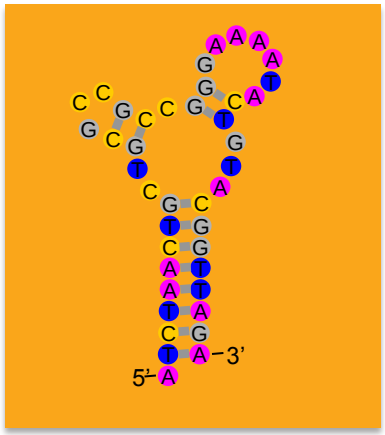
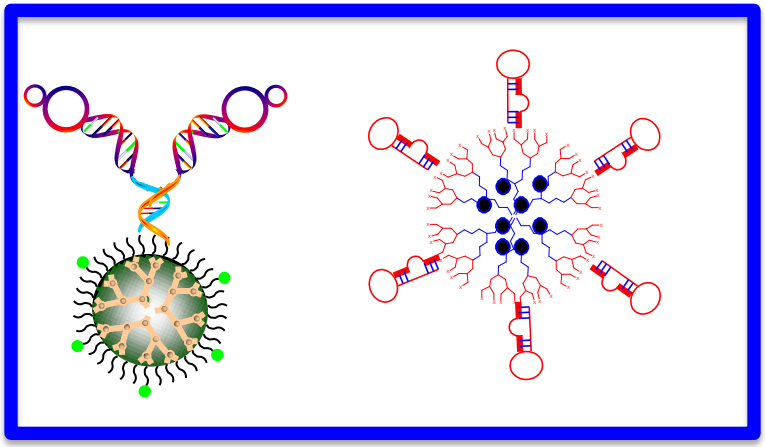
Programmable Materials for Drug Delivery and Regenerative Medicine

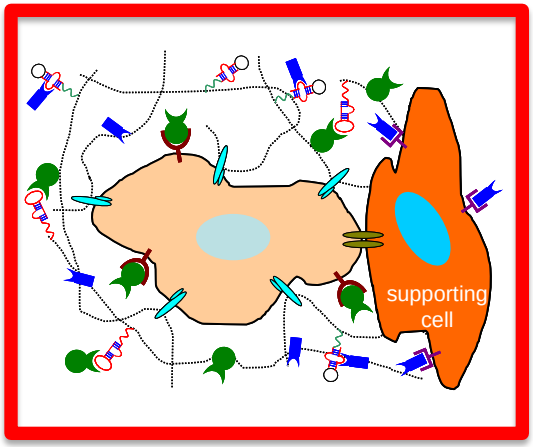
Yong Wang

Department of Biomedical Engineering
Pennsylvania State University, University Park, PA 16802

Goal: To develop biomolecular and biomimetic materials whose multiple functions can be programmed in diverse ways.





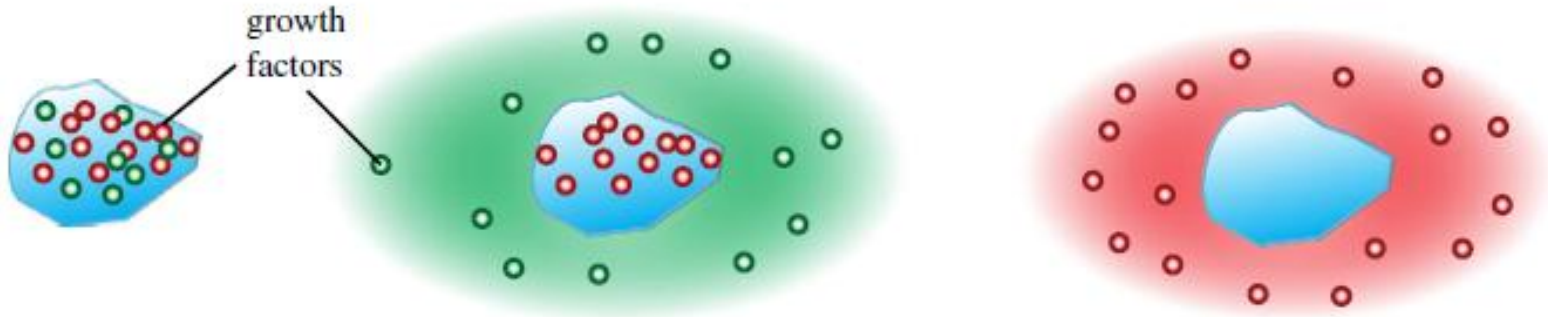


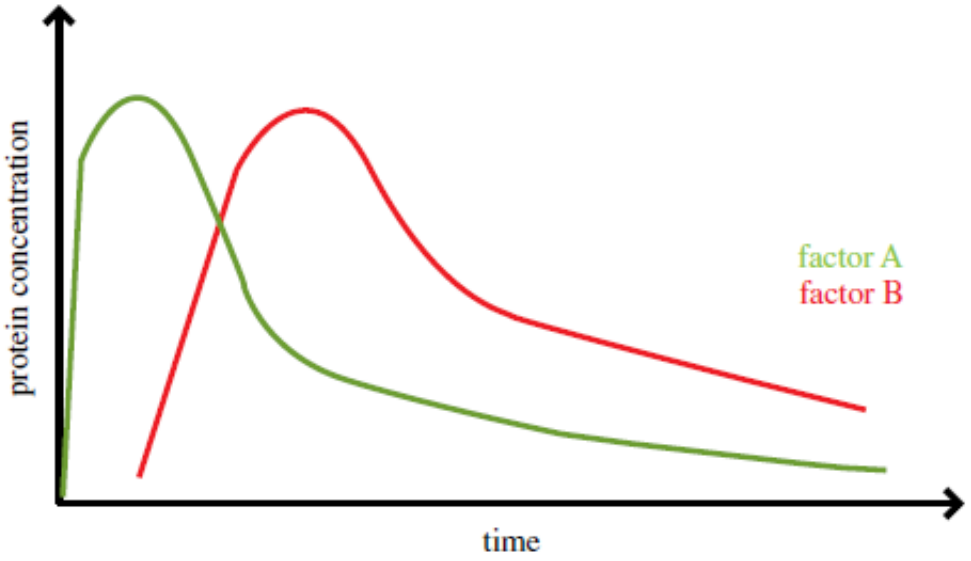
From affinity aptamers

To intelligent nanobiomaterials

To tissue-like biomaterials

On-Demand Release of Multiple Protein Drugs For Tissue Engineering and Regenerative Medicine

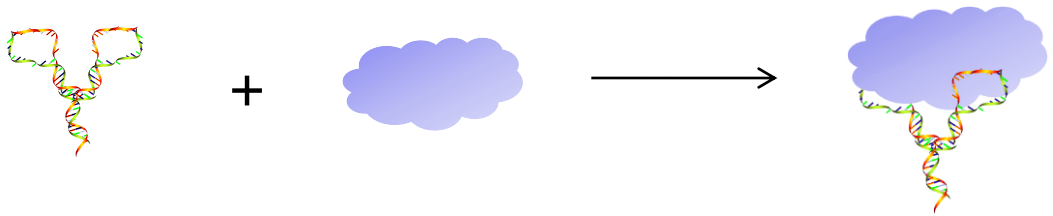




? Sequence
? Dose
? Time
? Duration

J. R. Soc. Interface (2011) 8, 153–170

***Principle*: Molecular Recognition**



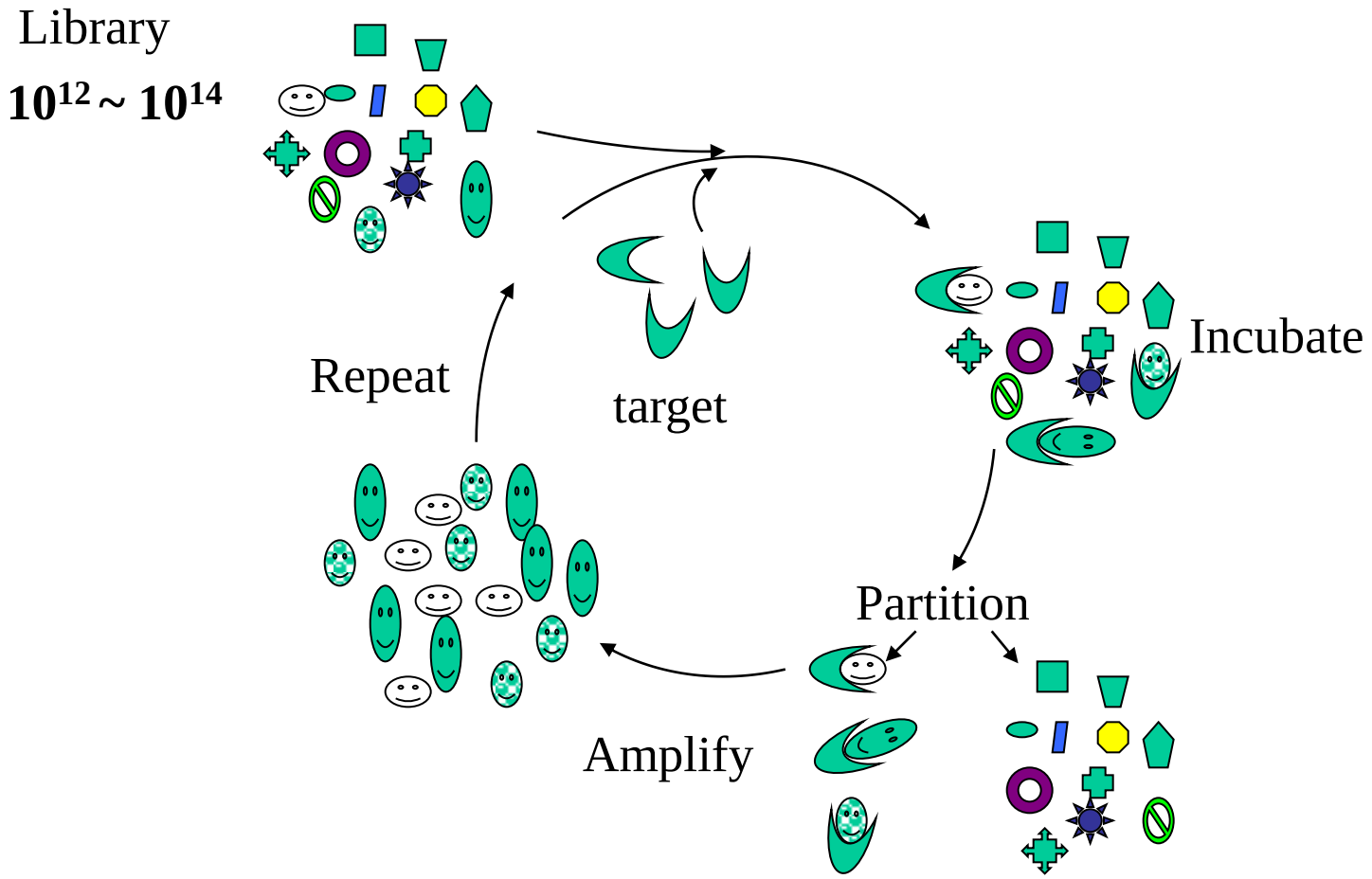
 **: aptamer**

 **: target**

Soontornworajit B, Zhou J, Shaw MT, Fan, TS, **Wang Y**. Chemical Communications 2010; 46:1857-1859
Soontornworajit, B. , Zhou, J. , Snipes, M., Battig, M., **Wang, Y.** *Biomaterials*. 2011, 32: 6839-6849.

Nucleic Acid Aptamers

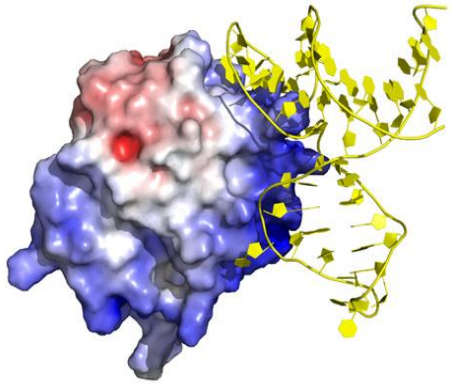
Single-stranded oligonucleotides screened from the library of synthetic oligonucleotides



- Tuerk C, and Gold L (1990) Science 249: 505-510
- Ellington AD, and Szostak JW (1990) Nature 346: 818-822

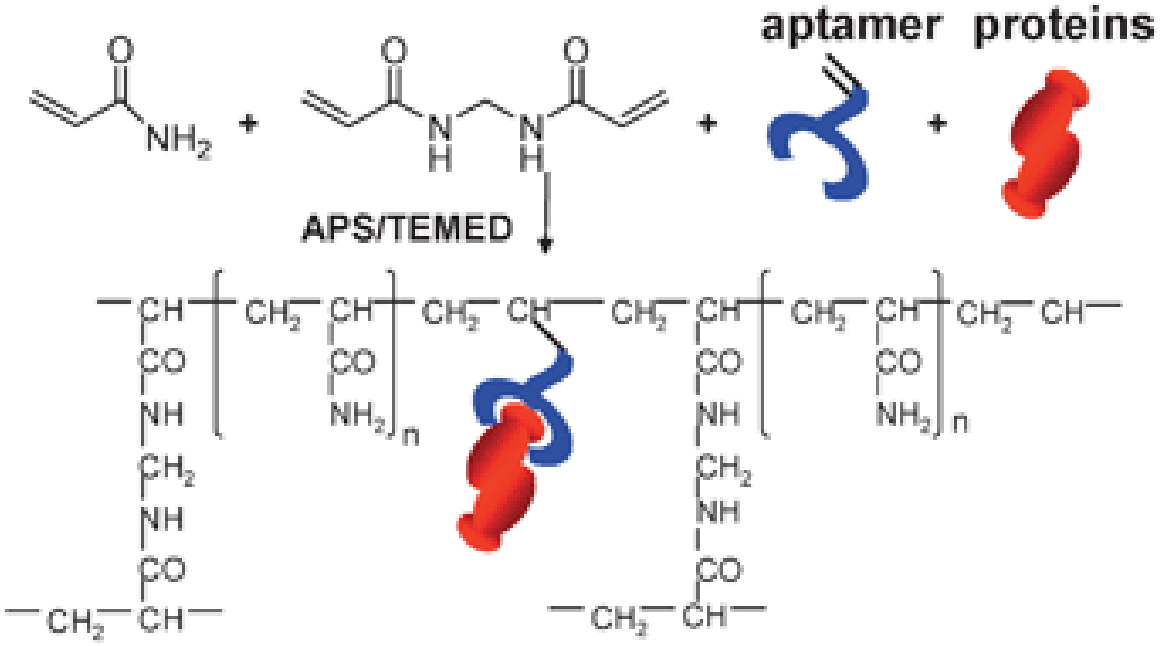
Nucleic Acid Aptamers

- High specificity
- High affinity
- Little immunogenicity
- Small size
- Easy synthesis
- Tolerant of harsh chemical/physical conditions
- **High resistance against nuclease degradation**
- **Controllable reversibility in molecular recognition**



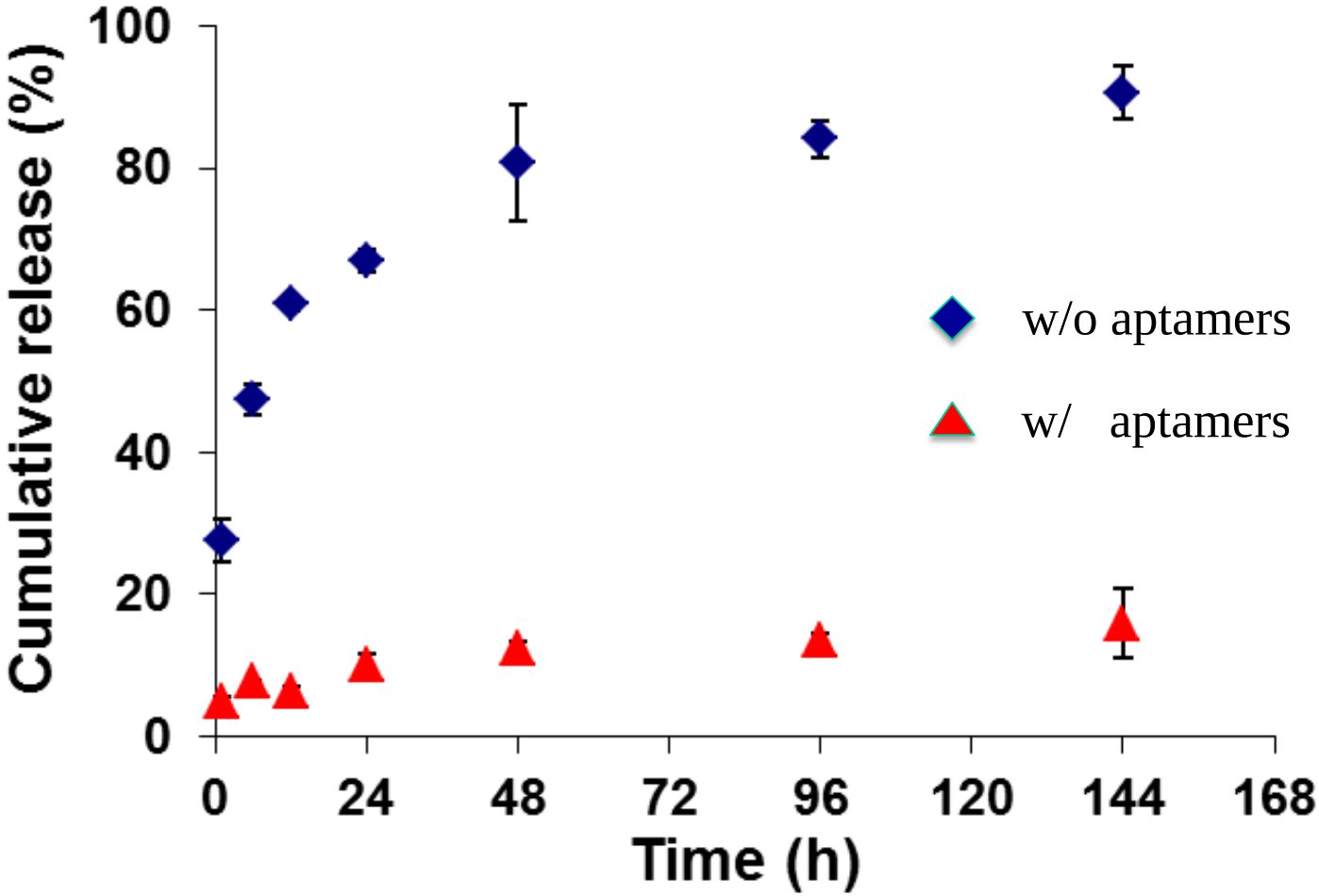
(2009) Structure 17: 1476-1484

Synthesis of Aptamer-Functionalized Hydrogels via Free Radical Polymerization



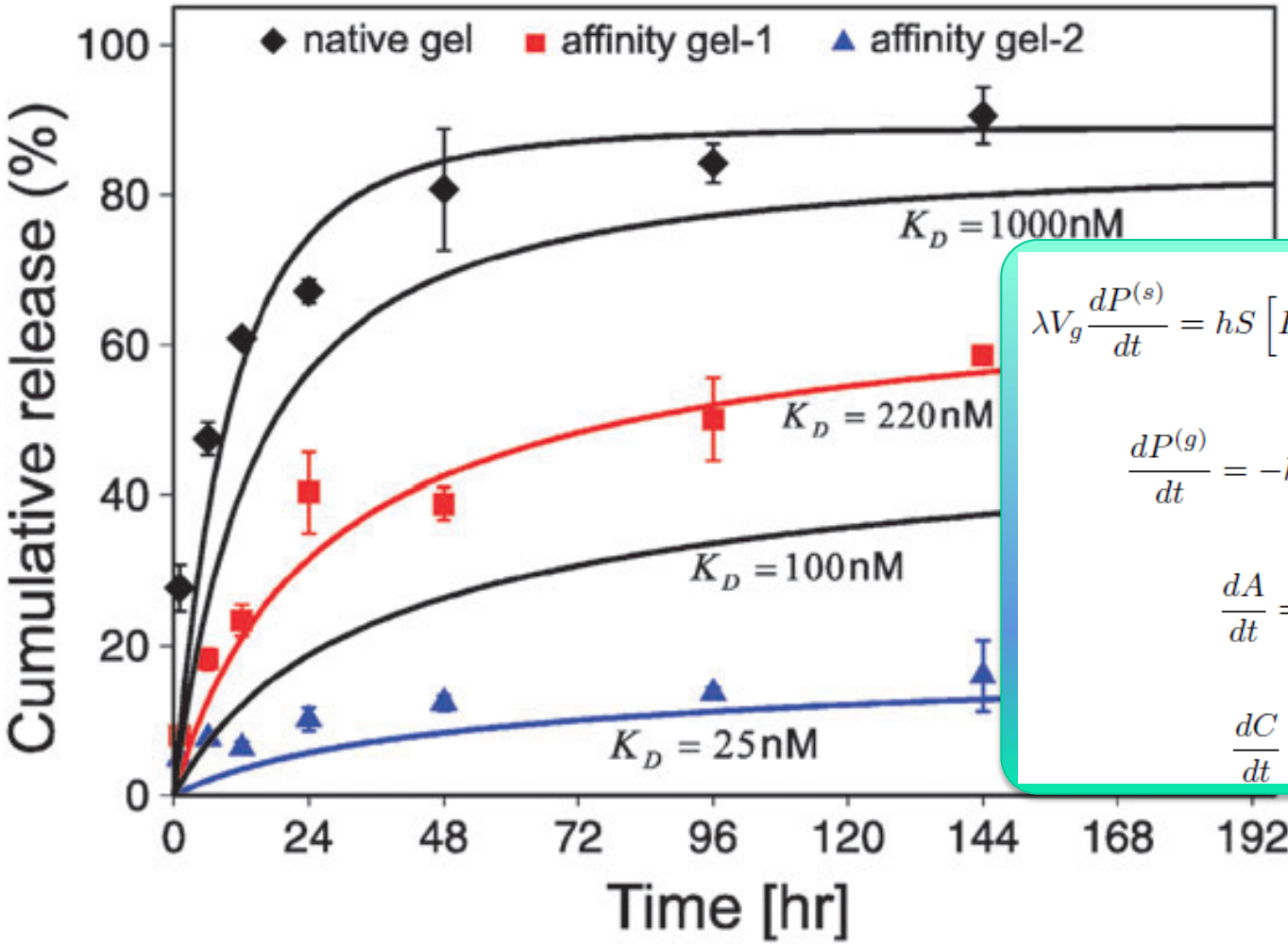
Soontornworajit B, Zhou J, Shaw MT, Fan, TS, **Wang Y**. Chemical Communications 2010; 46:1857-1859

Retention/Release of Growth Factors



Soontornworajit B, Zhou J, Shaw MT, Fan, TS, **Wang Y**. Chemical Communications 2010; 46:1857-1859

Effect of Binding Affinity on Retention/Release of Growth Factors



$$\lambda V_g \frac{dP^{(s)}}{dt} = hS\left[P^{(g)} - P^{(s)} - P_\infty^{(g)} + P_\infty^{(s)}\right],$$

$$\frac{dP^{(g)}}{dt} = -kAP^{(g)} + k'C - \lambda\frac{dP^{(s)}}{dt},$$

$$\frac{dA}{dt} = -kAP^{(g)} + k'C,$$

$$\frac{dC}{dt} = kAP^{(g)} - k'C,$$

Soontornworajit B, Zhou J, Shaw MT, Fan, TS, **Wang Y**. Chemical Communications 2010; 46:1857-1859

Pros & Cons

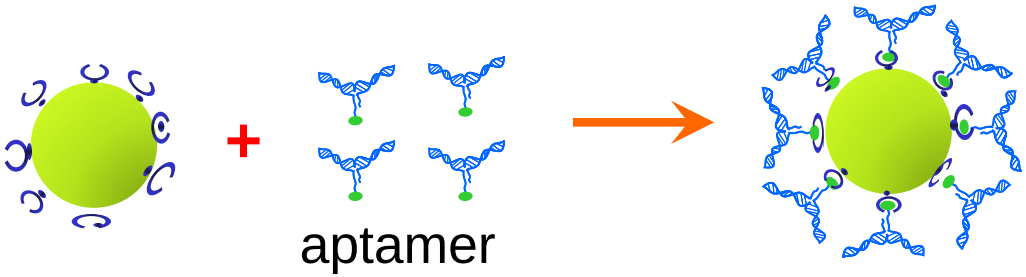
Good:

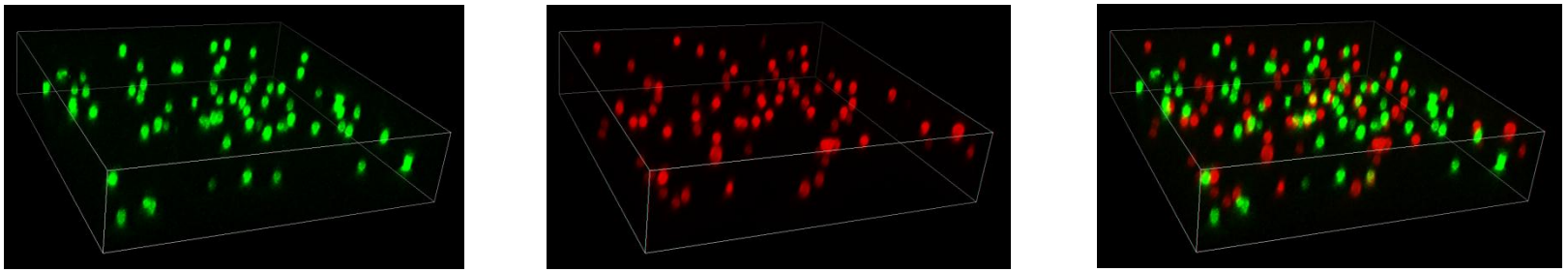
- *Aptamers were able to retain growth factors in the hydrogels;*
- *The retention/release could be modulated by varying the binding affinity of the aptamer.*

Bad:

- *Some growth factors were significantly or completely denatured during the synthesis of hydrogels.*
- *We also tried other methods like photoinitiated polymerization. It did not work well for us.*

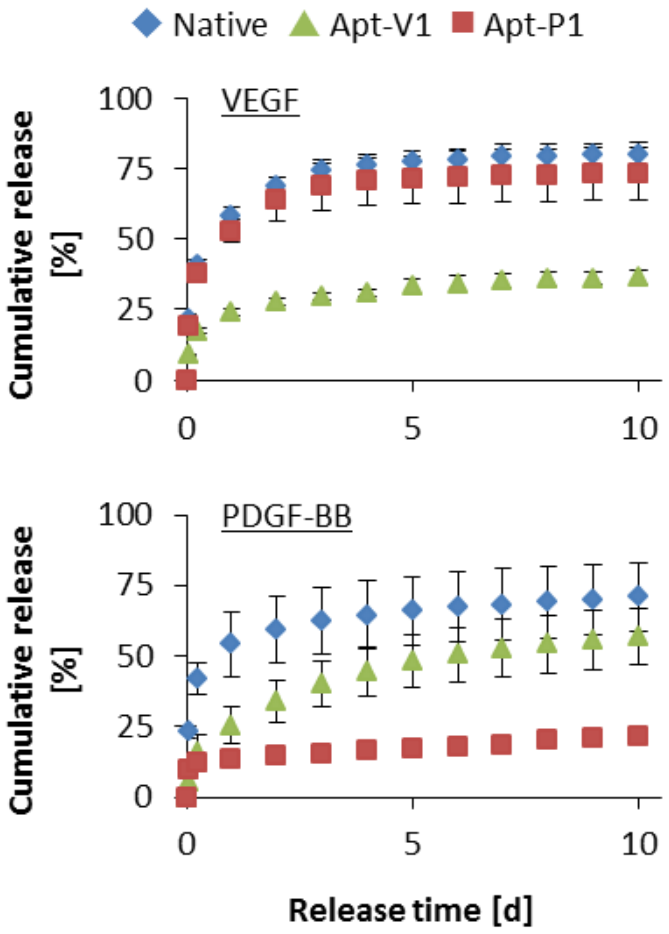
Synthesis of Aptamer-Functionalized Hydrogels Using Thermoresponsive Solutions





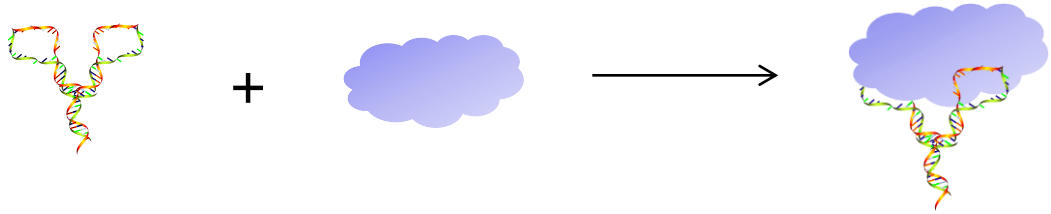
Battig, M.R., Soontornworajit, B. **Wang, Y.*** Programmable release of multiple protein drugs from aptamer-functionalized hydrogels via nucleic acid hybridization. ***Journal of the American Chemical Society***. 2012, 134, 12410-12413

Release of Growth Factors from Aptamer-Functionalized Agarose Hydrogels

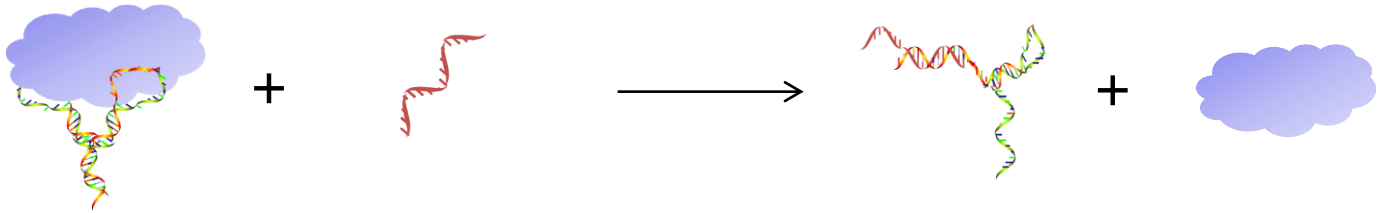


Battig, M.R., Soontornworajit, B. **Wang, Y.*** Programmable release of multiple protein drugs from aptamer-functionalized hydrogels via nucleic acid hybridization. ***Journal of the American Chemical Society***. 2012, 134, 12410-12413

Retention



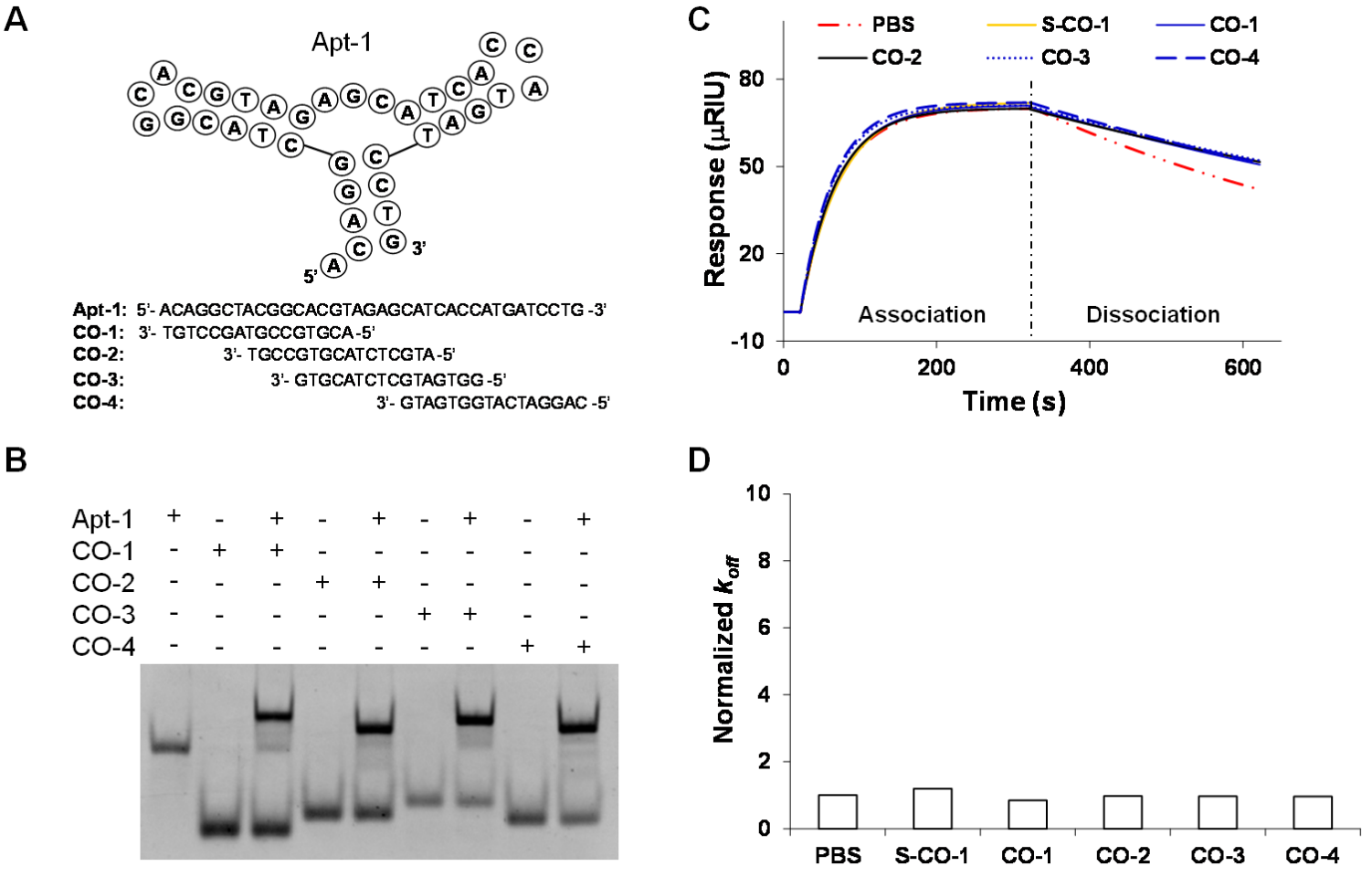
Programmable Release



Soontornworajit, B. , Zhou, J. , Snipes, M., Battig, M., **Wang, Y.** *Biomaterials*. 2011, 32: 6839-6849.

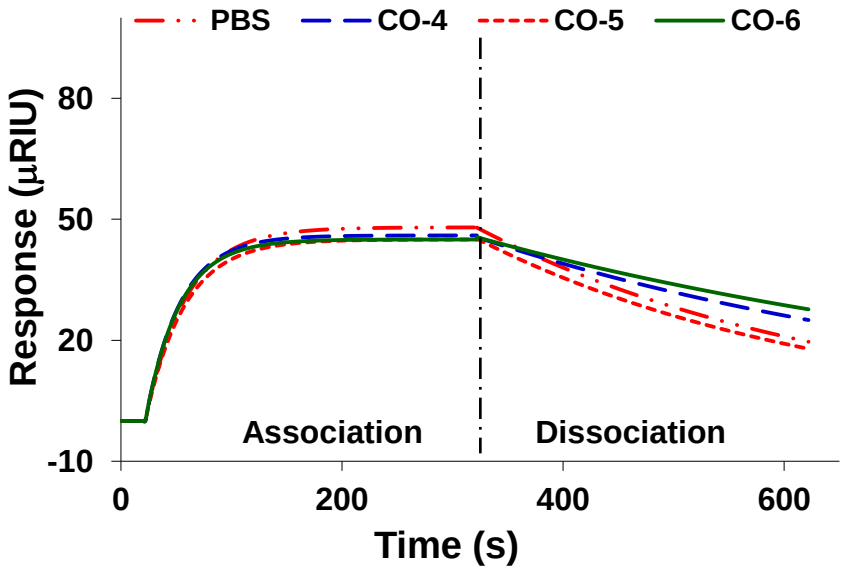
Battig, M.R., Soontornworajit, B. **Wang, Y.**. ***Journal of the American Chemical Society***. 2012, 134, 12410-12413.

Region for Hybridization



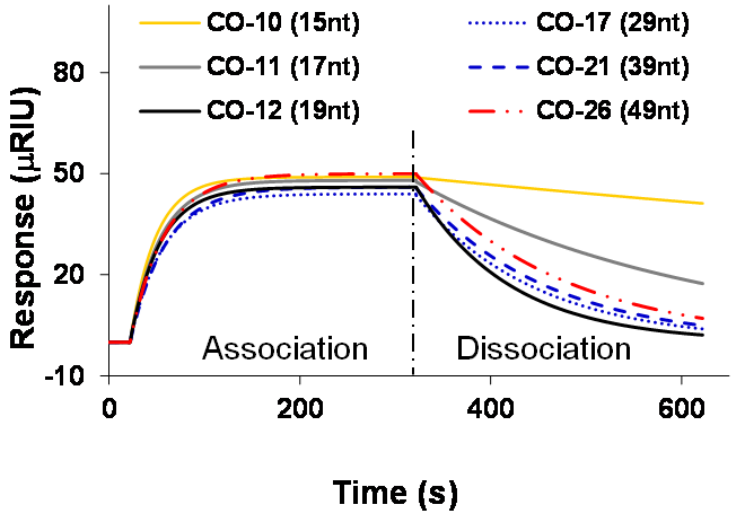
Length of Hybridization

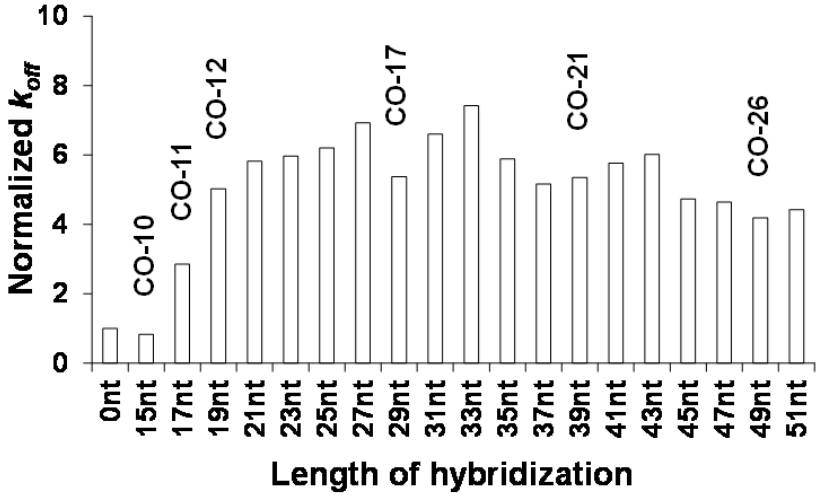
Apt-1: 5’- ACAGGCTACGGCACGTAGAGCATCACCATGATCCTG -3’
CO-4: 3’- GTAGTGGTACTAGGAC -5’
CO-5: 3’- CGTGCATCTCGTAGTGGTACTAGGAC -5’
CO-6: 3’- TGTCCGATGCCGTGCATCTCGTAGTGGTACTAGGAC -5’



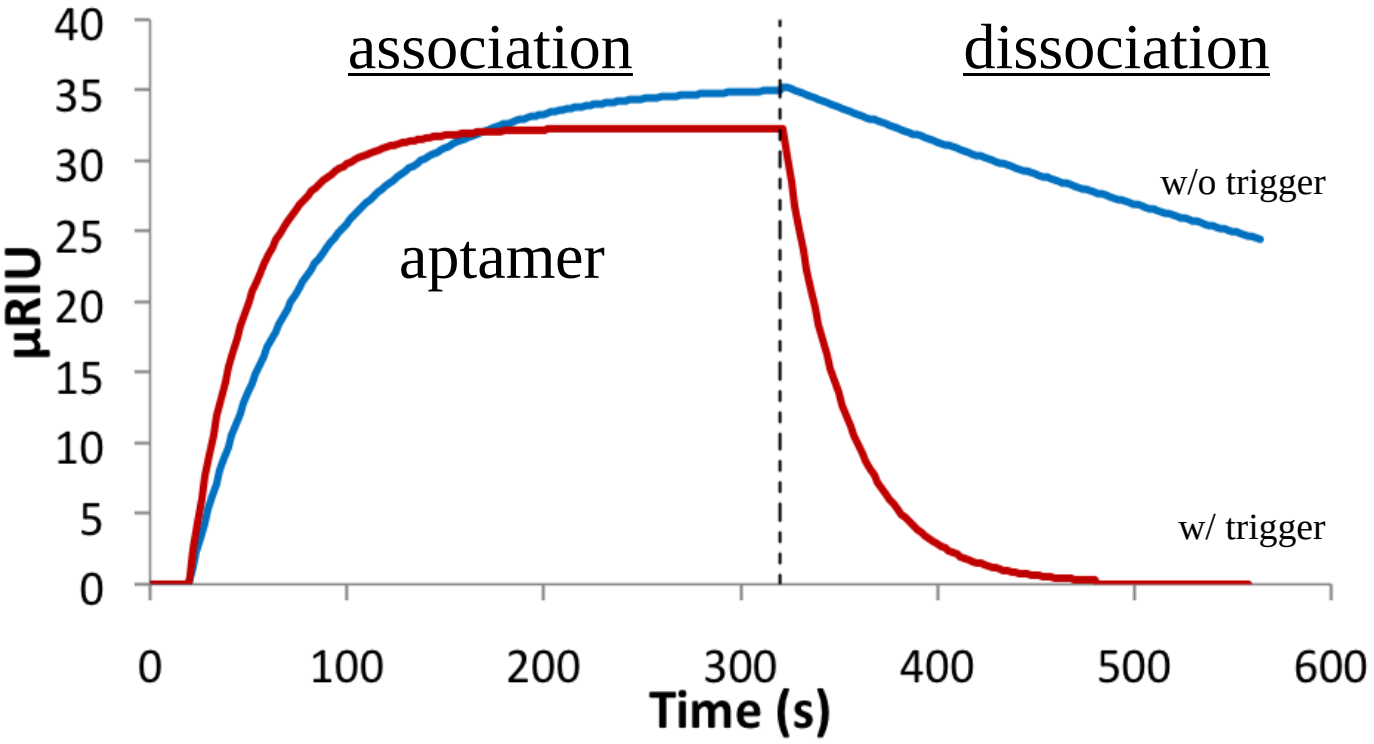
Synergistic Effect: Tail + Length

Apt-4:	5’- ACAGGCTACGGCACGTAGAGCATCACCATGATCCTGTGACTTGAGCAAAAT -3’
CO-10 (15nt)	3’- ACTGAACTCGTTTTA -5’
CO-11 (17nt)	3’-ACACTGAACTCGTTTTA-5’
CO-12 (19nt)	3’-GGACACTGAACTCGTTTTA-5’
CO-17 (29nt)	3’- AGTGGTACTAGGACACTGAACTCGTTTTA -5’
CO-21 (39nt)	3’- TGCATCTCGTAGTGGTACTAGGACACTGAACTCGTTTTA -5’
CO-26 (49nt)	3’- TCCGATGCCGTGCATCTCGTAGTGGTACTAGGACACTGAACTCGTTTTA -5’

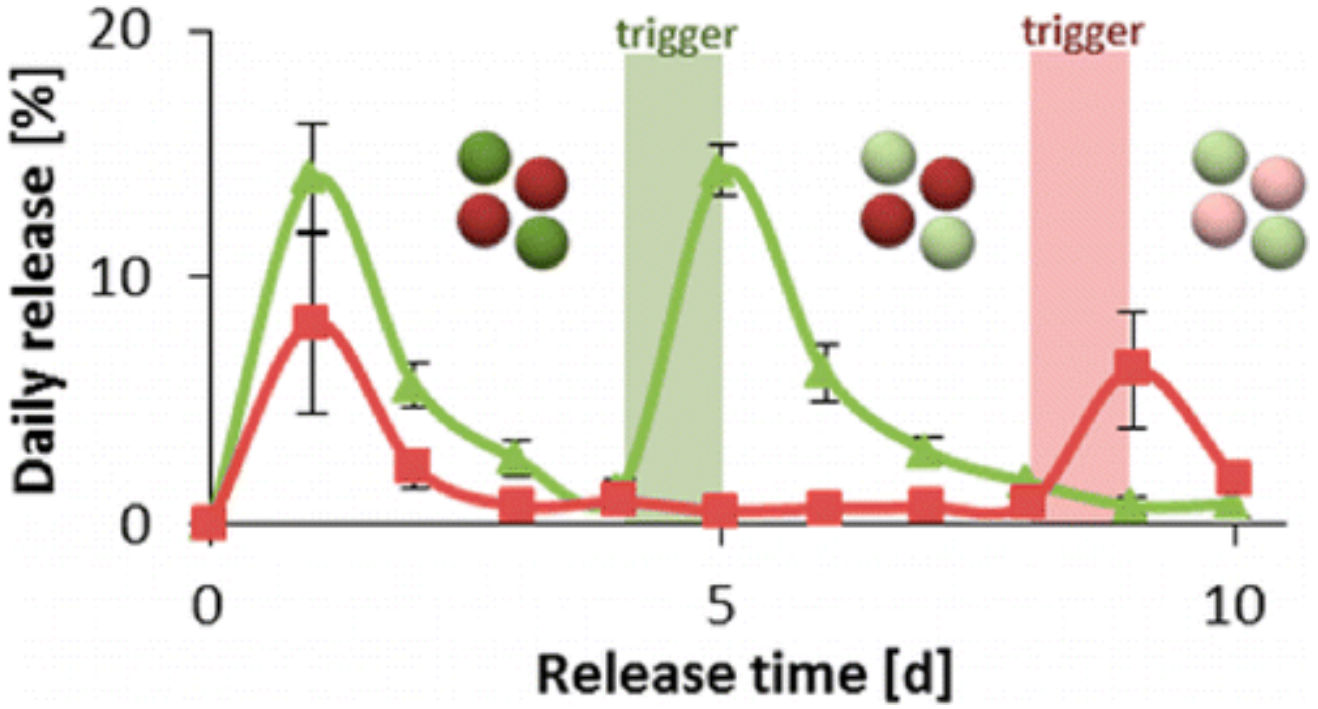




SPR Analysis of Programmable Molecular Recognition



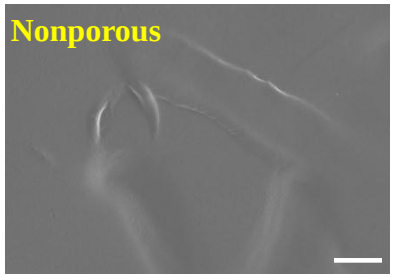
Programmable Release of Multiple Protein Drugs

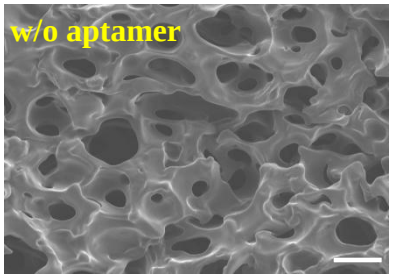


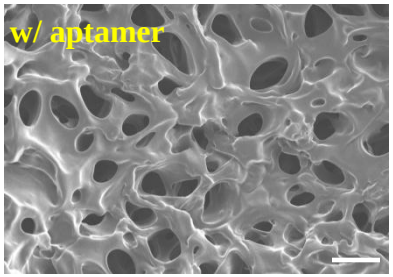
Two different protein drugs were programmed to release at days 5 and 10.

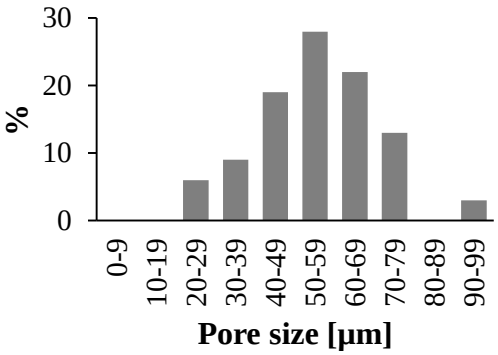
Battig, M.R., Soontornworajit, B. Wang, Y.* Programmable release of multiple protein drugs from aptamer-functionalized hydrogels via nucleic acid hybridization. ***Journal of the American Chemical Society***. 2012, 134, 12410-12413

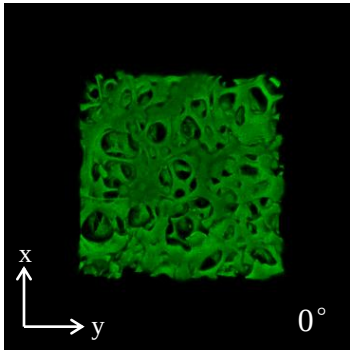
Structures of Superporous Hydrogels

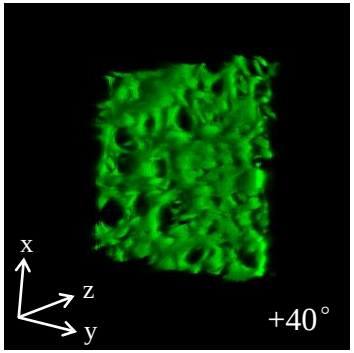








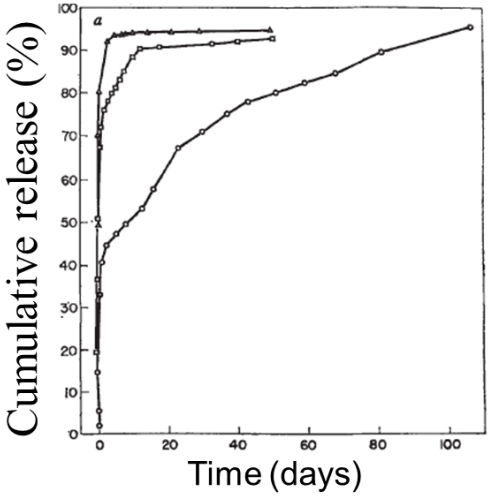


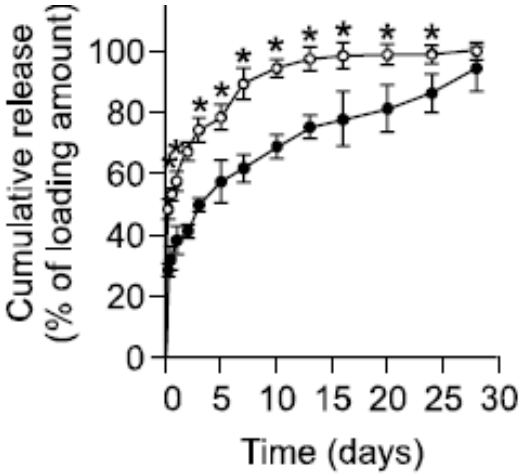


Hydrogels for the Delivery of Protein Drugs - Past & Current

Past

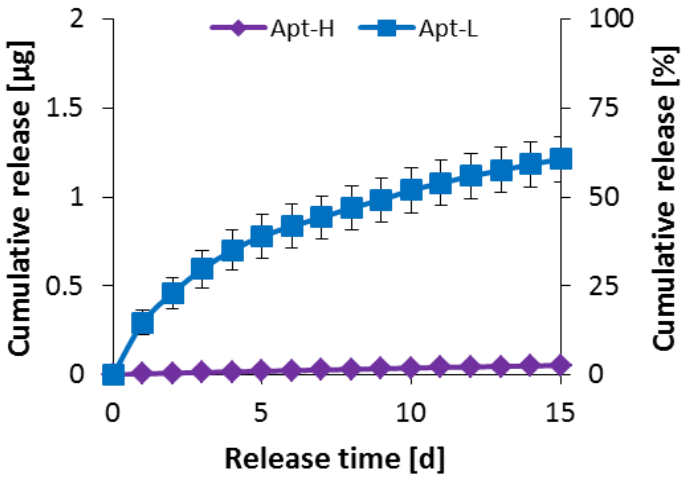
Nature; **1976** (263): 797-800

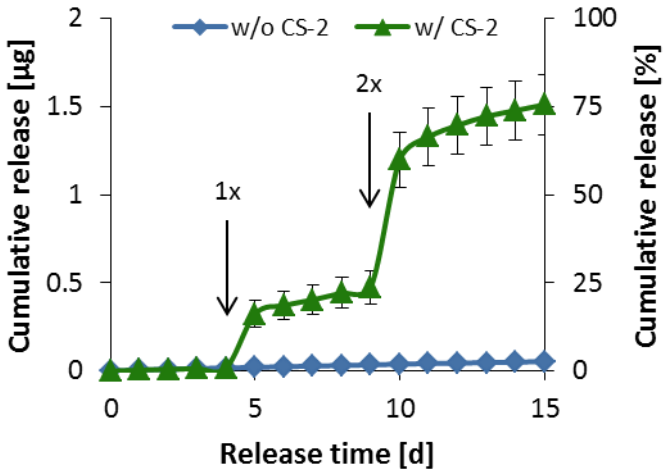




Experimental & Molecular Medicine **2012** (44), 350-355

Current Biomaterials 2014; 35(27), 8040-8048





OMICS INTERNATIONAL

www.omicsonline.org

OMICS International (and its subsidiaries), is an Open Access publisher and international conference Organizer, which owns and operates peer-reviewed Clinical, Medical, Life Sciences, and Engineering & Technology journals and hosts scholarly conferences per year in the fields of clinical, medical, pharmaceutical, life sciences, business, engineering, and technology. Our journals have more than 3 million readers and our conferences bring together internationally renowned speakers and scientists to create exciting and memorable events, filled with lively interactive sessions and world-class exhibitions and poster presentations. Join us!

OMICS International is always open to constructive feedback. We pride ourselves on our commitment to serving the Open Access community and are always hard at work to become better at what we do. We invite your concerns, questions, even complaints. Contact us at contact.omics@omicsonline.org. We will get back to you in 24-48 hours. You may also call 1-800-216-6499 (USA Toll Free) or at +1-650-268-9744 and we will return your call in the same timeframe.

Journal of Tissue Science & Engineering Related Journals

- Journal of Biochips & Tissue Chips
- Journal of Stem Cell Research & Therapy
- Journal of Biomimetics Biomaterials and Tissue Engineering

Journal of Tissue Science & Engineering

Related Conferences

- http://www.conferenceseries.com/

OMICS Group **Open Access Membership**

OMICS publishing Group Open Access Membership enables academic and research institutions, funders and corporations to actively encourage open access in scholarly communication and the dissemination of research published by their authors.

For more details and benefits, click on the link below:

http://omicsonline.org/membership.php