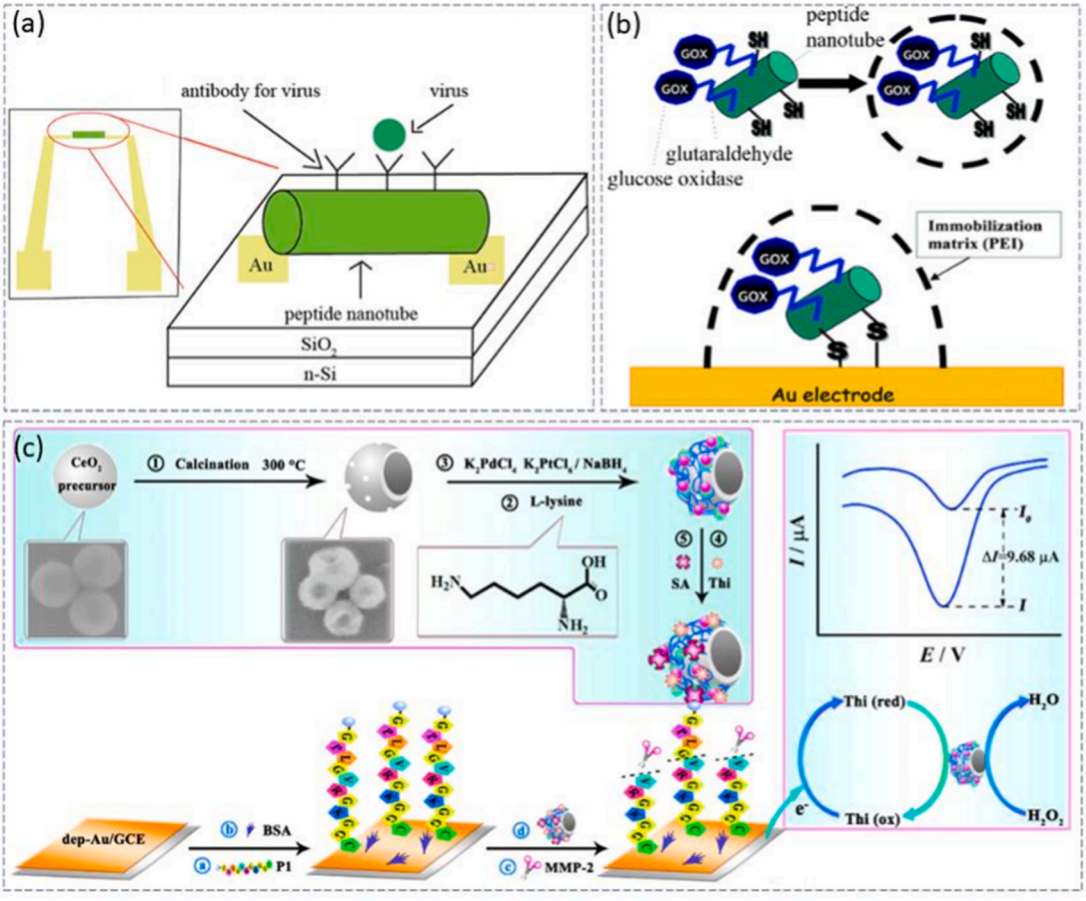

Fig. 6. Application of peptide nanomaterials as biosensing (a) Design of the pathogen-sensor platform assembled from peptide nanotubes [164]. (b) Schematic of the procedure used to manufacture enzymatic electrodes based on peptide nanotubes [165]. (c) Schematic of the peptide-based biosensor for MMP-2 detection [166].

self-aggregation of the molecules in vivo [168]. Besides, the in vivo assembly-induced tumor retention was also reported. Bellat et al. proposed a self-assembling nanofiber precursor (NFP) that is composed of multiple components, which could optimize tumoral delivery efficiency via using a combination of shape-controlled tumoral delivery, charge-assisted penetration, and enzyme-induced drug retention [169]. Cheng et al. designed a therapeutic peptide assembling nanoparticle with dual responsivity and intrinsic therapeutic potential for tumor-targeted delivery and precisely controllable drug release [170]. Zhang et al. designed a small molecular precursor composed of purpurin 18 as a functionality and a Pro-Leu-Gly-Val-Arg-Gly (PLGVRG) peptide as the enzyme-responsive linker, which can self-assemble into nanofibers in the tumor microenvironment. Due to the assembly-induced retention effect, the photoacoustic imaging signal and tumor therapeutic efficacy were improved [171]. In addition, the specific peptide sequence is a specific enzyme substrate, which plays a vital role in the determination of enzyme activity and the screening of enzyme inhibitors. Due to these special properties, peptides are ideal candidates for the development of sensitive and convenient biosensors [172,173]. The above examples show that peptide-nanotubes biosensing integrates the multiple disciplines of materials research, nanoscience and molecular biotechnology. These interdisciplinary approaches help to develop the novel field of bio-nanosensing technology.

5.3. Drug delivery

Compared with other delivery platforms, peptide-based nanostructures have some advantages, including their chemical diversity, biocompatibility, and specific binding to target proteins, making them great potential for biomedical applications, such as drug delivery.

Nanoparticles self-assembled from doxorubicin conjugated peptides have been considered as an effective modality for cancer treatment. Rubert et al. proposed a method of hierarchically assembling of peptide-based nanofibers with alginate to form microparticles [8], in which doxorubicin is conjugated to the alginate core while the shell is functionalized to target folate receptor (Fig. 7a.) [10,174].

Nucleic acid drugs have been used to treat viral infections, cancer, AIDS. siRNA is easy to synthesize and can target any protein

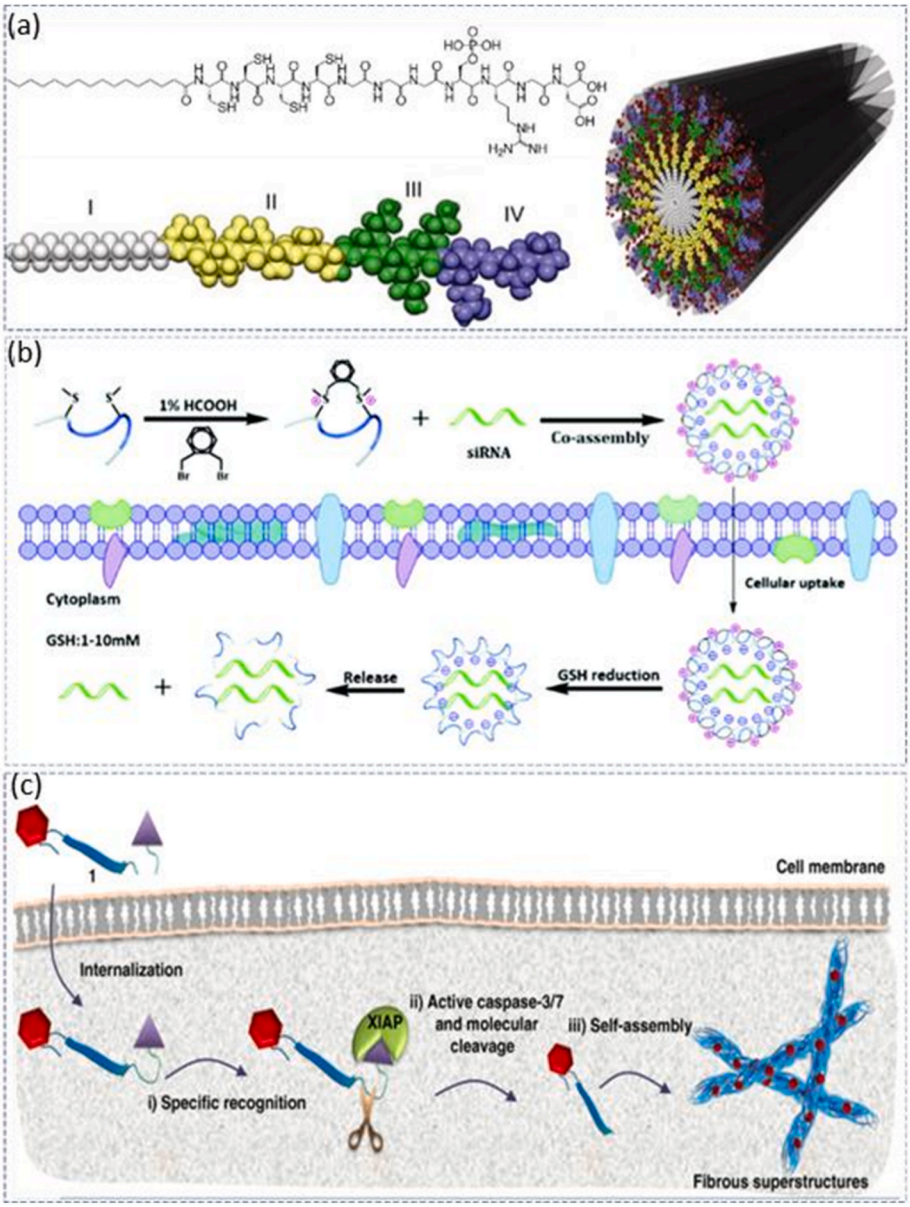

Fig. 7. Application of Drug delivery (a) Schematic representation of the chemical structure and self-assembled PA nanofibers of a classic peptide amphiphile [10]. (b) Schematic presentation of the Wpc peptide [178]. (c) The mechanism of peptide molecular specific recognition, molecular cleavage and in-situ self-assembly [181].

theoretically. The siRNA drugs have captured more and more attention these years [175]. However, RNA drugs are easily degraded and cannot penetrate cell membranes; there is an imperative need to develop efficient and biocompatible nucleic acid delivery systems [176]. As a class of self-existing biomolecules in living organisms, polypeptides are highly biocompatible and have been proved to be effective nucleic acid carriers, and their applications in biomedicine have attracted much attention [177]. At present, the polypeptide carrier system is generally long (longer than 20 amino acids), which is difficult to prepare and expensive. Li et al. reported a novel siRNA-induced peptide co-assembly nanocarrier, with high efficiency of RNA silencing, which has low cytotoxicity and good biocompatibility both in vitro and vivo (Fig. 7b.) [178]. This system is based on peptides modified with methionine, and the peptide-nucleotides nanoparticle is with only nine amino acids.

Traditional molecular drugs have poor efficacy due to rapid metabolic clearance in vivo, while nano-drugs can improve drug solubility, tumor passive targeting, and blood circulation time [179,180]. An et al. designed a TCASS system for tumor imaging and drug delivery(Fig. 7c.) [181]. In this system, small-molecule peptides specifically recognize the over-expressed X-linked inhibitor of apoptosis (XIAP) in tumors, which triggers the activation of Caspase-3 in tumor cells that triggers molecular splicing, enrichment and retention of self-assembled nanofibers in tumor tissues. In addition, TCASS is metabolically similar to small molecules that can be excreted quickly from the liver and kidneys, reducing systemic toxicity. This work optimizes accumulation, infiltration, and organ competition, reveals the mechanisms of effective retention and accumulation in tumor sites, and analyzes the pharmacokinetics of the system.

Anti-cancer chemotherapy drug, especially taxol, are widely used in clinical practice. However, the taxol exhibits poor water solubility, which limits its application and modification. Nanospheres, as rigid as metal nanoparticles [182], formed by di-phenylalanine derivatives, can be used to deliver single-stranded DNA and quantum dots [183]. It is within this context that Wang et al. designed a Folic acid (FA)–Taxol conjugate of FA-GpYK-Taxol [184], and reported a novel gelation system.

Molecular hydrogels possess huge potential for drug delivery. A molecular hydrogel mainly formed by taxol was proposed, which might be developed into novel self-delivery systems. In this work, the ester bond of taxol derivative(Tax-SA-GSSG) hydrolyzed to form the hydrogel that can hinder the growth and metastasis of solid tumors. Side effects of taxol during chemotherapy could be reduced due to the local administration of taxol hydrogels which lower the concentration of taxol in blood [185].

6. Conclusions and future perspectives

Peptides self-assembly means the spontaneous association of molecules under specific conditions into well-ordered and fairly stable structures. As one of the most common molecular self-organization phenomena in nature, the study of self-assembly behavior is of great significance for understanding the molecular interaction among biological molecules and creating novel functional materials. In addition, as a kind of molecule with biological homology, peptides are ideal self-assembling building blocks with superior biological and chemical properties. First, through rational molecular design and diversified peptide synthesis methods, millions of peptides with different structures and specific functions can be generated, providing adequate sequence analogs for parallel screening and optimization. Second, with good biocompatibility, versatility, and biological activity, one can easily customize the functions of self-assembly peptide nanomaterials for unique applications, such as drug delivery, bioengineering, and others.

Self-assembled peptides can be categorized into four classes based on their characteristics and functions, including “molecular Lego” “molecular switches” “molecular Velcro” “nanotubes” and “nanovesicles”. The peptide self-assembly is mainly driven by non-covalent interactions. The main forms of non-covalent interactions include electrostatic, hydrogen-bonding, hydrophobic, π-π stacking, and van der Waals interactions. Peptides can self-assemble into various nanostructures, which may exhibit intriguing properties, such as high thermostability and mechanical stability, semiconductivity, piezoelectricity, and optical properties, attracting more and more attention in biomedical and material fields. Although peptide self-assembly is widely present in nature and involves in regulating various life activities, the research on peptide self-assembly and the construction of various functional bionanomaterials using self-assembly methods is still in its infancy. At present, the synthesis and application of self-assembled peptide nanomaterials are still impeded by several limitations. Although self-assembled peptide nanomaterials have good biocompatibility and biodegradability, their mechanical and functional properties need further polish. Besides, as a scaffold material for in vivo drug release, the peptide self-assembly is easily affected by the physiological environment, and the self-assembly is not stable enough. Incorporating inorganic molecules can expand the properties of peptide assemblies, such as mechanical and structural diversity. In the future, self-assembled peptide materials should integrate more functions, such as targeting ability, sensitivity, and direct therapeutic effects. Although there are many forms of peptide assemblies, it is currently challenging to directly predict and regulate accurately from the molecular structure of peptides. As great effort has been made, new methods of researching these peptide structures including microfluidic and super-resolution microscopy could provide views of the peptide self-assembly process and peptide structures. Although peptide-based nanomaterials are still challenging to explore and use, they present huge promising future research.

This review summarizes the basic properties and applications of peptide-based nanomaterials from the aspects of mechanisms, properties, and applications. Based on their ability to self-assemble, peptide nanomaterials offer great potential applications in biomedicine and biotechnology. The application of peptide nanomaterials in various fields, such as supercapacitors, nanogenerators, biosensors, and drug delivery platforms, has been established. The widespread applications of peptide nanomaterials can significantly influence our daily life in the future. Although many challenges will be confronted in exploring peptide self-assembly, the future of peptide-based self-assembly nanomaterials is promising and achievable.

Declaration of competing interest

The authors declare that they have no conflict of interest

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References

[1] G.M. Whitesides, J.P. Mathias, C.T. Seto, Molecular self-assembly and nanochemistry: a chemical strategy for the synthesis of nanostructures, Science 254 (5036) (1991) 1312–1319.
[2] T.H. Han, J.K. Oh, G.J. Lee, S.I. Pyun, O.K. Sang, Hierarchical assembly of diphenylalanine into dendritic nanoarchitectures, Colloids Surf., B 79 (2) (2010) 440–445.
[3] C. Chen, L. Kai, J. Li, X. Yan, Functional architectures based on self-assembly of bio-inspired dipeptides: structure modulation and its photoelectronic applications, Adv. Colloid. Interfac. 225 (NOV) (2015) 177–193.
[4] S. Fleming, R.V. Ulijn, Design of nanostructures based on aromatic peptide amphiphiles, Chem. Soc. Rev. 43 (23) (2014) 8150–8177.
[5] S. Zhang, S. Zhang, Fabrication of novel materials through molecular self-assembly, Nat. Biotechnol. 21 (10) (2003) 1171–1178.

[6] J. Li, Y. Kuang, Y. Gao, X. Du, J. Shi, B. Xu, D-amino acids boost the selectivity and confer supramolecular hydrogels of a nonsteroidal anti-inflammatory drug (NSAID), J. Am. Chem. Soc. 135 (2) (2013) 542–545.
[7] X. Zhao, F. Pan, X. Hai, M. Yaseen, R.L. Jian, Molecular self-assembly and applications of designer peptide amphiphiles, ChemInform 39 (9) (2010) 3480–3498.
[8] C.M. Rubert Pérez, N. Stephanopoulos, S. Sur, S.S. Lee, C. Newcomb, S.I. Stupp, The powerful functions of peptide-based bioactive matrices for regenerative medicine, Ann. Biomed. Eng. 43 (3) (2015) 501–514.
[9] N. Habibi, N. Kamaly, A. Memic, H. Shafiee, Self-assembled peptide-based nanostructures: smart nanomaterials toward targeted drug delivery, Nano Today (2016) 41–60.
[10] J.B. Matson, R.H. Zha, S.I. Stupp, Peptide self-assembly for crafting functional biological materials, Curr. Opin. Solid. St. M. 15 (6) (2011) 225–235.
[11] A. Levin, T.A. Hakala, L. Schnaider, G.J.L. Bernardes, E. Gazit, T.P.J. Knowles, Biomimetic peptide self-assembly for functional materials, Nat. Rev. Chem. 4 (11) (2020) 615–634.
[12] V. Apostolopoulos, J. Bojarska, T.T. Chai, S. Elnagdy, K. Kaczmarek, J. Matsoukas, R. New, K. Parang, O.P. Lopez, H. Parhiz, C.O. Perera, M. Pickholz, M. Remko, M. Saviano, M. Skwarczynski, Y.F. Tang, W.M. Wolf, T. Yoshiya, J. Zabrocki, P. Zielenkiewicz, M. AlKhazindar, V. Barriga, K. Kelaidonis, E. M. Sarasia, I. Toth, A global review on short peptides: frontiers and perspectives, Molecules 26 (2) (2021).
[13] C.O. Pabo, E. Peisach, R.A. Grant, Design and selection of novel Cys(2)His(2) zinc finger proteins, Annu. Rev. Biochem. 70 (2001) 313–340.
[14] J.L. Battiste, H.Y. Mao, N.S. Rao, R.Y. Tan, D.R. Muhandiram, L.E. Kay, A. D. Frankel, J.R. Williamson, α-helix-RNA major groove recognition in an HIV-1 Rev peptide RRE RNA complex, Science 273 (5281) (1996) 1547–1551.
[15] M. Uesugi, G.L. Verdine, The α-helical FXX π-π motif in p53: TAF interaction and discrimination by MDM2, P. Natl. Acad. Sci. USA 96 (26) (1999) 14801–14806.
[16] J. Liu, D. Wang, Q. Zheng, M. Lu, P.S. Arora, Atomic structure of a short α-helix stabilized by a main chain hydrogen-bond surrogate, J. Am. Chem. Soc. 130 (13) (2008) 4334–4337.
[17] K. Hu, W. Xiong, C. Sun, C. Wang, J. Li, F. Yin, Y. Jiang, M.-R. Zhang, Z. Li, X. Wang, Z. Li, Self-assembly of constrained cyclic peptides controlled by ring size, CCS Chem 2 (1) (2020) 42–51.
[18] K. Hu, F. Yin, Z. Zhou, C. Lian, Y. Liu, C. Sun, W. Li, J. Zhang, Z. Li, Directional assembly of a stapled α-helical peptide, Chem. Commun. 55 (70) (2019) 10484–10487.
[19] K. Hu, Y. Jiang, W. Xiong, H. Li, P.-Y. Zhang, F. Yin, Q. Zhang, H. Geng, F. Jiang, Z. Li, X. Wang, Z. Li, Tuning peptide self-assembly by an in-tether chiral center, Sci. Adv. 4 (5) (2018) eaar5907.
[20] F. Ruan, Y. Chen, P.B. Hopkins, Metal ion-enhanced helicity in synthetic peptides containing unnatural, metal-ligating residues, J. Am. Chem. Soc. 112 (25) (2002) 9403–9404.
[21] S. Marqusee, R.L. Baldwin, Helix stabilization by Glu-...Lys+ salt bridges in short peptides of de novo design, P. Natl. Acad. Sci. USA 84 (24) (1987) 8898–8902.
[22] S. Sakamoto, A. Ueno, H. Mihara, Molecular assembly of two-α-helix peptide induced by haem binding, Chem. Commun. 10 (1998) 1073–1074.
[23] S. Mondal, L. Adler-Abramovich, A. Lampel, Y. Bram, S. Lipstman, E. Gazit, Formation of functional super-helical assemblies by constrained single heptad repeat, Nat. Commun. 6 (2015).
[24] K. Hu, H. Geng, Q.Z. Zhang, Q.S. Liu, M.S. Xie, C.J. Sun, W.J. Li, H.C. Lin, F. Jiang, T. Wang, Y.D. Wu, Z.G. Li, An in-tether chiral center modulates the helicity, cell permeability, and target binding affinity of a peptide, Angew. Chem. Int. Ed. 55 (28) (2016) 8013–8017.
[25] Y.X. Jiang, W. Zhang, F.D. Yang, C. Wan, X. Cai, J.B. Liu, Q.L. Zhang, Z.G. Li, W. Han, Molecular design of stapled pentapeptides as building blocks of self-assembled coiled coil-like fibers, Sci. Adv. 7 (4) (2021).
[26] Y.B. Lim, K.S. Moon, M. Lee, Stabilization of an α-helix by β-sheet-mediated self-assembly of a macrocyclic peptide, Angew. Chem. Int. Ed. 48 (9) (2009) 1601–1605.
[27] S. Zhang, T. Holmes, L.A. Rich, Spontaneous assembly of a self-complementary oligopeptide to form a stable macroscopic membrane, P. Natl. Acad. Sci. USA 90 (8) (1993) 3334–3338.
[28] S.G. Zhang, C. Lockshin, R. Cook, A. Rich, Unusually stable β-sheet formation in an ionic self-complementary oligopeptide, Biopolymers 34 (5) (1994) 663–672.
[29] S. Zhang, T.C. Holmes, C.M. Dipersio, R.O. Hynes, A. Rich, Self-complementary oligopeptide matrices support mammalian cell attachment, Biomaterials 16 (18) (1995) 1385–1393.
[30] M.P. Hendricks, K. Sato, L.C. Palmer, S.I. Stupp, Supramolecular assembly of peptide amphiphiles, Accounts Chem. Res. 50 (10) (2017) 2440–2448.
[31] H. Yokoi, T. Kinoshita, S. Zhang, Dynamic reassembly of peptide RADA16 nanofiber scaffold, P. Natl. Acad. Sci. USA 102 (24) (2005) 8414–8419.
[32] M.R. Ghadiri, J.R. Granja, R.A. Milligan, D. Mcree, N. Khazanovich, Self-assembling organic nanotubes based on a cyclic peptide architecture, Nature 366 (6453) (1993) 324.
[33] J. Couet, J. Samuel, A. Kopyshev, S. Santer, M. Biesalski, Peptide-polymer hybrid nanotubes, Angew. Chem. Int. Ed. 44 (21) (2005) 3297–3301.
[34] C. Reiriz, R.J. Brea, R. Arranz, J.L. Carrascosa, A. Garibotti, B. Manning, J. M. Valpuesta, R. Eritja, L. Castedo, J.R. Granja, alpha,gamma-Peptide nanotube templating of one-dimensional parallel fullerene arrangements, J. Am. Chem. Soc. 131 (32) (2009) 11335–+.
[35] H.S. Kim, J.D. Hartgerink, M.R. Ghadiri, Oriented self-assembly of cyclic peptide nanotubes in lipid membranes, J. Am. Chem. Soc. 120 (18) (1998) 4417–4424.
[36] T.D. Clark, J.M. Buriak, K. Kobayashi, M.P. Isler, D.E. McRee, M.R. Ghadiri, Cylindrical β-sheet peptide assemblies, J. Am. Chem. Soc. 120 (35) (1998) 8949–8962.
[37] J.P. Schnei De R, D.J. Pochan, B. Ozbas, K. Rajagopal, L. Pakstis, J. Kretsinger, Responsive hydrogels from the intramolecular folding and self-assembly of a designed peptide, J. Am. Chem. Soc. 124 (50) (2002) 15030–15037.
[38] M.S. Lamm, K. Rajagopal, J.P. Schneider, D.J. Pochan, Laminated morphology of nontwisting β-sheet fibrils constructed via peptide self-assembly, J. Am. Chem. Soc. 127 (47) (2005) 16692–16700.
[39] C. Veerman, K. Rajagopal, C.S. Palla, D.J. Pochan, J.P. Schneider, E.M. Furst, Gelation kinetics of β-Hairpin peptide hydrogel networks, Macromolecules 39 (19) (2006) 6608–6614.
[40] T.C. Holmes, S. de Lacalle, X. Su, G.S. Liu, A. Rich, S.G. Zhang, Extensive neurite outgrowth and active synapse formation on self-assembling peptide scaffolds, P. Natl. Acad. Sci. USA 97 (12) (2000) 6728–6733.
[41] H.M. Wang, J.F. Shi, Z.Q.Q. Feng, R. Zhou, S.Y. Wang, A.A. Rodal, B. Xu, An in situ dynamic continuum of supramolecular phosphoglycopeptides enables formation of 3D cell spheroids, Angew. Chem. Int. Ed. 56 (51) (2017) 16297–16301.
[42] S. Toledano, R.J. Williams, V. Jayawarna, R.V. Ulijn, Enzyme-triggered self-assembly of peptide hydrogels via reversed hydrolysis, J. Am. Chem. Soc. 128 (4) (2006) 1070–1071.
[43] Z.M. Yang, H.W. Gu, D.G. Fu, P. Gao, J.K. Lam, B. Xu, Enzymatic formation of supramolecular hydrogels, Adv. Mater. 16 (16) (2004) 1440. -+.
[44] J. Gao, J. Zhan, Z.M. Yang, Enzyme-instructed self-assembly (EISA) and hydrogelation of peptides, Adv. Mater. 32 (3) (2020).
[45] Z. Feng, H. Wang, B. Xu, Instructed assembly of peptides for intracellular enzyme sequestration, J. Am. Chem. Soc. 140 (48) (2018) 16433–16437.
[46] H.M. Wang, Z.Q.Q. Feng, B. Xu, Instructed assembly as context-dependent signaling for the death and morphogenesis of cells, Angew. Chem. Int. Ed. 58 (17) (2019) 5567–5571.
[47] Z.M. Yang, G.L. Liang, B. Xu, Enzymatic control of the self-assembly of small molecules: a new way to generate supramolecular hydrogels, Soft Matter 3 (5) (2007) 515–520.
[48] L.A. Estroff, A.D. Hamilton, Water gelation by small organic molecules, Chem. Rev. 104 (3) (2004) 1201–1217.
[49] H. Wang, X. Yang, H. Lu, Y. Tao, L. Zhou, Spatiotemporal control over chemical assembly in living cells by integration of acid catalyzed hydrolysis and enzymatic reaction, Angew. Chem. Int. Ed. (2021), https://doi.org/10.1002/adfm.202104092.
[50] J.N. Israelachvili, Contrasts between intermolecular, interparticle, and intersurface forces, Intermolecular & Surface Forces 2 (3) (2011) 205–222.
[51] J. Wang, K. Liu, R.R. Xing, X.H. Yan, Peptide self-assembly: thermodynamics and kinetics, Chem. Soc. Rev. 45 (20) (2016) 5589–5604.
[52] V. Palermo, P. Samori, Molecular self-assembly across multiple length scales, Angew. Chem. Int. Ed. 46 (24) (2007) 4428–4432.
[53] T.D. Do, W.M. Kincannon, M.T. Bowers, Phenylalanine oligomers and fibrils: the mechanism of assembly and the importance of tetramers and counterions, J. Am. Chem. Soc. 137 (32) (2015) 10080–10083.
[54] T.D. Do, N.D. Almeida, N.E. Lapointe, A. Chamas, M.T. Bowers, Amino acid metaclusters: implications of growth trends on peptide self-assembly and structure, Anal. Chem. 88 (1) (2016) 868–876.
[55] L. Adler-Abramovich, L. Vaks, O. Carny, D. Trudler, A. Magno, A. Caflisch, D. Frenkel, E. Gazit, Phenylalanine assembly into toxic fibrils suggests amyloid etiology in phenylketonuria, Nat. Chem. Biol. 8 (8) (2012) 701.
[56] T.P. Knowles, A.W. Fitzpatrick, S. Meehan, H.R. Mott, M. Vendruscolo, C. M. Dobson, M.E. Welland, Role of intermolecular forces in defining material properties of protein nanofibrils, Science 318 (5858) (2007) 1900–1903.
[57] M.G. Krone, L. Hua, P. Soto, R.H. Zhou, B.J. Berne, J.E. Shea, Role of water in mediating the assembly of Alzheimer amyloid-β Aβ16-22 protofilaments, J. Am. Chem. Soc. 130 (33) (2008) 11066–11072.
[58] P.L. Zhu, X.H. Yan, Y. Su, Y. Yang, J.B. Li, Solvent-induced structural transition of self-assembled dipeptide: from organogels to microcrystals, Chem. Eur J. 16 (10) (2010) 3176–3183.
[59] S. Toksoz, H. Acar, M.O. Guler, Self-assembled one-dimensional soft nanostructures, Soft Matter 6 (23) (2010) 5839–5849.
[60] J.J. Richardson, M. Bjornmalm, F. Caruso, Technology-driven layer-by-layer assembly of nanofilms, Science 348 (6233) (2015) 12.
[61] C.F.J. Faul, M. Antonietti, Ionic self-assembly: facile synthesis of supramolecular materials, Adv. Mater. 15 (9) (2003) 673–683.
[62] T.H. Rehm, C. Schmuck, Ion-pair induced self-assembly in aqueous solvents, Chem. Soc. Rev. 39 (10) (2010) 3597–3611.
[63] G.M. Whitesides, B. Grzybowski, Self-assembly at all scales, Science 295 (5564) (2002) 2418–2421.
[64] J. Wang, L.Q. Chen, J.D. Wu, W. Li, K. Liu, T. Masuda, A. Zhang, Supramolecular assembly of C_3-peptides into helical fibers stabilized through dynamic covalent chemistry, Chem. Asian J. 13 (23) (2018) 3647–3652.
[65] H.V. Schroder, Y. Zhang, A.J. Link, Dynamic covalent self-assembly of mechanically interlocked molecules solely made from peptides, Nat. Chem. 13 (2021) 850–857.
[66] J.F. Reuther, J.L. Dees, I.V. Kolesnichenko, E.T. Hernandez, D.V. Ukraintsev, R. Guduru, M. Whiteley, E.V. Anslyn, Dynamic covalent chemistry enables formation of antimicrobial peptide quaternary assemblies in a completely abiotic manner, Nat. Chem. 10 (1) (2018) 45–50.

[67] C. Bortolini, N.C. Jones, S.V. Hoffmann, F. Besenbacher, M. Dong, The influence of the localised charge of C- and N-termini on peptide self-assembly, Soft Matter 12 (2) (2015) 373–377.
[68] H. Cui, A.G. Cheetham, E.T. Pashuck, S.I. Stupp, Amino acid sequence in constitutionally isomeric tetrapeptide amphiphiles dictates architecture of one-dimensional nanostructures, J. Am. Chem. Soc. 136 (35) (2014) 12461–12468.
[69] N.R. Lee, C.J. Bowerman, B.L. Nilsson, Effects of varied sequence pattern on the self-assembly of amphipathic peptides, Biomacromolecules 14 (9) (2013) 3267–3277.
[70] W. Liyanage, B.L. Nilsson, Substituent effects on the self-assembly/coassembly and hydrogelation of phenylalanine derivatives, Langmuir 32 (3) (2016) 787–799.
[71] N.R. Lee, C.J. Bowerman, B.L. Nilsson, Sequence length determinants for self-assembly of amphipathic β-sheet peptides, Peptide Sci 100 (6) (2013) 738–750.
[72] D.M. Marini, W. Hwang, D.A. Lauffenburger, S. Zhang, R.D. Kamm, Left-handed helical ribbon intermediates in the self-assembly of a β-sheet peptide, Nano Lett. 2 (4) (2002) 295–299.
[73] M. Reches, E. Gazit, Formation of closed-cage nanostructures by self-assembly of aromatic dipeptides,, Nano Lett. 4 (4) (2004) 581–585.
[74] M. Reches, E. Gazit, Casting metal nanowires within discrete self-assembled peptide nanotubes, Science 300 (5619) (2003) 625–627.
[75] Q. Meng, Y. Kou, M. Xin, Y. Liang, K. Liu, Tunable self-assembled peptide amphiphile nanostructures, Langmuir 28 (11) (2012) 5017–5022.
[76] F. Qiu, Y.Z. Chen, C.K. Tang, Q.H. Zhou, C. Wang, Y.K. Shi, X.J. Zhao, De Novo design of a bolaamphiphilic peptide with only natural amino acids, Macromol. Biosci. 8 (11) (2008) 1053–1059.
[77] H. Xu, J. Wang, S. Han, J. Wang, R.L. Jian, Hydrophobic-region-induced transitions in self-assembled peptide nanostructures, Langmuir 25 (7) (2009) 4115–4123.
[78] F.Q. A, Y.C. A, X. Z, A.B. C, Comparative studies on the self-assembling behaviors of cationic and catanionic surfactant-like peptides - ScienceDirect, J. Colloid Interface Sci. 336 (2) (2009) 477–484.
[79] J. Wang, S. Han, G. Meng, H. Xu, D. Xia, X. Zhao, R. Schweins, J.R. Lu, Dynamic self-assembly of surfactant-like peptides A_6K and A_9K, Soft Matter 5 (20) (2009) 3870–3878.
[80] M.R. Tiné, M. Alderighi, C. Duce, L. Ghezzi, R. Solaro, Effect of temperature on self-assembly of an ionic tetrapeptide, J. Therm. Anal. Calorim. 103 (1) (2011) 75–80.
[81] Z. Luo, X. Zhao, S. Zhang, L. Hilal, Structural dynamic of a self-assembling peptide d-EAK16 made of only d-amino acids, PloS One 3 (5) (2008), e2364.
[82] J.E. Goldberger, E.J. Berns, R. Bitton, C.J. Newcomb, S.I. Stupp, Electrostatic control of bioactivity, Angew. Chem. 50 (28) (2011) 6292–6295.
[83] A. Ghosh, M. Haverick, K. Stump, X. Yang, M.F. Tweedle, J.E. Goldberger, Fine-tuning the pH trigger of self-assembly, J. Am. Chem. Soc. 134 (8) (2012) 3647–3650.
[84] Y. Zhao, H. Yokoi, M. Tanaka, T. Kinoshita, T. Tan, Self-assembled pH-responsive hydrogels composed of the RATEA16 peptide, Biomacromolecules 9 (6) (2008) 1511–1518.
[85] S.L. Zhou, S. Matsumoto, H.D. Tian, H. Yamane, A. Ojida, S. Kiyonaka, I. Hamachi, pH-Responsive shrinkage/swelling of a supramolecular hydrogel composed of two small amphiphilic molecules, Chemistry 11 (4) (2010) 1130–1136.
[86] H. Cui, T. Muraoka, A.G. Cheetham, S.I. Stupp, Self-assembly of giant peptide nanobelts, Nano Lett. 9 (3) (2009) 945–951.
[87] J. Cui, A. Liu, Y. Guan, J. Zheng, Z. Shen, X. Wan, Tuning the helicity of self-assembled structure of a sugar-based organogelator by the proper choice of cooling rate, Langmuir 26 (5) (2010) 3615.
[88] R. Huang, Q. Wei, R. Su, J. Zhao, Z. He, Solvent and surface controlled self-assembly of diphenylalanine peptide: from microtubes to nanofibers, Soft Matter 7 (14) (2011) 6418.
[89] Y. Zhao, J. Wang, L. Deng, P. Zhou, S. Wang, Y. Wang, H. Xu, J.R. Lu, Tuning the self-assembly of short peptides via sequence variations, Langmuir 29 (44) (2013) 13457–13464.
[90] Y. Zhao, L. Deng, J. Wang, X. Hai, R.L. Jian, Solvent controlled structural transition of KI_4K self-assemblies: from nanotubes to nanofibrils, Langmuir 31 (47) (2015).
[91] Y. Li, B. Li, Y. Fu, S. Lin, Y. Yang, Solvent-induced handedness inversion of dipeptide sodium salts derived from alanine, Langmuir 29 (31) (2013) 9721–9726.
[92] Q. Song, Z. Cheng, M. Kariuki, S.C.L. Hall, S.K. Hill, J.Y. Rho, S. Perrier, Molecular self-assembly and supramolecular chemistry of cyclic peptides, Chem. Rev. (2021), https://doi.org/10.1021/acs.chemrev.0c01291.
[93] H.Y. Chow, Y. Zhang, E. Matheson, X.C. Li, Ligation Technologies for the synthesis of cyclic peptides, Chem. Rev. 119 (17) (2019) 9971–10001.
[94] M. Reches, E. Gazit, Controlled patterning of aligned self-assembled peptide nanotubes, Nat, Nanotechnology 1 (3) (2006) 195–200.
[95] L. Adler-Abramovich, D. Aronov, P. Beker, M. Yevnin, S. Stempler, L. Buzhansky, G. Rosenman, E. Gazit, Self-assembled arrays of peptide nanotubes by vapour deposition, Nat, Nanotechnology 4 (12) (2009) 849–854.
[96] J.R. Chen, S.Y. Qin, X.L. Wu, P.K. Chut, Morphology and pattern control of diphenylalanine self-assembly via evaporative dewetting, ACS Nano 10 (1) (2016) 832–838.
[97] V. Nguyen, R. Zhu, K. Jenkins, R.S. Yang, Self-assembly of diphenylalanine peptide with controlled polarization for power generation, Nat. Commun. 7 (2016) 6.
[98] M. Reches, E. Gazit, Designed aromatic homo-dipeptides: formation of ordered nanostructures and potential nanotechnological applications, Phys. Biol. 3 (1) (2006) 10–19.
[99] Singh, Jasprit, Semiconductor Optoelectronics : Physics and Technology, Semiconductor Optoelectronics : Physics and Technology1995.
[100] L. Adler-Abramovich, M. Badihi-Mossberg, E. Gazit, J. Rishpon, Characterization of peptide-nanostructure-modified electrodes and their application for ultrasensitive environmental monitoring, Small 6 (7) (2010) 825–831.
[101] N. Amdursky, I. Koren, E. Gazit, G. Rosenman, Adjustable photoluminescence of peptide nanotubes coatings, J. Nanosci. Nanotechnol. 11 (10) (2011) 9282–9286.
[102] P. Beker, I. Koren, N. Amdursky, E. Gazit, G. Rosenman, Bioinspired peptide nanotubes as supercapacitor electrodes, J. Mater. Sci. 45 (23) (2010) 6374–6378.
[103] H. Inouye, P.E. Fraser, D.A. Kirschner, Structure of β-crystallite assemblies formed by Alzheimer β-amyloid protein analogs: analysis by x-ray diffraction, Biophys. J. 64 (2) (1993) 502–519.
[104] H. Inouye, D.A. Kirschner, X-ray diffraction analysis of scrapie prion: intermediate and folded structures in a peptide containing two putative alpha-helices, J. Mol. Biol. 268 (2) (1997) 375–389.
[105] R.J.A. Hill, V.L. Sedman, S. Allen, P.M. Williams, M. Paoli, L. Adler-Abramovich, E. Gazit, L. Eaves, S.J.B. Tendler, Alignment of aromatic peptide tubes in strong magnetic fields, Adv. Mater. 19 (24) (2007) 4474–4479.
[106] E. Gazit, A possible role for π-stacking in the self-assembly of amyloid fibrils, Faseb. J. 16 (1) (2002) 77–83.
[107] Porat Yair, Stepensky Alex, Ding Fa-Xiang, Naider Fred, Gazit Ehud, Completely different amyloidogenic potential of nearly identical peptide fragments, Biopolymers 69 (2) (2003) 161–164.
[108] S.B. Malinchik, H. Inouye, K.E. Szumowski, D.A. Kirschner, Structural analysis of Alzheimer's β(1-40) amyloid: protofilament assembly of tubular fibrils, Biophys. J. 74 (1) (1998) 537–545.
[109] L.C. Serpell, C. Blake, P.E. Fraser, Molecular structure of a fibrillar Alzheimer's Aβ fragment, Biochemistry 39 (43) (2000) 13269.
[110] P. Sikorski, E. Atkins, L.C. Serpell, Structure and texture of fibrous crystals formed by Alzheimer's Aβ(11–25) peptide fragment, Structure 11 (8) (2003) 915–926.
[111] V. Nguyen, K. Jenkins, R.S. Yang, Epitaxial growth of vertically aligned piezoelectric diphenylalanine peptide microrods with uniform polarization, Nano Energy 17 (2015) 323–329.
[112] C.M. Kelly, T. Northey, K. Ryan, B.R. Brooks, A.L. Kholkin, B.J. Rodriguez, N. V. Buchete, Conformational dynamics and aggregation behavior of piezoelectric diphenylalanine peptides in an external electric field, Biophys. Chem. 196 (2015) 16–24.
[113] L. Adler-Abramovich, M. Reches, V.L. Sedman, S. Allen, E. Gazit, Thermal and chemical stability of diphenylalanine peptide nanotubes: implications for nanotechnological applications, Langmuir 22 (3) (2006) 1313–1320.
[114] V.L. Sedman, L. Adler-Abramovich, S. Allen, E. Gazit, S.J.B. Tendler, Direct observation of the release of phenylalanine from diphenylalanine nanotubes, J. Am. Chem. Soc. 128 (21) (2006) 6903–6908.
[115] M. Stolz, R. Raiteri, A.U. Daniels, M.R. VanLandingham, W. Baschong, U. Aebi, Dynamic elastic modulus of porcine articular cartilage determined at two different levels of tissue organization by indentation-type atomic force microscopy, Biophys. J. 86 (5) (2004) 3269–3283. §.
[116] P.D. Pablo, I. Schaap, F.C. Mackintosh, C.F. Schmidt, Deformation and collapse of microtubules on the nanometer scale, Phys. Rev. Lett. 91 (9) (2003), 098101.
[117] N. Kol, L. Adler-Abramovich, D. Barlam, R.Z. Shneck, E. Gazit, I. Rousso, Self-assembled peptide nanotubes are uniquely rigid bioinspired supramolecular structures, Nano Lett. 5 (7) (2005) 1343–1346.
[118] B. Wetzel, P. Rosso, F. Haupert, K. Friedrich, Epoxy nanocomposites - fracture and toughening mechanisms, Eng. Fract. Mech. 73 (16) (2006) 2375–2398.
[119] V. Chechik, Using the bending beam model to estimate the elasticity of diphenylalanine nanotubes, Langmuir 23 (14) (2007) 7443–7446.
[120] N. Even, L. Adler-Abramovich, L. Buzhansky, H. Dodiuk, E. Gazit, Improvement of the mechanical properties of epoxy by peptide nanotube fillers, Small 7 (8) (2011) 1007–1011.
[121] Z. Fan, L.M. Sun, Y.J. Huang, Y.Z. Wang, M.J. Zhang, Bioinspired fluorescent dipeptide nanoparticles for targeted cancer cell imaging and real-time monitoring of drug release, Nat. Nanotechnol. 11 (4) (2016) 388–+.
[122] B. Akdim, R. Pachter, R.R. Naik, Self-assembled peptide nanotubes as electronic materials: an evaluation from first-principles calculations, Appl. Phys. Lett. 106 (18) (2015) 4.
[123] K. Tao, W. Hu, B. Xue, D. Chovan, N. Brown, L. Shimon, O. Maraba, Y. Cao, S. Tofail, D. Thompson, Bioinspired stable and photoluminescent assemblies for power generation, Adv. Mater. 31 (12) (2019).
[124] K. Tao, B. Xue, Q. Li, W. Hu, L.J.W. Shimon, P. Makam, M.S. Si, X.H. Yan, M. J. Zhang, Y. Cao, R.S. Yang, J.B. Li, E. Gazit, Stable and optoelectronic dipeptide assemblies for power harvesting, Mater. Today 30 (2019) 10–16.
[125] L. Adler-Abramovich, Z.A. Arnon, X.M. Sui, I. Azuri, H. Cohen, O. Hod, L. Kronik, L.J.W. Shimon, H.D. Wagner, E. Gazit, Bioinspired flexible and tough layered peptide crystals, Adv. Mater. 30 (5) (2018) 6.
[126] X. Zhao, S. Zhang, Molecular designer self-assembling peptides, Chem. Soc. Rev. 35 (2006).
[127] E. Gazit, Self-assembled peptide nanostructures: the design of molecular building blocks and their technological utilization, Chem. Soc. Rev. 36 (8) (2007) 1263–1269.
[128] T.S. Fiona Chan, Structure-specific Intrinsic Fluorescence of Protein Amyloids Used to Study Their Kinetics of Aggregation, Elsevier Inc., 2014, pp. 147–155.

[129] N. Santhanamoorthi, Diphenylalanine peptide nanotube: charge transport, band gap and its relevance to potential biomedical applications, Adv. Mater. Lett. 2 (2) (2011) 100–105.
[130] Y. Wu, H. Yan, M. Huang, B. Messer, J.H. Song, P. Yang, Inorganic semiconductor nanowires: rational growth, assembly, and novel properties, Chemistry 8 (6) (2002) 1260–1268.
[131] X. Fang, Y. Bando, U.K. Gautam, C. Ye, D. Golberg, Inorganic semiconductor nanostructures and their field-emission applications, J. Mater. Chem. 18 (2008).
[132] N. Amdursky, M. Molotskii, E. Gazit, G. Rosenman, Elementary building blocks of self-assembled peptide nanotubes, J. Am. Chem. Soc. 132 (44) (2010) 15632–15636.
[133] N. Amdursky, M. Molotskii, E. Gazit, G. Rosenman, Self-assembled bioinspired quantum dots: optical properties, Appl, Phys. Lett. 94 (26) (2009) 1283.
[134] N. Amdursky, P. Beker, I. Koren, B. Bank-Srour, E. Mishina, S. Semin, T. Rasing, Y. Rosenberg, Z. Barkay, E. Gazit, Structural transition in peptide nanotubes, Biomacromolecules 12 (4) (2011) 1349.
[135] Nadav Amdursky, Enhanced solid-state electron transport via tryptophan containing peptide networks, Phys. Chem. Chem. Phys. 15 (32) (2013) 13479–13482.
[136] Fabio Andrade-Filho, Ferreira Furlan, Andrade Wendel, Alexandre Alves, Reily, Rocha, The effects of water molecules on the electronic and structural properties of peptide nanotubes, Phys. Chem. Chem. Phys. 15 (20) (2013) 7555–7559.
[137] A. Gruverman, B.J. Rodriguez, S.V. Kalinin, Electromechanical Behavior in Biological Systems at the Nanoscale, Springer, New York, 2007.
[138] M.H. Shamos, L.S. Lavine, Piezoelectricity as a fundamental property of biological tissues, Nature 213 (5073) (1967) 267–269.
[139] Z.X. Gan, X.L. Wu, X.B. Zhu, J.C. Shen, Light-induced ferroelectricity in bioinspired self-assembled diphenylalanine nanotubes/microtubes, Angew. Chem. Int. Ed. 52 (7) (2013) 2055–2059.
[140] V. Nguyen, S. Kelly, R. Yang, Piezoelectric peptide-based nanogenerator enhanced by single-electrode triboelectric nanogenerator, Apl. Mater. 5 (7) (2017) 5.
[141] A. Kholkin, N. Amdursky, I. Bdikin, E. Gazit, G. Rosenman, Strong piezoelectricity in bioinspired peptide nanotubes, ACS Nano 4 (2) (2010) 610–614.
[142] A. Heredia, I. Bdikin, S. Kopyl, E. Mishina, S. Semin, A. Sigov, K. German, V. Bystrov, J. Gracio, A.L. Kholkin, FAST TRACK COMMUNICATION Temperature-driven phase transformation in self-assembled diphenylalanine peptide nanotubes, J. Phys. D Appl. Phys. 43 (46) (2010) 462001–462006, 6.
[143] I. Bdikin, V. Bystrov, I. Delgadillo, J. Gracio, S. Kopyl, M. Wojtas, E. Mishina, A. Sigov, A.L. Kholkin, Polarization switching and patterning in self-assembled peptide tubular structures, J. Appl. Phys. 111 (7) (2012) 7.
[144] S. Vasilev, P. Zelenovskiy, D. Vasileva, A. Nuraeva, V.Y. Shur, A.L. Kholkin, Piezoelectric properties of diphenylalanine microtubes prepared from the solution, J. Phys. Chem. Solid. 93 (2016) 68–72.
[145] E.D. Bosne, A. Heredia, S. Kopyl, D.V. Karpinsky, A.G. Pinto, A.L. Kholkin, Piezoelectric resonators based on self-assembled diphenylalanine microtubes, Appl. Phys. Lett. 102 (7) (2013) 625–653.
[146] R. Rica, E. Mendoza, H. Matsui, Bioinspired target-specific crystallization on peptide nanotubes for ultrasensitive Pb ion detection, Small 6 (16) (2010) 1753–1756.
[147] S. Kim, J.H. Kim, J.S. Lee, C.B. Park, Beta-Sheet-Forming, Self-assembled peptide nanomaterials towards optical, energy, and healthcare applications, Small 11 (30) (2015) 3623–3640.
[148] O. Berger, L. Adler-Abramovich, M. Levy-Sakin, A. Grunwald, Y. Liebes-Peer, M. Bachar, L. Buzhansky, E. Mossou, V.T. Forsyth, T. Schwartz, Y. Ebenstein, F. Frolow, L.J.W. Shimon, F. Patolsky, E. Gazit, Light-emitting self-assembled peptide nucleic acids exhibit both stacking interactions and Watson-Crick base pairing, Nat. Nanotechnol. 10 (4) (2015) 353–360.
[149] K. Tao, P. Makam, R. Aizen, E. Gazit, Self-assembling peptide semiconductors, Science 358 (6365) (2017), eaam9756.
[150] F. Yin, K. Hu, S. Chen, D. Wang, J. Zhang, M. Xie, D. Yang, M. Qiu, H. Zhang, Z.-g. Li, Black phosphorus quantum dot based novel siRNA delivery systems in human pluripotent teratoma PA-1 cells, J. Mater. Chem. B 5 (27) (2017) 5433–5440.
[151] N. Amdursky, M. Molotskii, D. Aronov, L. Adler-Abramovich, E. Gazit, G. Rosenman, Blue luminescence based on quantum confinement at peptide nanotubes, Nano Lett. 9 (9) (2009) 3111–3115.
[152] X. Gao, Y. Cui, R.M. Levenson, L. Chung, S. Nie, In vivo cancer targeting and imaging with semiconductor quantum dots, Nat. Biotechnol. 22 (8) (2004) 969–976.
[153] A.M. Derfus, W. Chan, S.N. Bhatia, Probing the cytotoxicity of semiconductor quantum dots, Nano Lett. 4 (1) (2004).
[154] T. Kai, Z. Fan, L. Sun, M. Pan De Eswar, Z. Tian, R. Mark, S.N. Shira, H. De Rek, A. Ruth, Z. Pan, Quantum confined peptide assemblies with tunable visible to near-infrared spectral range, Nat. Commun. 9 (1) (2018) 3217.
[155] M. Wang, S. Xiong, X. Wu, P.K. Chu, Effects of water molecules on photoluminescence from hierarchical peptide nanotubes and water probing capability, Small 7 (19) (2011) 2801–2807.
[156] L. Adler-Abramovich, D. Aronov, E. Gazit, G. Rosenman, Patterned arrays of ordered peptide nanostructures, J. Nanosci. Nanotechnol. 9 (3) (2009) 1701–1708.
[157] Kuan, Chao Zheng, Xiaohui Miao, Lu Wang, A peptide-based supercapacitor and its performance improvement via TiO2 coating, J. Mater. Chem. 6 (17) (2018) 8047–8052.
[158] K. Hu, Y.X. Jiang, W. Xiong, H. Li, P.Y. Zhang, F. Yin, Q.L. Zhang, H. Geng, F. Jiang, Z. Li, X.W. Wang, Z.G. Li, Tuning peptide self-assembly by an in-tether chiral center, Sci. Adv. 4 (5) (2018) 8.
[159] W. Xiong, K. Hu, Z. Li, Y. Jiang, Z. Li, Z. Li, X. Wang, A wearable system based on core-shell structured peptide-Co9S8 supercapacitor and triboelectric nanogenerator, Nano Energy 66 (2019).
[160] P.B. Liu, J. Yan, Z.X. Guang, Y. Huang, X.F. Li, W.H. Huang, Recent advancements of polyaniline-based nanocomposites for supercapacitors, J. Power Sources 424 (2019) 108–130.
[161] D.J. Jiang, B.J. Shi, H. Ouyang, Y.B. Fan, Z.L. Wang, Z. Li, Emerging implantable energy harvesters and self-powered implantable medical electronics, ACS Nano 14 (6) (2020) 6436–6448.
[162] T.P. Nguyen, A.D. Easley, N.A. Kang, S. Khan, S.M. Lim, Y.H. Rezenom, S. Y. Wang, D.K. Tran, J.W. Fan, R.A. Letteri, X. He, L. Su, C.H. Yu, J.L. Lutkenhaus, K.L. Wooley, Polypeptide organic radical batteries, Nature 593 (7857) (2021) 61–+.
[163] X. Gao, H. Matsui, Peptide-based nanotubes and their applications in bionanotechnology, Adv. Mater. 17 (17) (2005) 2037–2050.
[164] R. de la Rica, E. Mendoza, L.M. Lechuga, H. Matsui, Label-free pathogen detection with sensor chips assembled from peptide nanotubes, Angew. Chem. Int. Ed. 47 (50) (2008) 9752–9755.
[165] M. Yemini, M. Reches, E. Gazit, J. Rishpon, Peptide nanotube-modified electrodes for enzymebiosensor applications, Anal. Chem. 77 (16) (2005) 5155–5159.
[166] W. Xu, J. Pei, H. Yi, S. Xue, R. Yuan, Bimetallic Pt/Pd encapsulated mesoporous-hollow CeO_2 nanospheres for signal amplification toward electrochemical peptide-based biosensing for matrix metalloproteinase 2, Sensors Actuat. B-Chem. 230 (Jul) (2016) 345–352.
[167] M. Lian, C. Xu, X. Liu, Z. Yi, W. Yang, A self-assembled peptide nanotube–chitosan composite as a novel platform for electrochemical cytosensing, Sensors Actuat. B-Chem. 251 (2017).
[168] L.L. Li, H.L. Ma, G.B. Qi, D. Zhang, F.Q. Yu, Z.Y. Hu, H. Wang, Pathological-condition-driven construction of supramolecular nanoassemblies for bacterial infection detection, Adv. Mater. 28 (2) (2016) 254–262.
[169] V. Bellat, R. Ting, T.L. Southard, L. Vandat, H. Molina, J. Fernandez, O. Aras, T. Stokol, B. Law, Functional peptide nanofibers with unique tumor targeting and enzyme-induced local retention properties, Adv. Funct. Mater. 28 (44) (2018).
[170] K.M. Cheng, Y.P. Ding, Y. Zhao, S.F. Ye, X. Zhao, Y.L. Zhang, T.J. Ji, H.H. Wu, B. Wang, G.J. Anderson, L. Ren, G.J. Nie, Sequentially responsive therapeutic peptide assembling nanoparticles for dual-targeted cancer immunotherapy, Nano Lett. 18 (5) (2018) 3250–3258.
[171] D. Zhang, G.B. Qi, Y.X. Zhao, S.L. Qiao, C. Yang, H. Wang, In situ formation of nanofibers from purpurin18-peptide conjugates and the assembly induced retention effect in tumor sites, Adv. Mater. 27 (40) (2015) 6125–6130.
[172] Q. Liu, J. Wang, B.J. Boyd, Peptide-based biosensors, Talanta 136 (2015) 114–127.
[173] S. Pavan, F. Berti, Short peptides as biosensor transducers, Anal. Bioanal. Chem. 402 (10) (2012) 3055–3070.
[174] J.D. Hartgerink, E. Beniash, S.I. Stupp, Peptide-amphiphile nanofibers: a versatile scaffold for the preparation of self-assembling materials, P, Natl. Acad. Sci. USA 99 (8) (2002) 5133–5138.
[175] D. Bumcrot, M. Manoharan, V. Koteliansky, D.W.Y. Sah, RNAi therapeutics: a potential new class of pharmaceutical drugs, Nat. Chem. Biol. 2 (12) (2006) 711–719.
[176] F. Mingozzi, K.A. High, Gene transfer for genetic disease using AAV: progress and challenges, Nat. Rev. Genet. 12 (5) (2011) 341–355.
[177] L. Crombez, G. Aldrian-Herrada, K. Konate, Q.N. Nguyen, G.K. McMaster, R. Brasseur, F. Heitz, G. Divita, A new potent secondary amphipathic cell-penetrating peptide for sirna delivery into mammalian cells, Mol. Ther. 17 (1) (2009) 95–103.
[178] W.J. Li, D.Y. Wang, X.D. Shi, J.X. Li, Y. Ma, Y.D. Wang, T.T. Li, J.N. Zhang, R. T. Zhao, Z.Q. Yu, F. Yin, Z.G. Li, A siRNA-induced peptide co-assembly system as a peptide-based siRNA nanocarrier for cancer therapy, Mater, Horizons 5 (4) (2018) 745–752.
[179] A.L. Vahrmeijer, M. Hutteman, J.R. van der Vorst, C.J.H. van de Velde, J. V. Frangioni, Image-guided cancer surgery using near-infrared fluorescence, Nat. Rev. Clin. Oncol. 10 (9) (2013) 507–518.
[180] A.L. Antaris, H. Chen, K. Cheng, Y. Sun, G.S. Hong, C.R. Qu, S. Diao, Z.X. Deng, X. M. Hu, B. Zhang, X.D. Zhang, O.K. Yaghi, Z.R. Alamparambil, X.C. Hong, Z. Cheng, H.J. Dai, A small-molecule dye for NIR-II imaging, Nat. Mater. 15 (2) (2016) 235–+.
[181] H.W. An, L.L. Li, Y. Wang, Z.Q. Wang, D.Y. Hou, Y.X. Lin, S.L. Qiao, M.D. Wang, C. Yang, Y. Cong, Y. Ma, X.X. Zhao, Q. Cai, W.T. Chen, C.Q. Lu, W.H. Xu, H. Wang, Y.L. Zhao, A tumour-selective cascade activatable self-detained system for drug delivery and cancer imaging, Nat. Commun. 10 (2019) 15.
[182] L. Adler-Abramovich, N. Kol, I. Yanai, D. Barlam, R.Z. Shneck, E. Gazit, I. Rousso, Self-assembled organic nanostructures with metallic-like stiffness, Angew. Chem. Int. Ed. 49 (51) (2010) 9939–9942.
[183] X.H. Yan, P.L. Zhu, J.B. Li, Self-assembly and application of diphenylalanine-based nanostructures, Chem. Soc. Rev. 39 (6) (2010) 1877–1890.
[184] H.M. Wang, C.H. Yang, L. Wang, D.L. Kong, Y.J. Zhang, Z.M. Yang, Self-assembled nanospheres as a novel delivery system for taxol: a molecular hydrogel with nanosphere morphology, Chem. Commun. 47 (15) (2011) 4439–4441.
[185] H.M. Wang, J. Wei, C.B. Yang, H.Y. Zhao, D.X. Li, Z.N. Yin, Z.M. Yang, The inhibition of tumor growth and metastasis by self-assembled nanofibers of taxol, Biomaterials 33 (24) (2012) 5848–5853.