Biomaterials, Drug Delivery, Nanotechnology and Bioengineering

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“Smart” Drug Delivery

- The future of drug delivery systems will involve smart systems.

- These will address the issue of keeping the drug at the desired therapeutic level in the body thus avoiding frequent administration.

- Systems use detection of chemical signals in the body to prompt the release of drugs.

- The ultimate goal is to administer drugs at the right time, at the right dose anywhere in the body with specificity and efficiency.
Oral Delivery of Proteins

Challenges

- Protection of the drug from:
  - The **acidic** environment in the stomach
  - Degradation by proteolytic enzymes in the GI tract

- Penetration and absorption of drug across the intestinal mucosa and epithelium

Stomach pH ~2
Complexation and pH Responsive Hydrogels

Complexed
Small mesh size
Low pH

Uncomplexed
Increased mesh size
High pH

Protect drug

Release drug

\[
\begin{aligned}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{H}_2\text{C} & \quad \text{H}_2\text{C} \\
\text{C} & \quad \text{C} \\
\text{C} & \quad \text{C} \\
\cdots & \quad \cdots \\
\text{O} & \quad \text{HOOC} \\
\text{CH}_2\text{CH}_2 & \cdots \\
\text{OCH}_3 & \\
\end{aligned}
\]

\[
\begin{aligned}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{H}_2\text{C} & \quad \text{H}_2\text{C} \\
\text{C} & \quad \text{C} \\
\text{C} & \quad \text{C} \\
\cdots & \quad \cdots \\
\text{O} & \quad \text{OOC} \\
\text{CH}_2\text{CH}_2 & \cdots \\
\text{OCH}_3 & \\
\end{aligned}
\]
**In Vivo Study with pH-Responsive Complexation Hydrogels**

- P(MAA-g-EG) microspheres loaded with insulin
- Administered to diabetic rats → 40% drop in blood glucose levels

*Figure 1*- Blood glucose in diabetic, male Wistar rats following oral administration of 25 IU/kg body weight doses contained in (○) P(MAA-g-EG) microspheres and (●) insulin solutions (n = 5).
Oral siRNA Delivery

Polymeric polymers mediate endosome disruption through the proton sponge mechanism. Following endosomal escape, entrapped biomolecules can be released into the cytosol.

Fluorescently labeled siRNA with fluorescent tagged ovalbumin conjugated to surface

Intracellular Glutathione (GSH)

Nanoscale hydrogels for siRNA delivery
Bionanotechnology

Externally controlled drug delivery

Gold-polymer nanoparticle for triggered and targeted drug delivery
Upon laser irradiation, a thermo-sensitive polymer collapses to release therapeutics
Temperature sensitive nano-composites with Fe_3O_4 and gold nanoparticles shown schematically, with electron microscopy, and thermal-IR imaging.

Microdevices for biomarker detection and intelligent therapeutics

Microcantilever array with hydrogel patterned on surface.

Microcantilever patterned with an environmentally responsive hydrogel

Micropatterned array of biomimetic polymer networks
System-Responsive Therapy: Control-Based Design of Biomedical Systems
Configurational Biomimetic Imprinting

Making “artificial locks” for “molecular keys”

Molecular key
(template molecule)
- Small molecules
  - Drug substances, amino acids, steroid hormones
- Large molecules
  - Nucleic acids, proteins
- Cells and viruses

Lock
(polymer building blocks)
- Functional monomers
- Cross-linkers
Configurational Biomimetic Imprinting

Monomers → Template → Polymerization

Extraction and drying
BioMEMS Sensor Platform

Pattern **environmentally responsive hydrogels onto silicon microcantilevers** to create a BioMEMS/MEMS sensor device.

Change in **analyte, pH, temperature etc.** → hydrogel swells
**Bionanotechnology**

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System-Responsive Therapy: A Bright Future

- Need for *advanced intelligent materials*, more reliable devices, *miniaturized* systems

- Society asks for *improved treatment* of disease, advanced *detection* and *therapy*, and *cost effective processes*

- Improvement of *quality of life* is important