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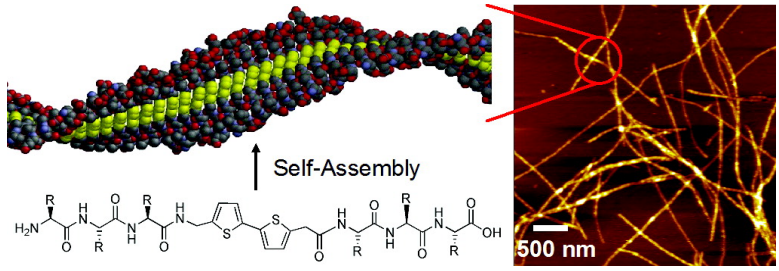

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One-Dimensional Optoelectronic Nanostructures Derived from the Aqueous Self-Assembly of π-Conjugated Oligopeptides

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Self-assembling supramolecular objects with π-electron functionality are of increasing interest for nanotechnology.[1] The vast majority of these approaches involve the association of molecular components in organic solvents. Notable exceptions are the water-soluble rod-coil oligophenylenes, but they are rendered soluble by oligo(ethylene oxide)s known in many cases to resist specific biological adhesion.[1h] Thus, the construction of discrete organic electronic nanostructures with biologically interactive function in aqueous environments remains a daunting challenge. We demonstrate herein how small peptide sequences with π-conjugated oligomers directly embedded in the backbone promote assembly into 1-D nanostructures with strong $\pi-\pi$ intermolecular electronic communication under completely aqueous and physiologically relevant conditions. This important step sets the stage for the presentation of bioactive small peptides and other molecular recognition elements on the periphery of the nanostructure. The synthetic approach is fundamentally different from covalent modification of preformed nanostructures or single proteins in that the peptidic structure encourages or enforces the formation of π-stacked conduits within the assembled objects.[2]

Synthetic biomaterials whose properties can be regulated by external stimuli offer useful scaffolds for cell adhesion and growth.[3] Biological architectures that incorporate π-conjugated materials are attracting substantial attention in this regard,[4] as evidenced in polypyrrole-based cell scaffolds and artificial muscles.[5] External stimuli can also provoke the assembly of biomolecular components into functional nanostructures. These strategies are inspired by the formation of β-amyloid plaques where misfolded soluble proteins undergo hierarchical assembly to yield fibrils 10−50 nm in diameter with lengths of several micrometers. A wide diversity of small peptides form amyloid fibrils, and substantial research efforts seek to describe their formation,[6] prevent their formation, and even *use* the process for advanced materials.[7]

The amyloid aggregation paradigm presents an attractive method to construct well-defined 1-D nanostructures with biologically responsive and electronically useful properties from molecular precursors. To harness this process to control $\pi-\pi$ interactions, we will need to embed the π-system directly into the peptide backbone. As proof of principle, we prepared bithiophene **1** bearing an Fmoc-protected amine and a free carboxylic acid (Scheme 1 and Supporting Information, S1),[8] representing the shortest member of the oligothiophene class of p-channel organic semiconductors. It mimics amino acid building blocks commonly employed in solid-phase peptide synthesis (SPPS) and enables direct incorporation of bithiophene into the backbones of known β-sheet forming motifs to yield molecules such as **2**.[7e] Previously, complex nonsymmetric π-systems have been embedded within *soluble* biological motifs.[9] With **2**, environmental conditions that promoted carboxylate charge screening (e.g., HCl or $CaCl_2$) initiated self-assembly resulting in the macroscopic formation of self-supporting gels suggestive of entangled 1-D structures.

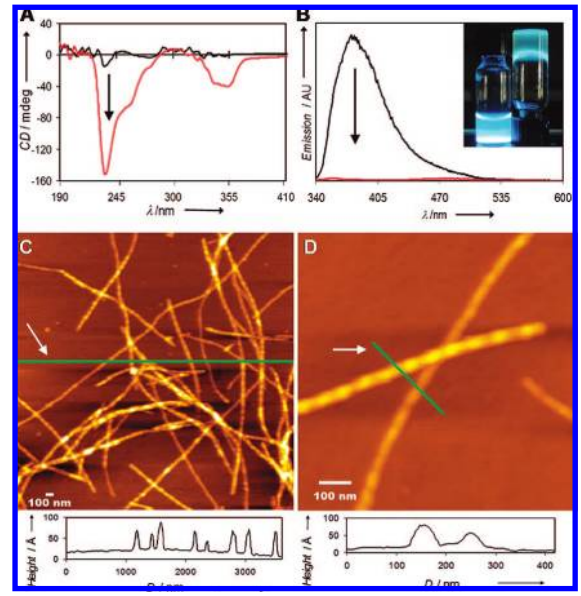
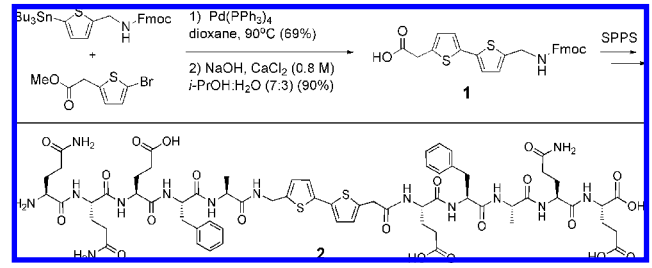


Figure 1. (A) CD and (B) fluorescence of **2** in basic (dissolved, black traces) and acidic (assembled, red traces) aqueous solutions. The inset of panel B depicts a concentrated solution (left) and a gel (right) irradiated at 365 nm. Tapping-mode AFM images and height profiles of the indicated line trace of (C) large area and (D) isolated structures formed after assembly and deposition on freshly cleaved mica surfaces.

Scheme 1. Endgame Construction of Bithiophene Fmoc-Amino Acid **1** Used To Construct Self-Assembling Peptides Such as **2**



The IR spectrum for **2** displayed characteristic β-sheet amide I bands at 1630 and 1641 cm^{-1} accompanied by minor random-coil contributions.[8] Circular dichroism (CD) of freely soluble **2** showed no meaningful absorption while assembled **2** had intense absorptions only associated with the π-conjugated unit (Figure 1A). Molecularly dissolved **2** exhibited a low-energy absorption λ_{max} at 320 nm. Excitation at 320 nm triggered strong photoluminescence at 380 nm (Figure 1B). Upon assembly, the absorption profile remained comparable but the emission was dramatically quenched. The bisignate CD response crossing over at 320 nm (coincident with the absorption λ_{max}) is a classic signature for exciton-coupled chromophores in chiral environments. Although formal H-ag-

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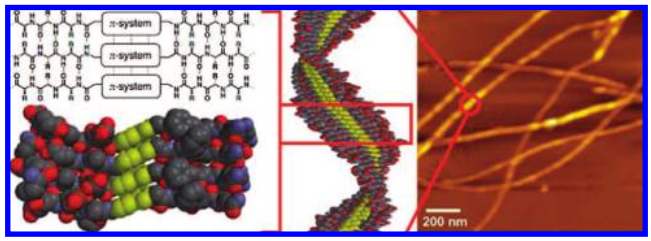

Figure 2. Energy-minimized illustration of β-sheets and π-stacks as line drawings and space-filling models (left, thiophenes in yellow) and the helical twist sense along a model aggregate (center, hydrogens omitted).

gregates require blue-shifted absorptions, the lower oscillator strength of **2** may have led to less-pronounced effects. The natural propensities for β-sheets to adopt macromolecular twists would also dictate *twisted* H-aggregates.[10] Although X-ray diffraction was inconclusive, the photophysics associated with the spectroscopic behavior above lead us to conclude that the bithiophene π-systems intimately associate within a twisted chiral environment imposed by β-sheet interactions throughout the assembled structure.

Atomic force microscopy (AFM) of gel samples deposited on mica revealed 1-D nanostructures with heights ranging from 2 to 6 nm (Figure 1C,D). Given that **2** is ca. 42 Å in length, these objects are consistent with coiled tape-like or even more complex fibrillar structures, early thermodynamic sinks on the assembly energy landscape that spans from free molecule to large amyloid-like fiber. The rigidity of these structures is evident in the larger height profiles near crossover junctions. In some cases we resolved 1-D structures resting over a monolayer of flat tapes passivating the mica surface (ca. 1 nm in height) attributed to strong interactions between flat tapes and the highly polar mica surface.[8,11] The influence of the backbone-embedded quadrupole moment of the π-cloud must play a role in affecting peptide−surface interactions: nanostructures deposited on nonpolar substrates did not show any evidence for monolayer passivation.[8]

Our working model (Figure 2) starts with the formation of β-sheets yielding twisted ribbon 1-D structures (akin to telephone cords) with the same handedness as natural β-sheets. We expect the more favorable antiparallel configuration shown at left but cannot unambiguously determine this from the data at hand. These structures can adsorb directly on the surface or they can aggregate with other tapes into larger fibrils as do other synthetic amyloid peptides. Regardless, the directionality of the hydrogen-bonding network coincides with the π-stacking axis with a calculated intermolecular $\pi-\pi$ distance of ca. 5 Å. This relatively long distance still enables electronic communication as discussed above and as witnessed by energy transfer among isolated chromophores within α-helical and β-sheet peptides.[2b,12] The AFM images reveal superstructural undulations with periodicities of ca. 76 nm (Figure 1D) as found in the right- and left-handed helical superstructures within natural amyloid sequences.[8,13] We also acknowledge prospects for "molecular torque" caused by competing thermodynamic preferences to maximize β-sheet hydrogen bonding and minimize electrostatic repulsion among the bithiophene π-clouds,[14] a subject of continued inquiry.

In conclusion, we report a new class of peptides bearing *internal* π-conjugated segments that can be manipulated and assembled into 1-D nanostructures in completely aqueous and physiologically relevant [Ca^{2+}] environments. The clear photophysical changes observed upon assembly highlight the strong electronic communication existing within the amyloidlike aggregates as mediated by π-stacking among molecular components, a critical component necessary for charge transport or exciton delocalization in nanostructures with semiconductive π-systems. We are currently exploring the scope of this assembly in terms of the π-conjugated amino acids and the bioactive peptide sequences used during SPPS, as well as the environmental conditions required to initiate assembly. Understanding how these variables impact supramolecular association will allow us to engineer and evaluate numerous biologically relevant and electronically functional nanostructures in a rapid manner.

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Supporting Information Available: Experimental details, characterization data, and additional microscopy. This material is available free of charge via the Internet at http://pubs.acs.org.

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