Institute for Biomaterials, Drug Delivery and Regenerative Medicine

Laboratory of Biomaterials, Drug Delivery and Bionanotechnology

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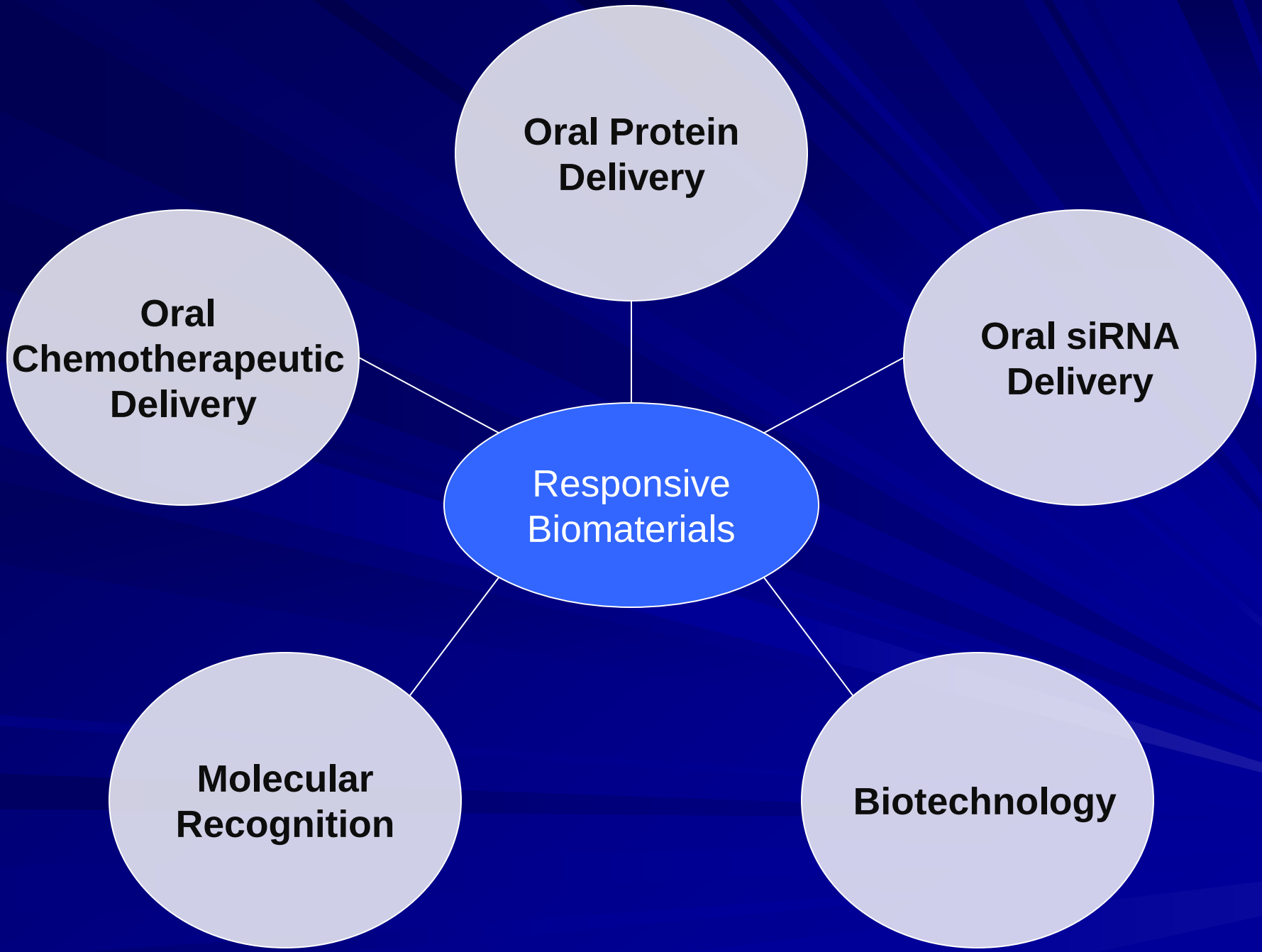
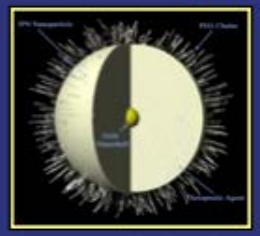
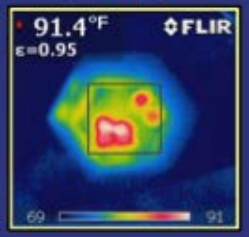

Oral Protein Delivery
Oral Chemotherapeutic Delivery
Oral siRNA Delivery
Responsive Biomaterials
Molecular Recognition
Biotechnology

Bionanotechnology

Externally Responsive Nanoparticles

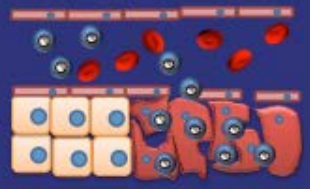




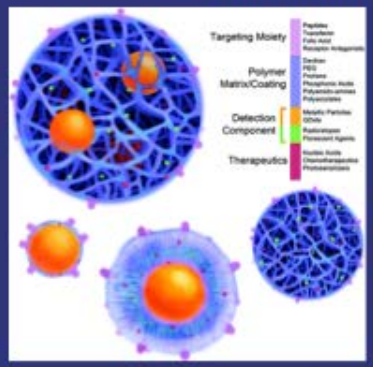
Gold-polymer nanoparticles
- Laser irradiation leads to polymer collapse and release of therapeutic

Fe3O4 nano-composites
- Temperature sensitive
- Thermal-IR imaging

Nanoparticle localization
- IV injection leads to localization due to leaky vasculature
- Surface chemistry manipulation can improve localization
- Drug carriers can be improved by modification of polymer chemistry



Targeted Delivery and Theranostics



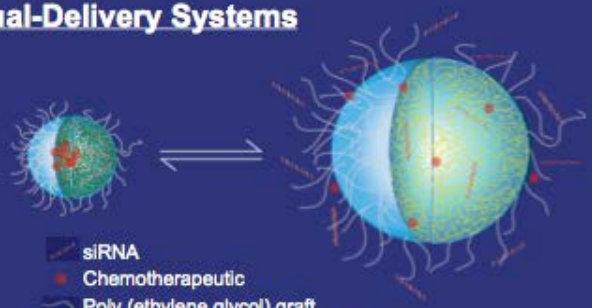
Molecularly decorated, intelligent nanoparticles take advantage of unique phenotypic features of diseased tissues and cells in order to deliver a particle or drug to the site of action.

Targeting Ligands:
- Small Molecules
- Aptamers
- Folate, Transferrin
- Antibodies
- Peptides
- Oligonucleotides

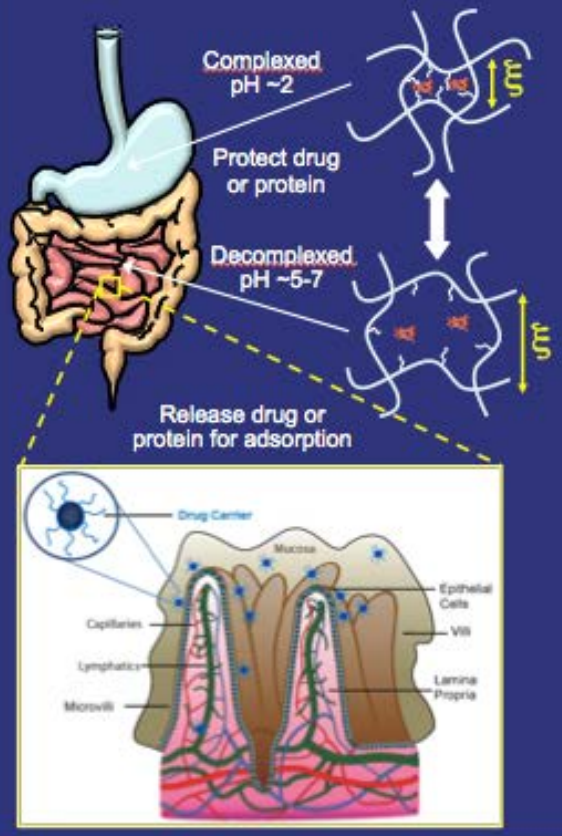
Dual-Delivery Systems

Drug-Resistant Cancer:
- Efflux pumps
- Anti-apoptotic pathways

Drug Delivery System:
- Injectable
- Amine methacrylates
- pKa ~6
- Simultaneous delivery

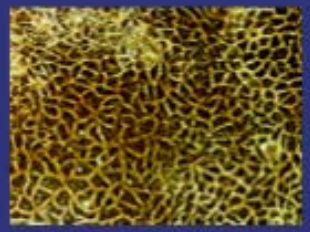


Background

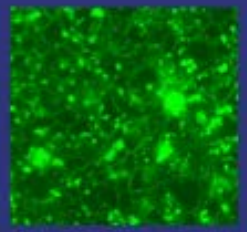


Major Disease Targets and Therapeutics

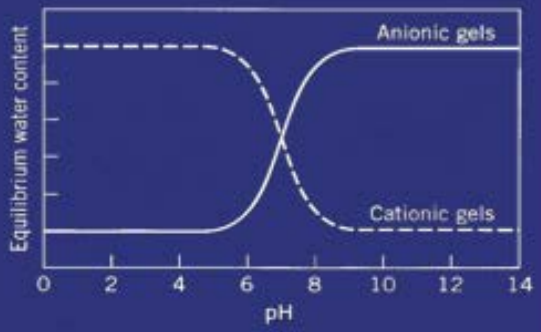
Multiple Sclerosis	Interferon-β
Crohn's Disease	"High Isoelectric Point Drugs"
Cancer	Chemotherapeutic Agents, siRNA, Interferon-α
Ulcerative Colitis	siRNA
Celiac Disease	siRNA
Osteoporosis	Calcitonin
Hemophilia	Hemophiliac Factor IX
GHD, Turner's Syndrome, Prader-Willi Syndrome	Human Growth Hormones



Caco-2 cells as a gastrointestinal model



Caco-2 cells with tight junction stained



Highlight of Recent Patents

- W. Liecthy and N.A. Peppas, "Delivery of Small Interfering RNA and Micro RNA Through Membrane-Disruptive, Responsive Nanoscale Hydrogels.", U.S. Patent (pending).
- N. A. Peppas, B. Ekerdt and M. Gomez: "Method and Process for the Production of Multicoated, Recognitive and Releasing Systems", U.S. Patent 8,821,899, September 2, 2014.
- N. A. Peppas and L. Brannon-Peppas: "Multilayer Modular Oral Release System", U.S. Patent (pending)

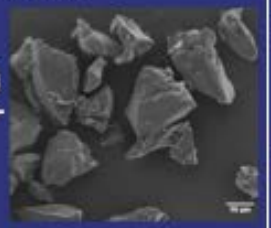
Oral Protein Delivery

Hemophilia

Treatment of hemophilia B, a bleeding disorder, relies on i.v. injections/infusions of blood clotting protein, factor IX.

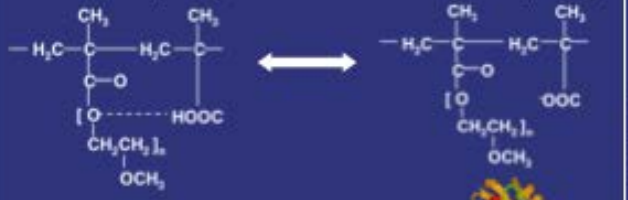
Goal: To improve hemophilia B treatment by offering a convenient, needle-free, and accessible protein replacement therapy

Objective: To develop a pH-sensitive polymeric carrier for the oral delivery of factor IX



Carrier System: P(MAA-g-EG)
Crosslinked poly(methacrylic acid)-grafted-poly(ethylene glycol)

Stomach (pH 2) ⟷ Intestine (pH 7)



Oral Delivery of High Molecular Weight Proteins

Insulin 5.8 kDa < Factor IX 57 kDa

Osteoporosis

Proteins exhibiting a high isoelectric point present delivery challenges due to charge interactions with our carriers.

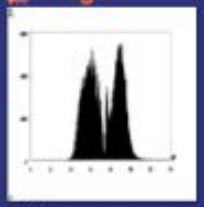
Salmon Calcitonin
- Osteoporosis medication
- Cationic in small intestine
- Anionic hydrogels

Nearly half of all proteins exhibit high isoelectric point, as do many best-selling drugs.

Urokinase

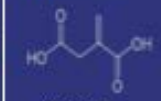
Rituxan

Notable High pI Drugs:
- Humira
- Enbrel
- Remicade
- Avastin
- Herceptin
- Lucentis

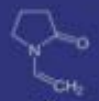


>$72 Billion sales

Using P(IA-co-NVP) hydrogels, we can deliver therapeutic levels of salmon calcitonin, in 1 daily capsule.



Itaconic acid (IA)



N-vinylpyrrolidone (NVP)

sCT

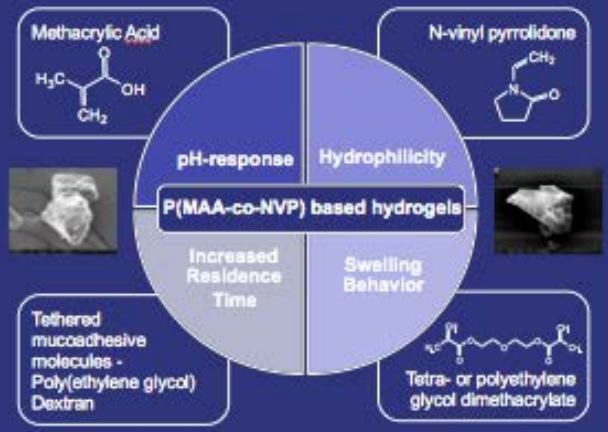
Growth-Related Disorders

22 kDa
pI 5.1

Human Growth Hormone

Replacement therapies can aid in the treatment of the following pediatric disorders:
- Growth hormone deficiency
- Turner's Syndrome
- Prader-Willi Syndrome

Research Goal: To develop a pH-responsive polymeric system for the oral delivery of hGH to replace once daily injections

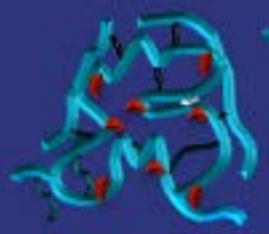


Oral siRNA and Chemotherapeutics Delivery

Chemotherapeutics

Goal: To improve treatment efficacy and patient quality of life by increasing the solubility and permeability of hydrophobic therapeutics

Oral delivery platform: Grafted, copolymer network for delivering hydrophobic therapeutics (e.g. doxorubicin)

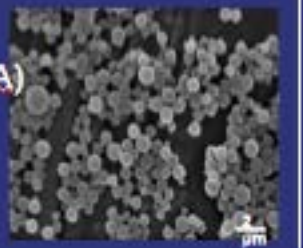


Graft Hydrophilic Network

Grafted PEG Chains

Hydrophobic Components

P(MAA-g-PEG-co-*t*BMA) nanoparticles



siRNA

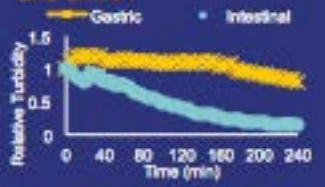
Challenges to the oral delivery of siRNA

- Preserving biological activity in harsh pH and enzymatic conditions
- Facilitating intracellular uptake and endosomal release
- Mitigating off-target gene silencing
- Effective RNAi-mediated gene silencing

Two-Part Oral Delivery of siRNA

I. Intestinal Delivery

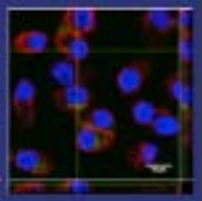
Microgels protect nanogels and siRNA



Microgels swell, undergo enzymatic degradation, and release nanogels

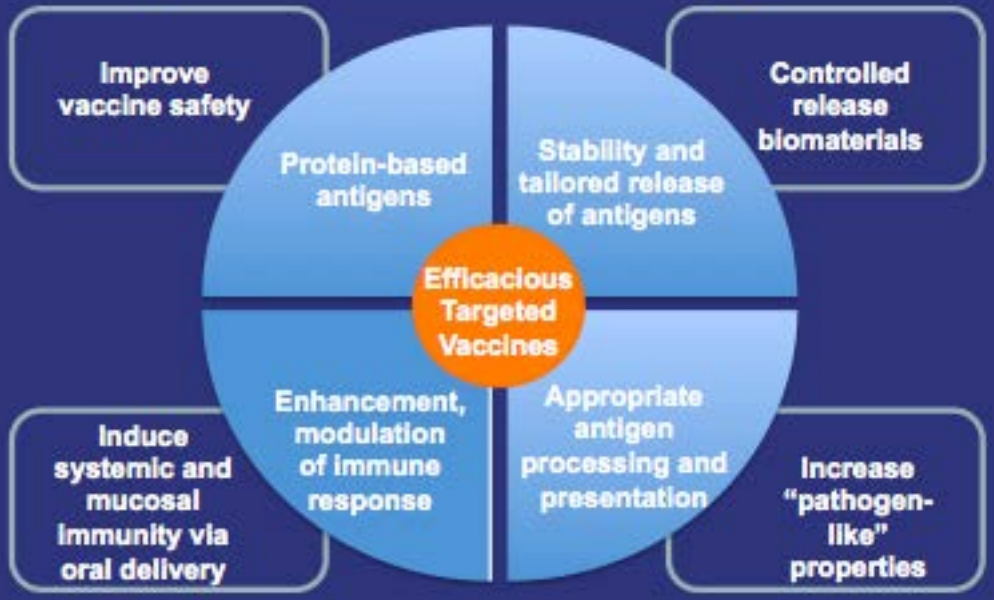
II. Intracellular Delivery

Polycationic nanogels facilitate cellular uptake, siRNA release, and endosomal escape into the cell cytosol.

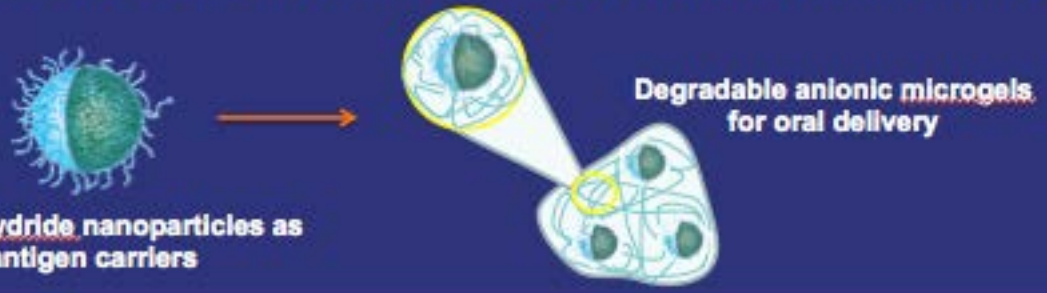


Right: Nanogels (green) internalized by RAW 264.7 cells.

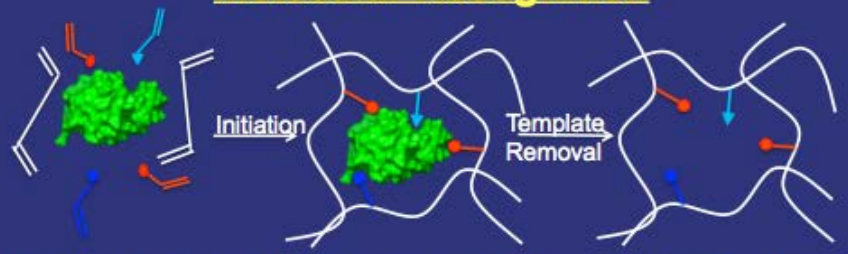
Oral Vaccine Delivery



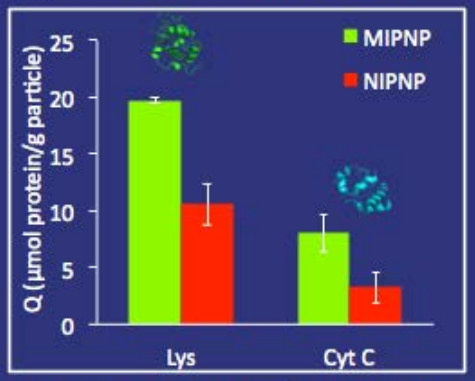
Proposed Solution: Dual system for targeted oral vaccine delivery



Molecular Recognition

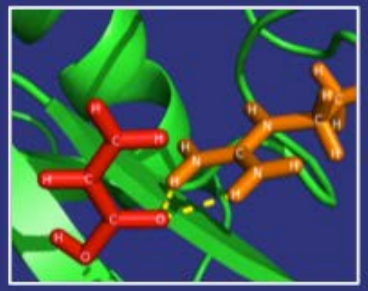


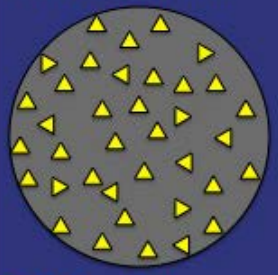
Functional monomers are polymerized in the presence of a biomolecule of interest. Following purification, these polymers have recognitive moieties. Applications include *low cost biosensors and drug delivery systems*.

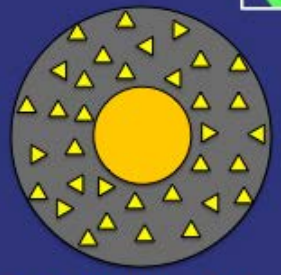


Imprinted particles preferentially bind template proteins

Specificity is achieved through numerous non-covalent interactions between templates and functional monomers



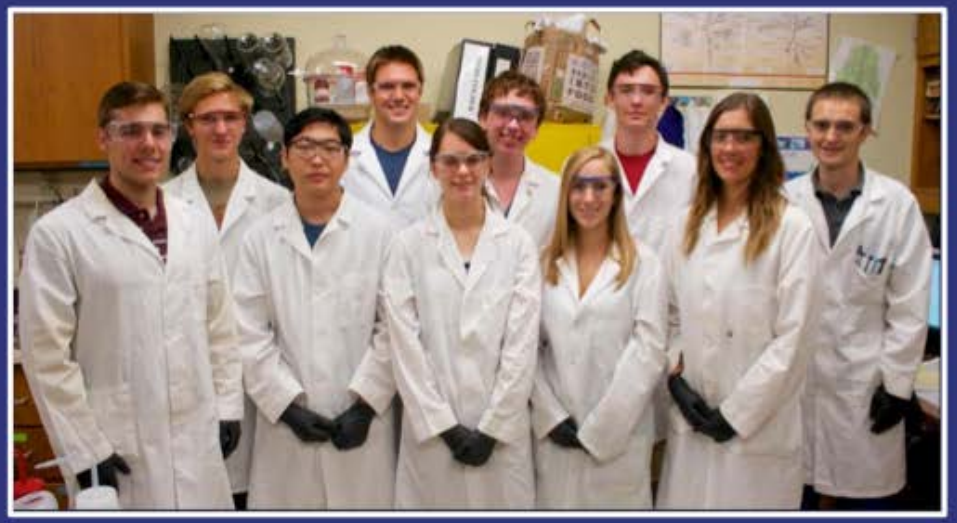




Bulk Imprinting:
Small molecules for SMART drug delivery

Core-Shell Imprinting:
Proteins for diagnostic applications

Surface Imprinting:
Cells for applications in regenerative medicine



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Chairman of Biomedical Engineering, Cockrell Family Regents Chair in Engineering #6
and Cockrell Family Chair for Departmental Leadership #1

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