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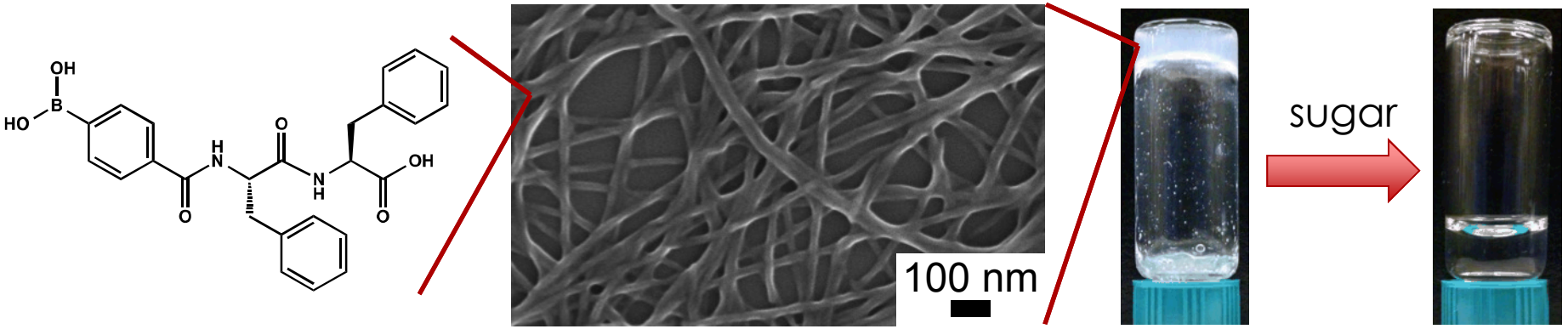

Responsive Self-Assembly of Boronic Acid-Functionalized Peptides

Brad H. Jones, Alina M. Martinez, Jill S. Wheeler,
Bonnie McKenzie, David R. Wheeler, and Erik D. Spoerke

April 7, 2015

U.S. DEPARTMENT OF ENERGY
NNSA National Nuclear Security Administration

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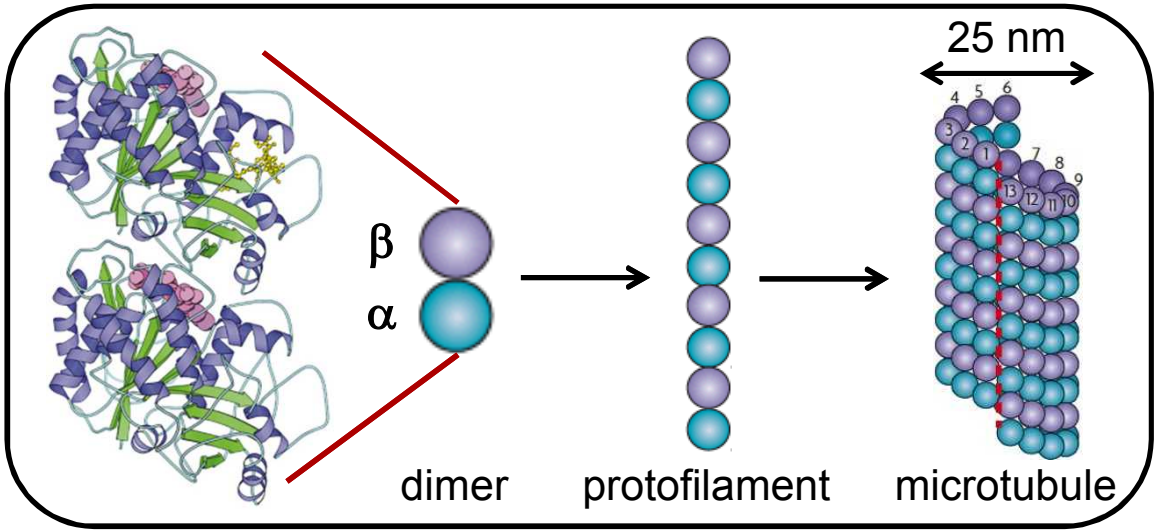
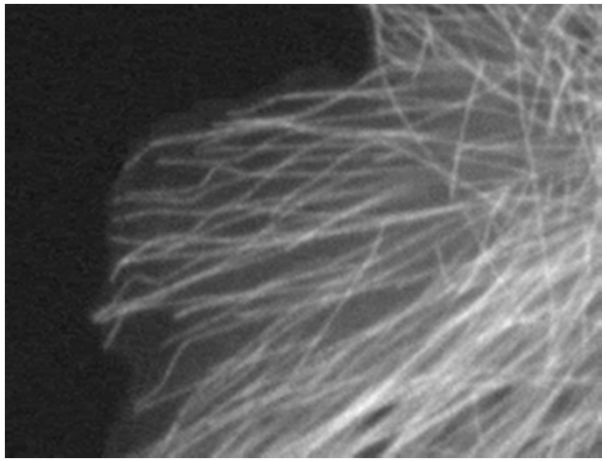
Microtubules: Dynamic Functional Assemblies

Microtubules are dynamic, self-assembling entities essential to cell function



Akhmanova, A.; Steinmetz, M.O. *Nat. Rev. Mol Cell. Bio*. **2008**, *9*, 309-322.
Nogales, E. *Annu. Rev. Biochem*. **2000**, *69*, 277-302.



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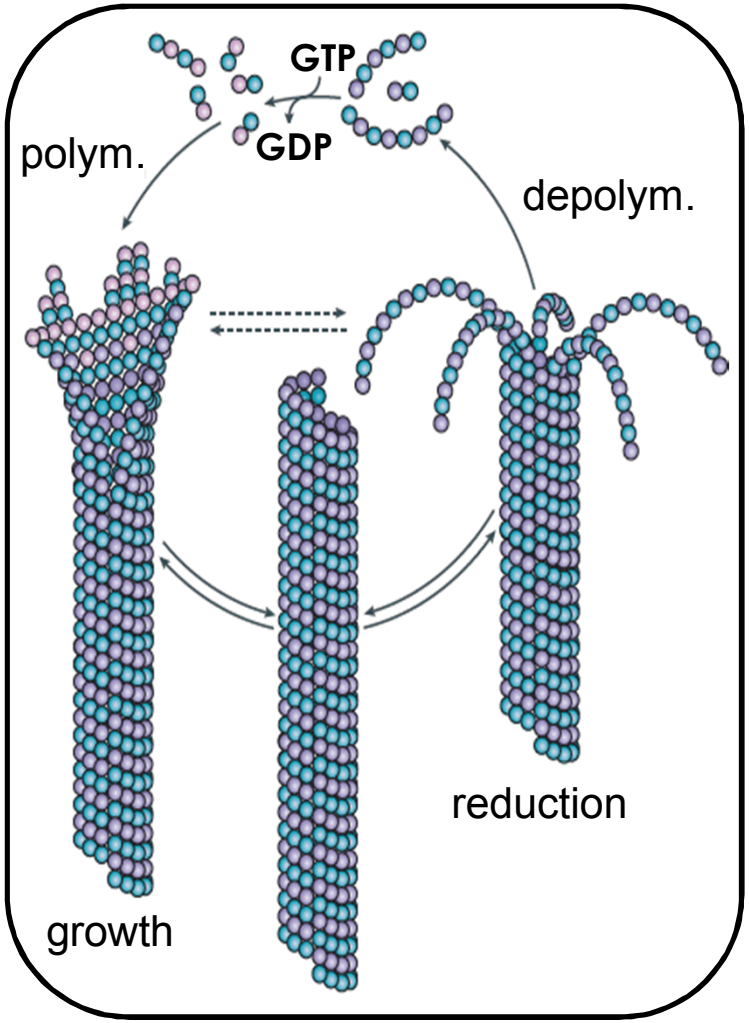
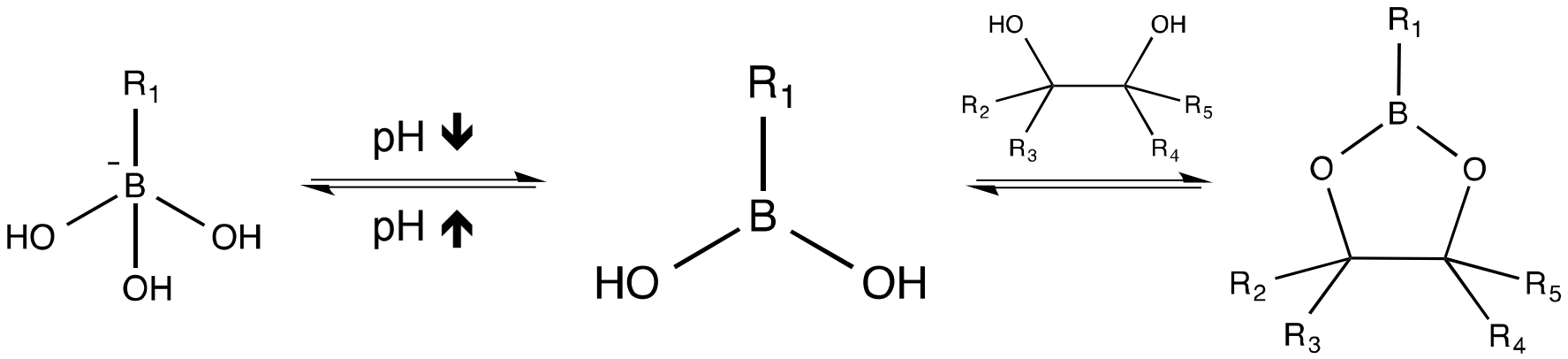
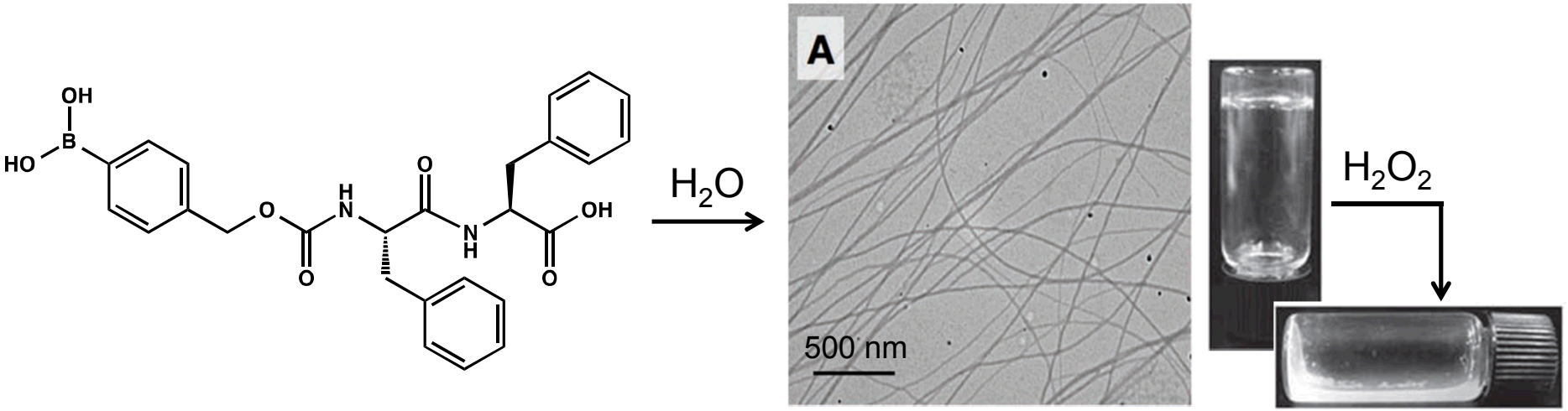


Akhmanova, A.; Steinmetz, M.O. *Nat. Rev. Mol Cell. Bio*. **2008**, *9*, 309-322.

Boronic Acids

Boronic acids are a convenient chemical functionality to impart responsive behavior to synthetic molecules

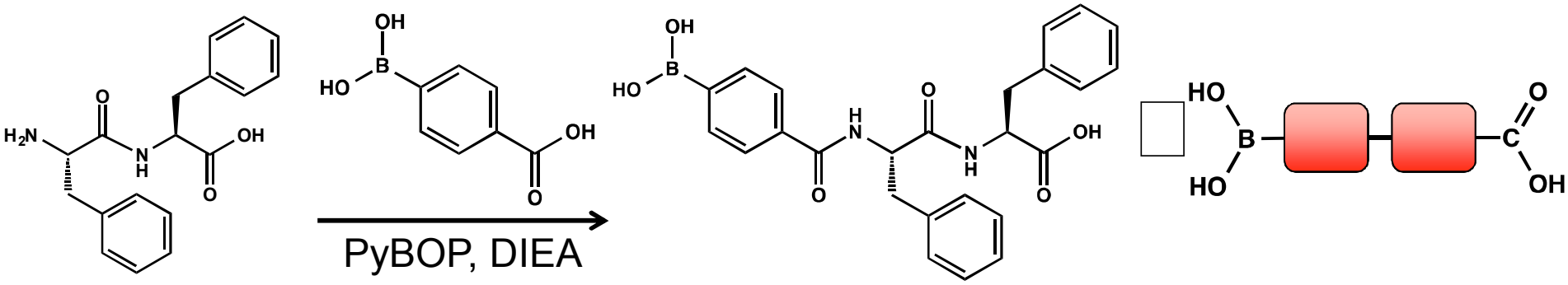




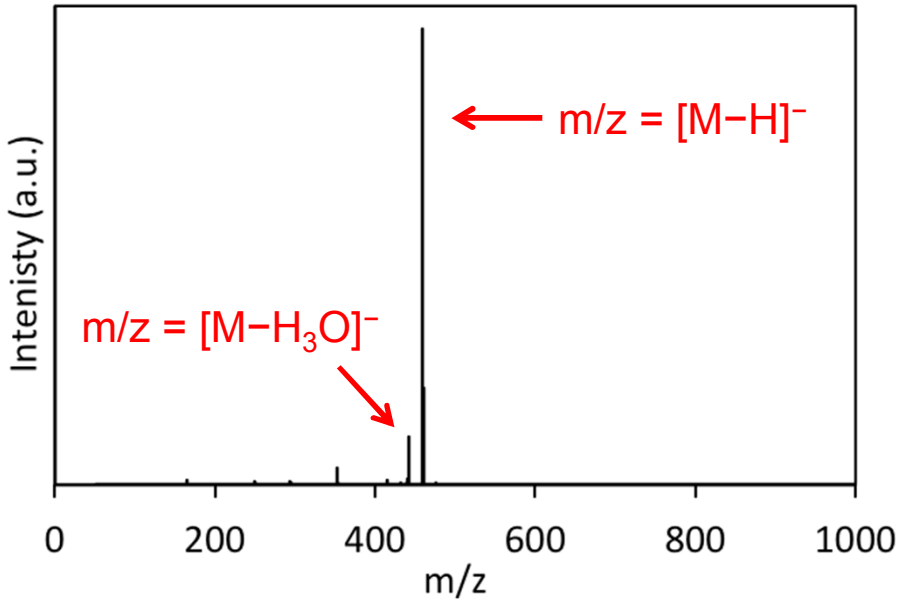
Ikeda, M.; *et al. Adv. Mater.* **2011**, *23*, 2819-2822.

Boronic Acid Dipeptide Synthesis

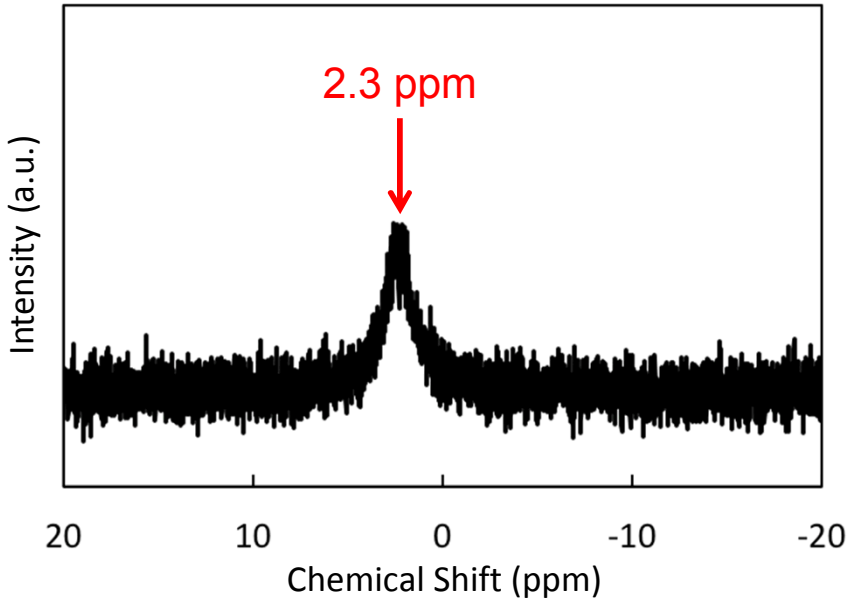
_N_-terminal coupling of carboxyboronic acids is a straightforward route to boronic acid-modified peptides



MS

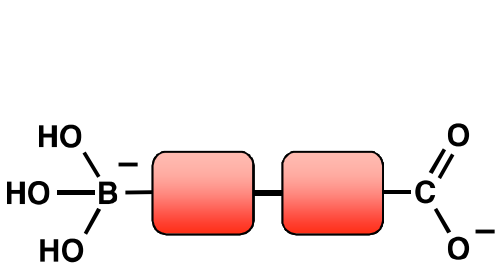


^{11}B NMR



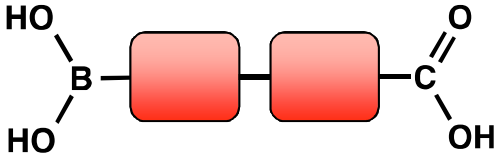
pH-Responsive Self-Assembly

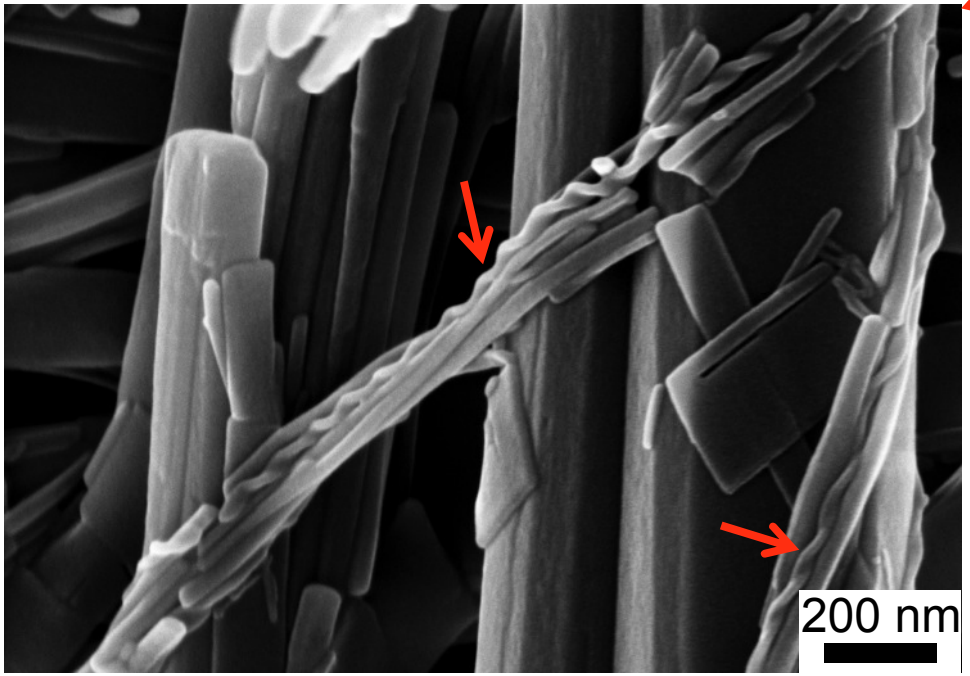
Nanoribbon assemblies are reversibly formed by changes in pH

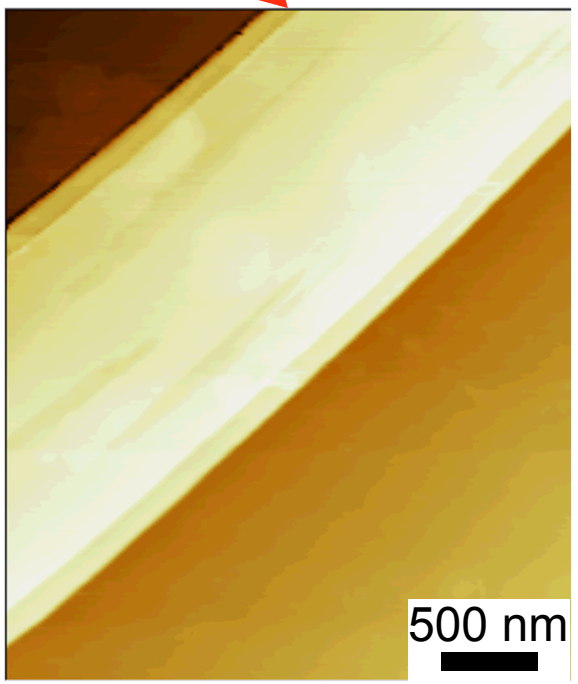


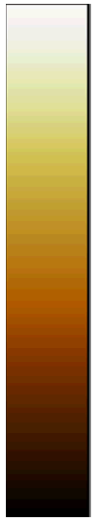
+ HCl, pH ≤ 5

+ NH_4OH, pH ≥ 5









Salt-Responsive Self-Assembly

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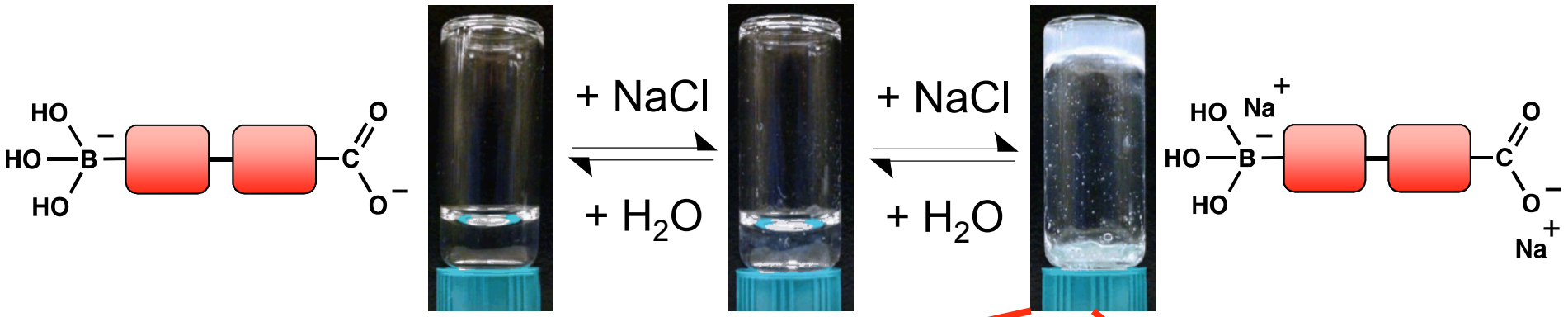
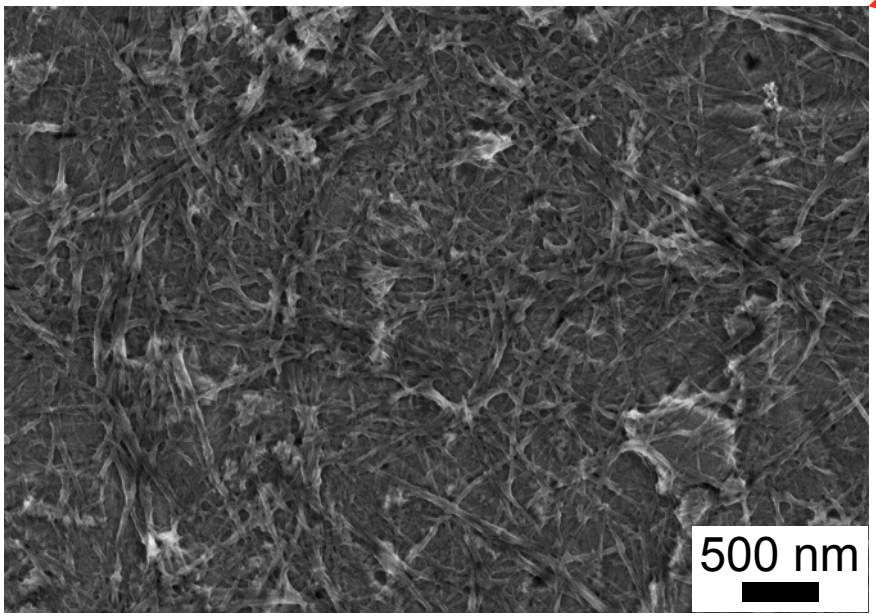
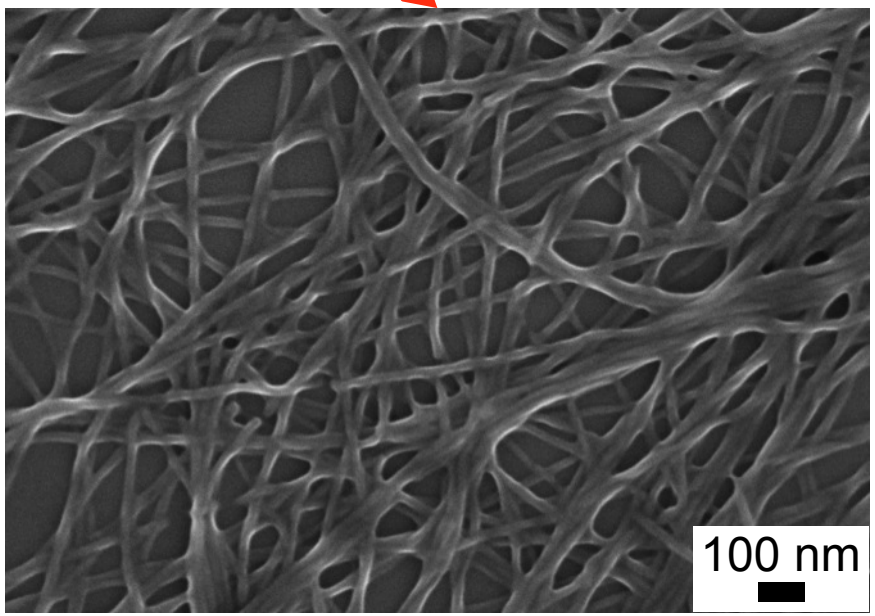
Nanoribbon assemblies are reversibly formed by changes in [salt]

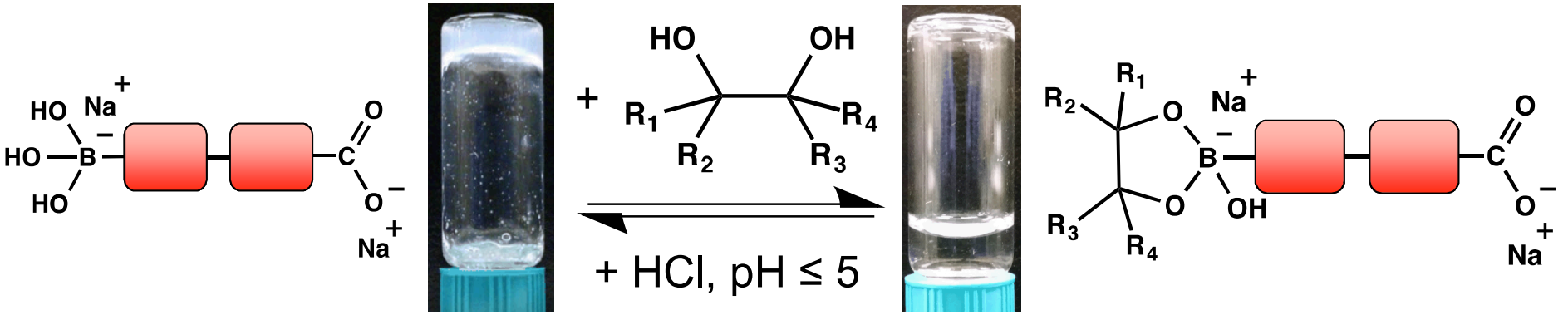


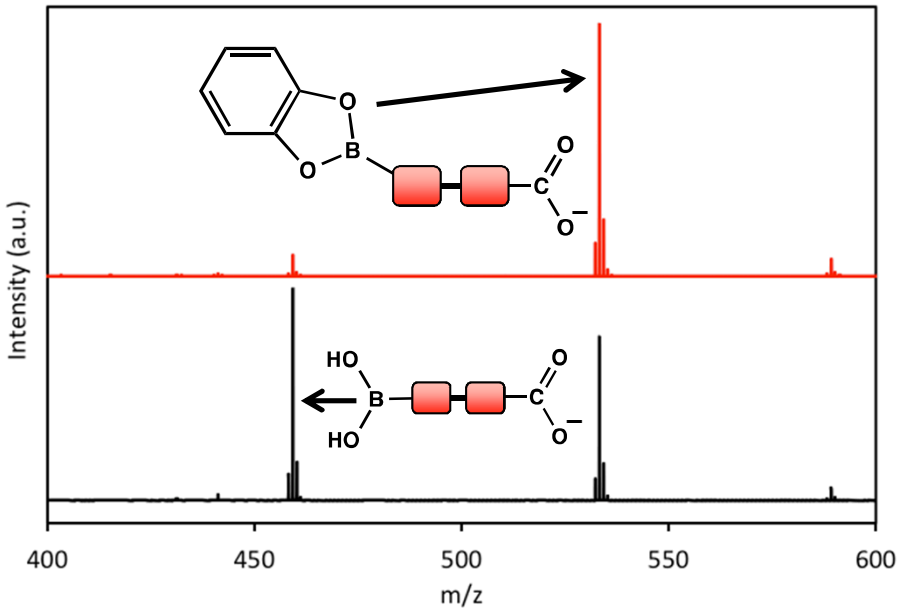




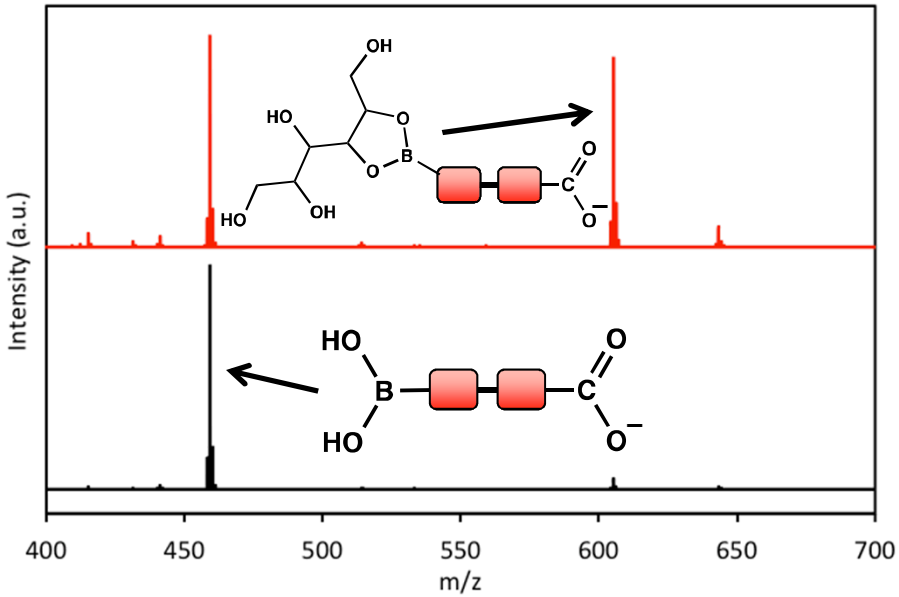
Saccharides/Polyols Induce Disassembly

Gel-sol transitions are triggered by addition of saccharides or polyols





[**catechol**]:[peptide] = 1:1 6:1

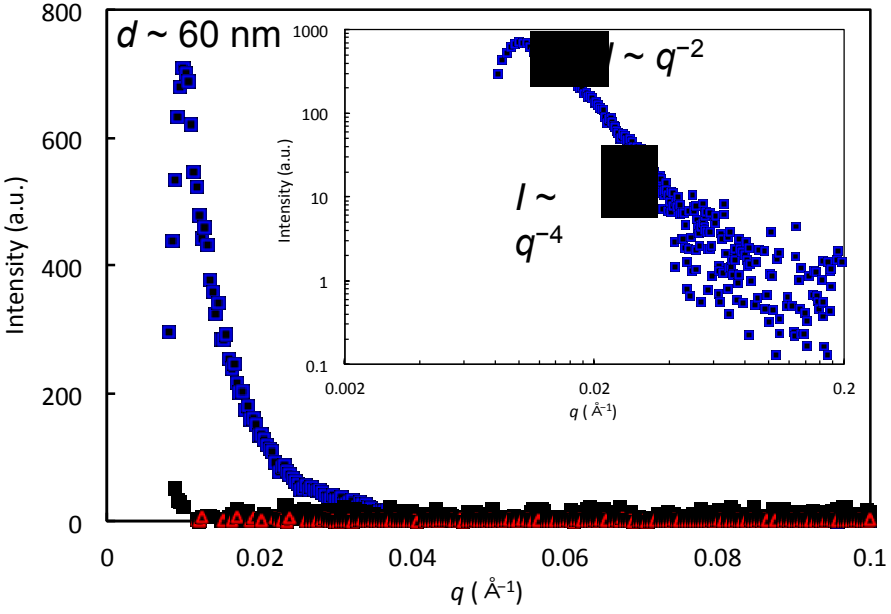


[**sorbitol**]:[peptide] = 1:1 6:1

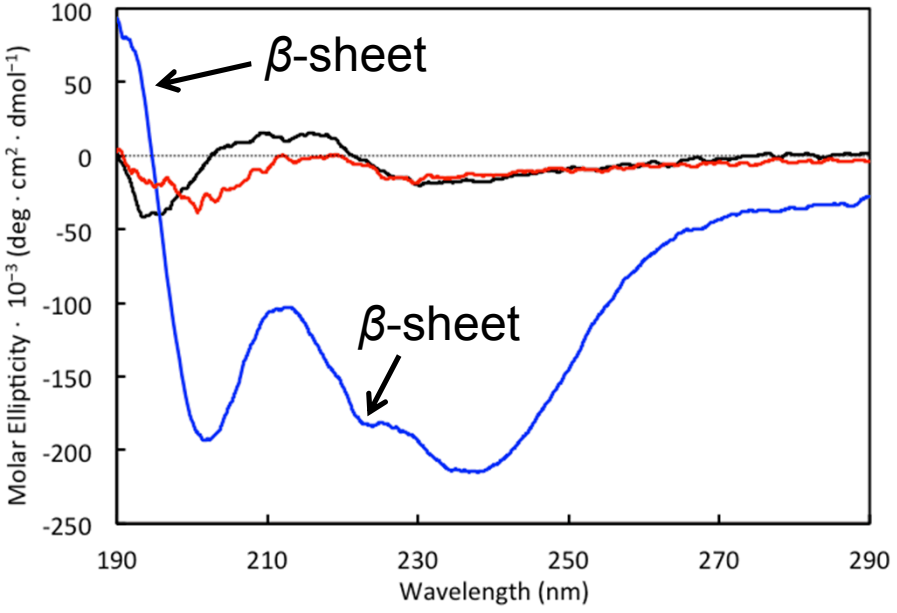
Structural Characterization

Small angle x-ray scattering (SAXS) and circular dichroism (CD) spectroscopy confirm stimulus-induced disorder-order-disorder transitions.

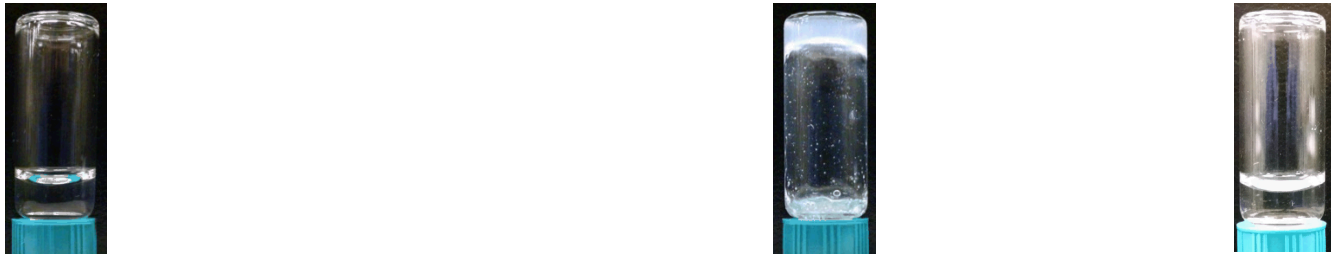
SAXS



CD

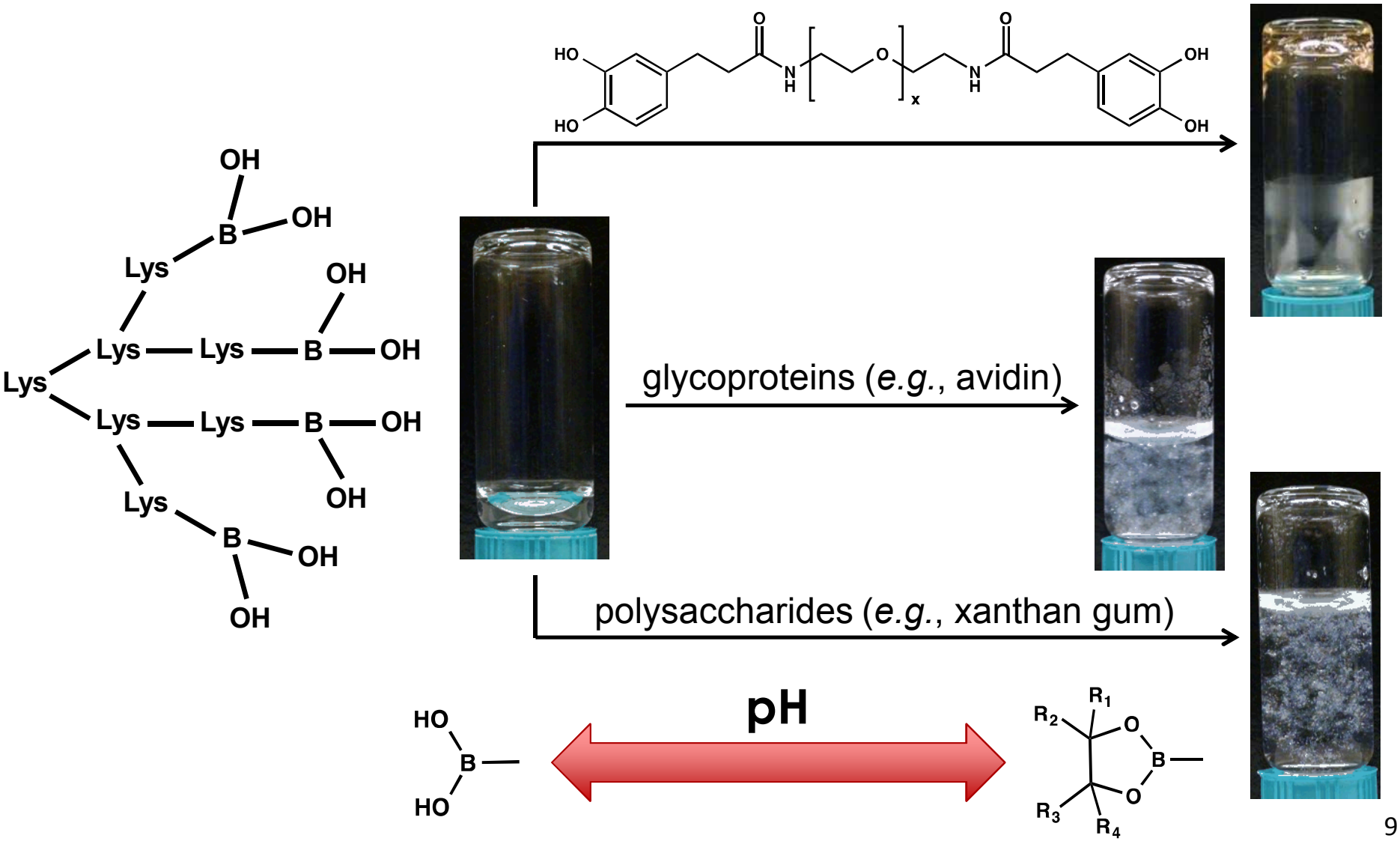


peptide in pH 7 buffer → + NaCl → + catechol



Multi-Functional Peptides

Boronic acid-polyol recognition can also trigger sol-gel transitions in peptides containing multiple boronic acids



Conclusions

- **Boronic acids are synthetically convenient handles for directing the self-assembly of peptides *via* external stimuli**
- **Boronic acid-modified di(phenylalanine) reversibly self-assembles into physically crosslinked nanoribbon networks in response to changes in pH or [salt]**
- **Physical networks can be disassembled by the conversion of boronic acids to boronate esters *via* introduction of polyols/saccharides**
- **The same interactions can be utilized in multi-functional peptides to reversibly introduce chemical crosslinks**

Acknowledgements

- **Lance Miller and Dr. James Hochrein** – mass spectrometry
- **This research was supported by the U.S. Department of Energy, Office of Basic Energy Sciences, Division of Materials Sciences and Engineering, Project KC0203010**