Controlled Self-Assembly of Metallated and Non-Metallated Peptidic Arrays

Geoffrey Vrla
Chemistry, Middlebury College

NNIN iREU Site: National Institute for Materials Science (NIMS), Tsukuba, Ibaraki, Japan
NNIN iREU Principal Investigator and Mentor: Dr. Kentaro Tashiro,
Reticular Materials Group, National Institute for Materials Science
Contact: gvrla@middlebury.edu, tashiro.kentaro@nims.go.jp

Abstract:

Peptide-based compounds are desirable targets for the development of novel nano-materials due to their propensity to form self-assembled, supramolecular architectures. Chemical modification of self-assembling peptides has been investigated as a route for the formation of functional nanostructures designed for specific applications. Here, we have modified the diphenylalanine (FF) peptide, previously shown to spontaneously form fibrous self-assemblies, with two organic chelating groups capable of coordinating various transition metals. We investigated the self-assembling behaviors of this peptide in coordination with several combinations of Pt(II), Re(I), or Rh(III) using Fourier transform infrared (FTIR) spectroscopy, circular dichroism (CD) spectroscopy, and scanning electron microscopy (SEM). SEM analysis indicated that both homo-metallated species of Pt(II) and Re(I) as well as the non-metallated species form fibrous self-assemblies. However, the heterometallic peptide coordinating Pt(II)and Rh(III) did not form distinguishable fibrous structures under identical conditions. We propose that the charge states of the metal centers may affect the self-assembly properties of these peptide compounds. Further investigation into possible self-assembling heterometallic dipeptides could be beneficial for the future development of more complex, metallated nanostructures.

Introduction:

Peptide-based compounds are desirable targets for the development of novel nano-materials due to their propensity to form self-assembled, supramolecular architectures. Short, aromatic peptides such as diphenylalanine (FF) exhibit particularly strong tendencies to self assemble; FF has been previously shown to self-assemble into discrete, robust nanotubes [1]. The biocompatibility of these peptide nanostructures, as well as the ability to modify the peptide backbone with numerous function groups, has given these compounds versatility and usefulness in a wide range of applications [2].

The incorporation of transition metals into the structure of self-assembling peptides may provide a route towards the development of more complex metallic nanostructures with novel properties. Recently, the FF structural motif has been incorporated into a Ru(II) complex, resulting in the first metallo-hydrogellator capable of redox-responsive self-assembly and gelation [3]. The incorporation of multiple chelating functional groups capable of coordinating a broader range of transition metals into a self-assembling peptide could significantly increase the complexity of these nanostructures, and provide potential catalytic or fluorescent properties.

Here, we have developed a method for the incorporation of heterometallic complexes into the backbone structure of a self-assembling peptide. We modified the FF structural motif with two organic chelating groups capable of coordinating either Pt(II), Re(I), Rh(III), or Ru(II). This technique not only allows for the synthesis of heterometallic peptidic arrays, but also allows for the sequential addition of amino acid subunits to achieve peptide chains with more than two metal centers.

Experimental Procedure:

Metallated peptides were synthesized previously using either a conventional solution phase synthesis technique or a modified form of the Merrifield solid-phase synthesis technique [4]. One non-metallated and three metallated peptides studied here are shown in Figure 1.

SEM Analysis. A 0.1 mM sample stock solution was prepared by suspending 0.5 mg (0.3 μmol) of peptide in 3 mL acetonitrile (ACN). The suspension was sonicated for 30 s followed by heating at 50°C for one min; this process was repeated until the solid had fully dissolved. After 24 hr of incubation at 22°C, the solution was spotted onto a silicon substrate and visualized using a Hitachi SU8000 scanning electron microscope.

CD Analysis. Samples were prepared identically to SEM samples, with the addition of a 10-fold dilution to achieve a proper concentration for CD analysis. Their CD spectra were recorded on a JASCO Type J-820 spectropolarimeter at -10°C.

FTIR Analysis. Samples were prepared as pellets in solid KBr and their spectra were recorded using a Thermo Scientific model Nicolet 4700 Fourier transform infrared spectrometer.

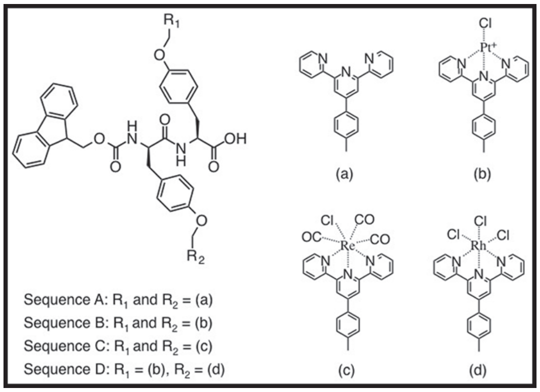

*Figure 1: Series of non-metallated (**A**) and metallated (**B**-**C**) peptides.*

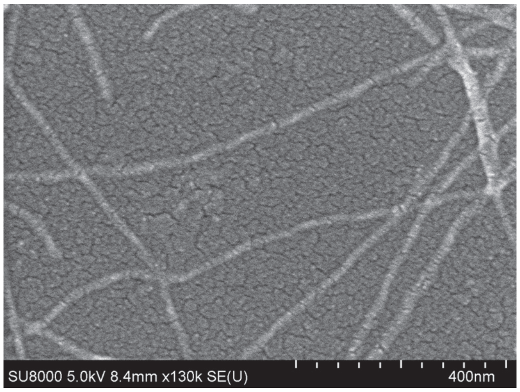

*Figure 2: SEM of non-metallated peptide (**A**) self-assemblies.*

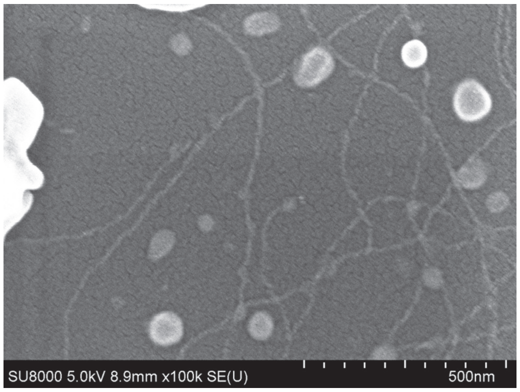

*Figure 3: SEM of Pt$^+$-Pt$^+$ peptide (**B**) self-assemblies.*

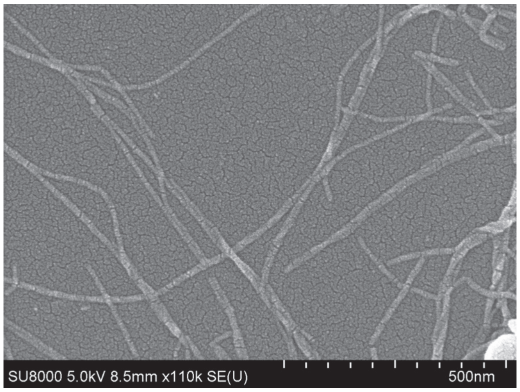

*Figure 4: SEM of Re-Re peptide (**C**) self-assemblies.*

Results and Conclusions:

All four peptide compounds were weakly soluble in ACN. After several hours of incubation at 22°C, the formation of solid aggregates was observed. SEM analysis indicated that sequences **A**, **B**, and **C**, but not **D**, formed fibrous assemblies shown in Figures 2-4. While the charge state of the metal centers was identical (either $^+1$ or 0) for **A**, **B**, and **C**, the charge state of the Pt(II) and Rh(III) in **D** were different ($^+1$ and 0, respectively). It is possible that the charge symmetry of the metal centers may affect the self-assembling properties of the compound, which may explain the absence of fibrous aggregates in the hetero-metallic species.

The non-metallated sequence (**A**) gave a relatively strong CD signal with a positive peak at 198 nm, while the CD signals of the metallated peptides were too weak to distinguish. Additionally, two strong bands between 1670-1690 cm^{-1} and 1607-1612 cm^{-1} in the infrared spectra of compounds **A**-**D** were observed. Previously studied FF-based nanostructures have characteristic IR stretching frequencies around 1630 cm^{-1}, attributed to peptide amide groups in the β-sheet conformation [1]. The absence of an amide stretch around 1630 cm^{-1} in the metallated peptides suggests that these monomers are not arranged in a β-sheet conformation.

Future Work:

Future work will investigate the conditions most appropriate for the formation of fibrous structures of hetero-metallated species. The ability to develop self-assembling peptides with hetero-metallic centers is useful for the development of more complex metallated architectures. Such compounds have not been reported previously, and may possess interesting catalytic or electronic properties. Additionally, field effect transistor measurements can be performed on homo-metallated dipeptides to measure the potential semi-conductive properties of these compounds.

Acknowledgements:

I would like to thank the Dr. Kentaro Tashiro and Reticular Materials Group for their guidance. I acknowledge the NSF and NNIN iREU Program for financial support, and the National Institute of Materials Science for hosting me.

References:

[1] Reches, M.; Gazit, E. Science 2003, 300, 625.
[2] Gazit, E. Chem. Soc. Rev. 2007, 36, 1263.
[3] Zhang, Y., et al., J. Am. Chem. Soc. 2013, 135, 5008.
[4] Vairaprakash, P., et al., J. Am. Chem. Soc. 2011, 133, 759.