Purdue University | Weldon School of Biomedical Engineering
The Convergence of Differences, The Future of Excellence

BME 695N

Engineering Nanomedical Systems

Lecture 2

"Basic concepts of nanomedicine"

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Features of Nanomedicine

Beyond the obvious application of nanotechnology to medicine, the approach is fundamentally different:

- Nanomedicine is a “nano-” approach NOT just due to the nano size. It is the nanotechnology “bottoms-up” rather than “tops-down” approach to medicine.
- Nanomedicine uses “nano-tools” (e.g. smart nanoparticles) that are roughly 1000 times smaller than a cell (knives to microsurgery to nanosurgery …)
- Nanomedicine is the treatment or repair (regenerative medicine, not just killing of diseased cells) of tissues and organs, WITHIN individually targeted cells, cell-by-cell.
- Nanomedicine typically combines use of molecular biosensors to provide for feedback control of treatment and repair. Drug use is targeted and adjusted appropriately for individual cell treatment at the proper dose for each cell (single cell medicine).

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Some Elements of Good Engineering Design Applicable to the Design of Nanomedical Systems

Principle 1: Whenever possible, use a general design that has already been tested.

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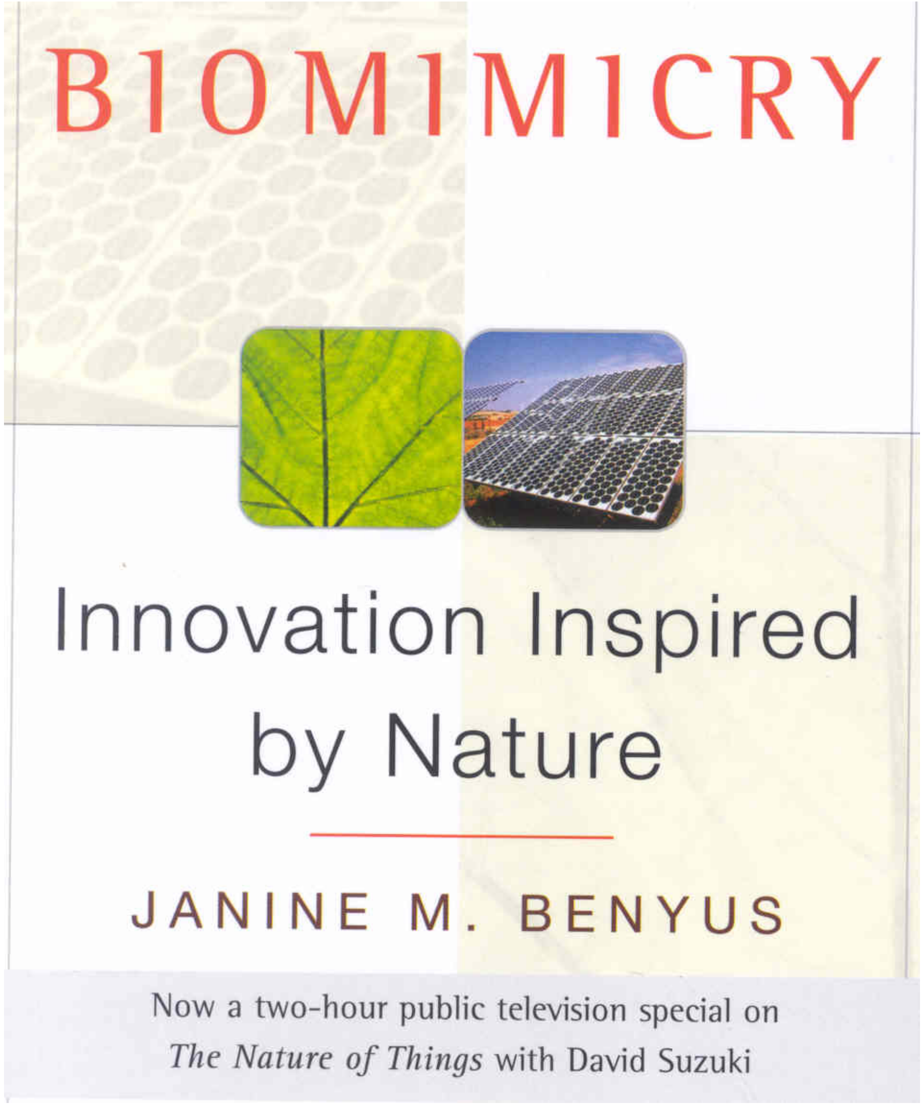
Biomimicry – Can Nature Provide Some of the Answers?



From the Greek “bios” = life and “mimesis” = imitation…

“Biomimicry (or Biomimetics) is a new science that studies nature’s models and then imitates or takes inspiration from these designs and processes to solve human problems.”

[from the preface of Biomimicry]

Nature has already solved similar problems with “Nature’s nanoparticle”, the virus. We are making artificial, non-biological viruses in the form of nano-machines but with some capabilities and features not present in biological viruses.

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A design tested by Mother nature…

One good biomimetic design that has been well tested is that of a virus. But in the case of a nanomedical device we construct a non-replicating, artificial virus made of well-defined molecular components that we can manufacture in a reproducible manner suitable for human in-vivo use.

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Some Elements of Good Engineering Design Applicable to the Design of Nanomedical Systems

Principle 2: Something that is a good general purpose design means that it is not particularly good for any particular function.

Use collections of specific designs to do each specific function well.

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A nanomedical device must do several functions well, so it must contain specific molecules that do well:

1. Cell targeting
2. Cell entry
3. Intracellular targeting
4. Controlled drug delivery

It is possible, but rare, for a single molecule to do two or even more functions. For example, we are currently using a single peptide sequence which does pretty good cell targeting, cell entry, and intracellular targeting to the nucleus of that cell.

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Some Elements of Good Engineering Design Applicable to the Design of Nanomedical Systems

Principle 3: By controlling the order of molecular assembly one can control the order of those specific molecular functions, leading to a "programmable" nanodevice.

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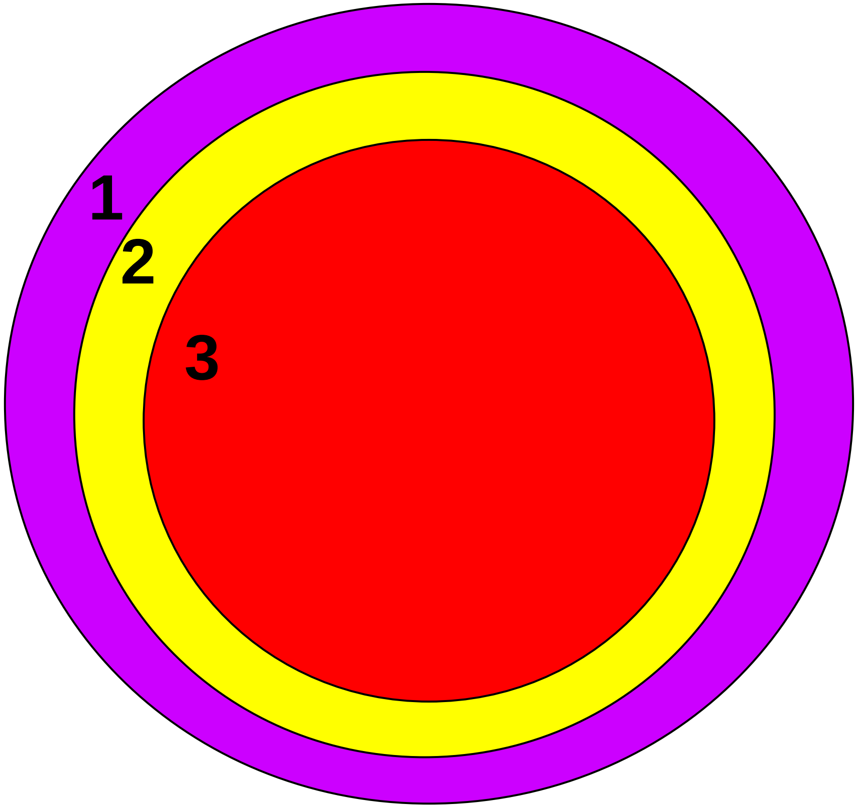

Whereby Step 1 must occur before Step 2 can happen, and Step 3 will not happen unless it is preceded by Steps 1 and 2

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“The first shall be last, and the last shall be first…”

Consequently we construct a multi-component nanomedical system in reverse order of controlling events, namely from the inside out. The outer components are the first to be used. The inner components are the last.

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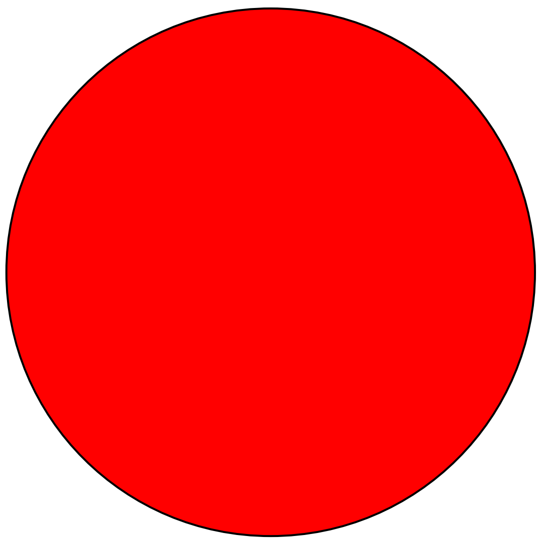
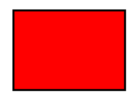
Basic Design – Building a Nanodevice

Step 1: Choice of Core Materials





Commonly used core materials include: gold, ferric oxide, silica, Qdots,

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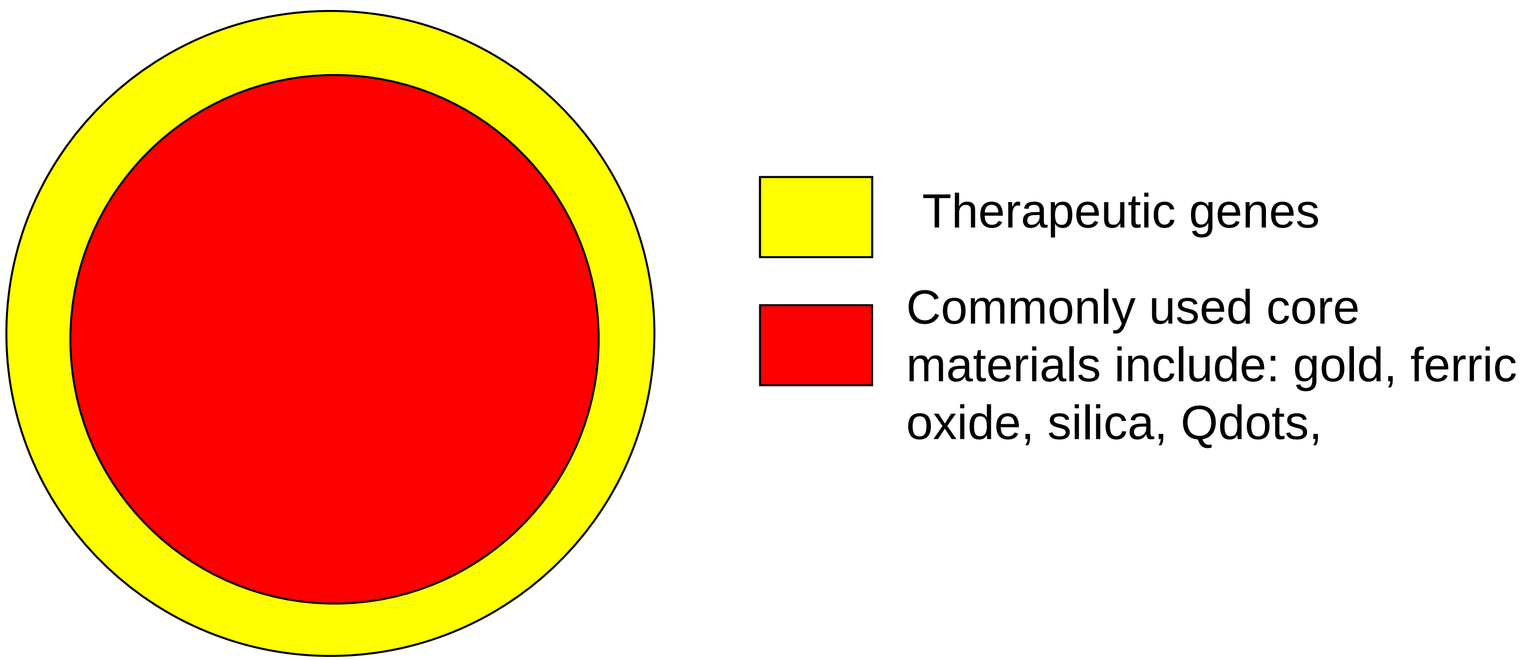
Basic Design – Building a Nanodevice

Step 2: Add drug or therapeutic gene



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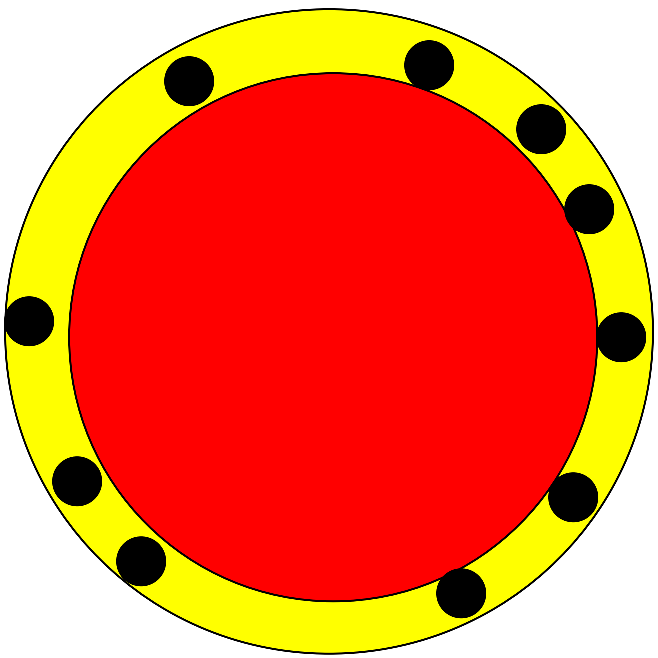
Basic Design – Building a Nanodevice

Step 3: Add Molecular Biosensors



Therapeutic genes

Commonly used core materials include: gold, ferric oxide, silica, Qdots,

Biomolecular sensors (for error-checking and/or gene switch)

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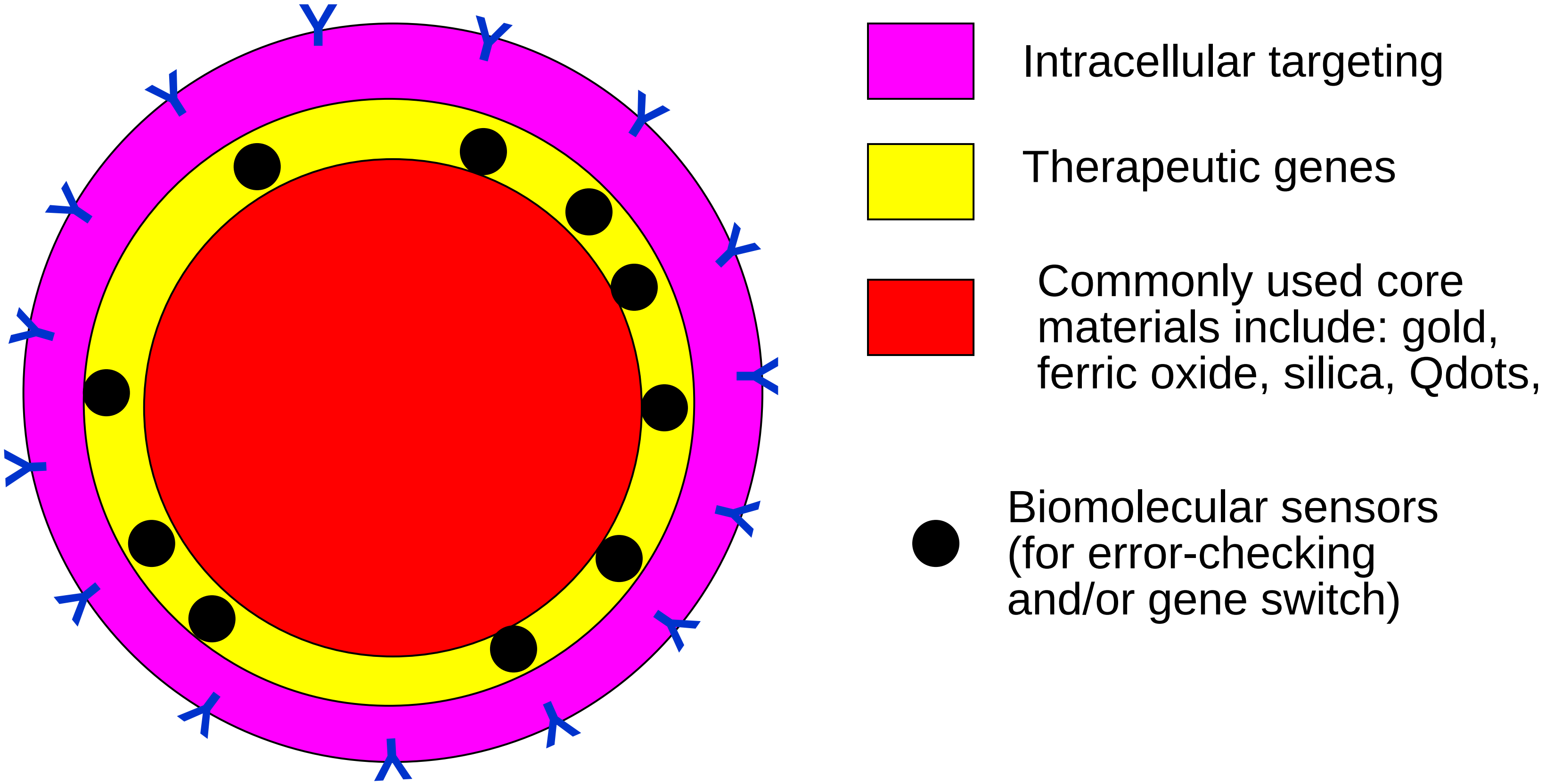
Basic Design – Building a Nanodevice

Step 4: Add Intracellular targeting molecules



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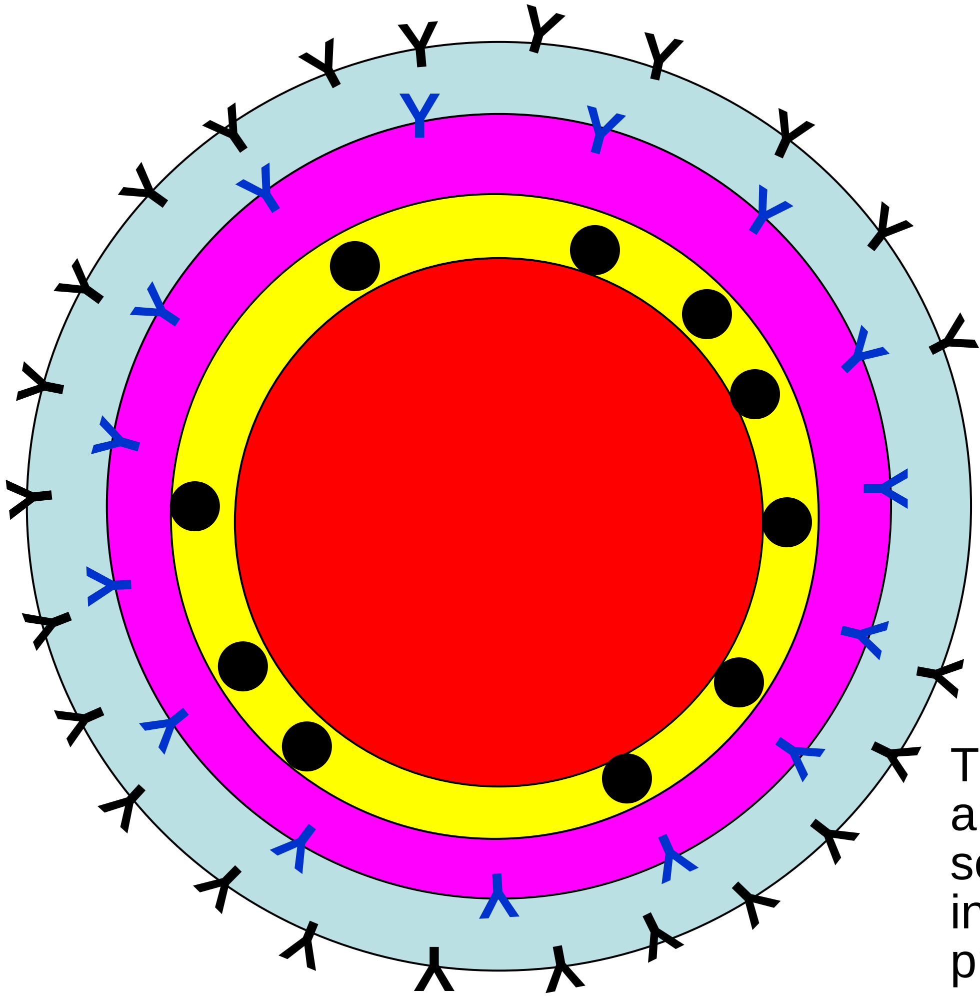
Result: A Multi-component, Multi-functional “Programmable” Nanodevice or Nanosystem



Cell targeting and entry

Intracellular targeting

Therapeutic genes

Commonly used core materials include: gold, ferric oxide, silica, Qdots,

Biomolecular sensors (for error-checking and/or gene switch)

Targeting molecules (e.g. an antibody, an DNA, RNA or peptide sequence, a ligand, a thioaptamer), in proper combinations for more precise nanoparticle delivery

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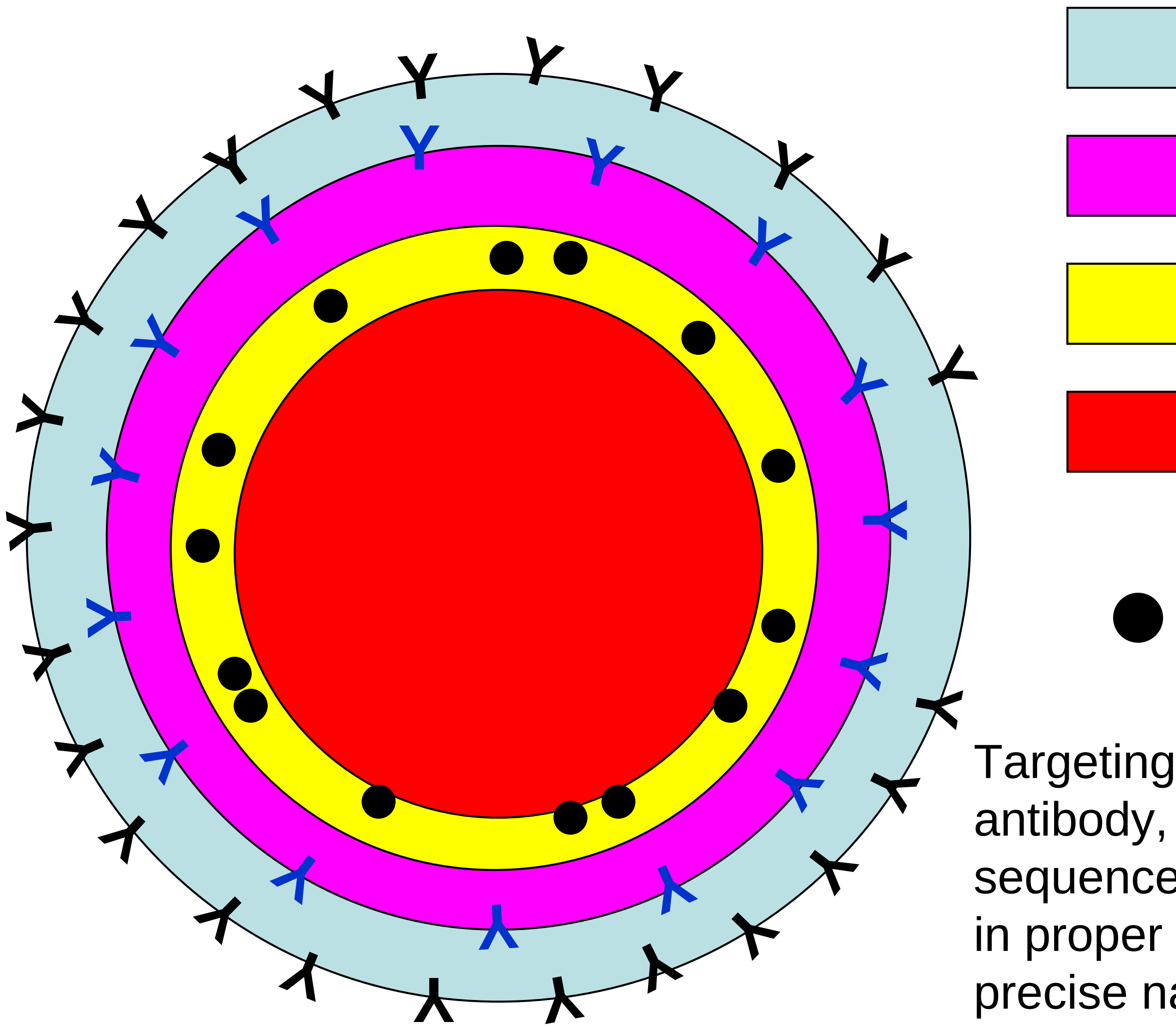
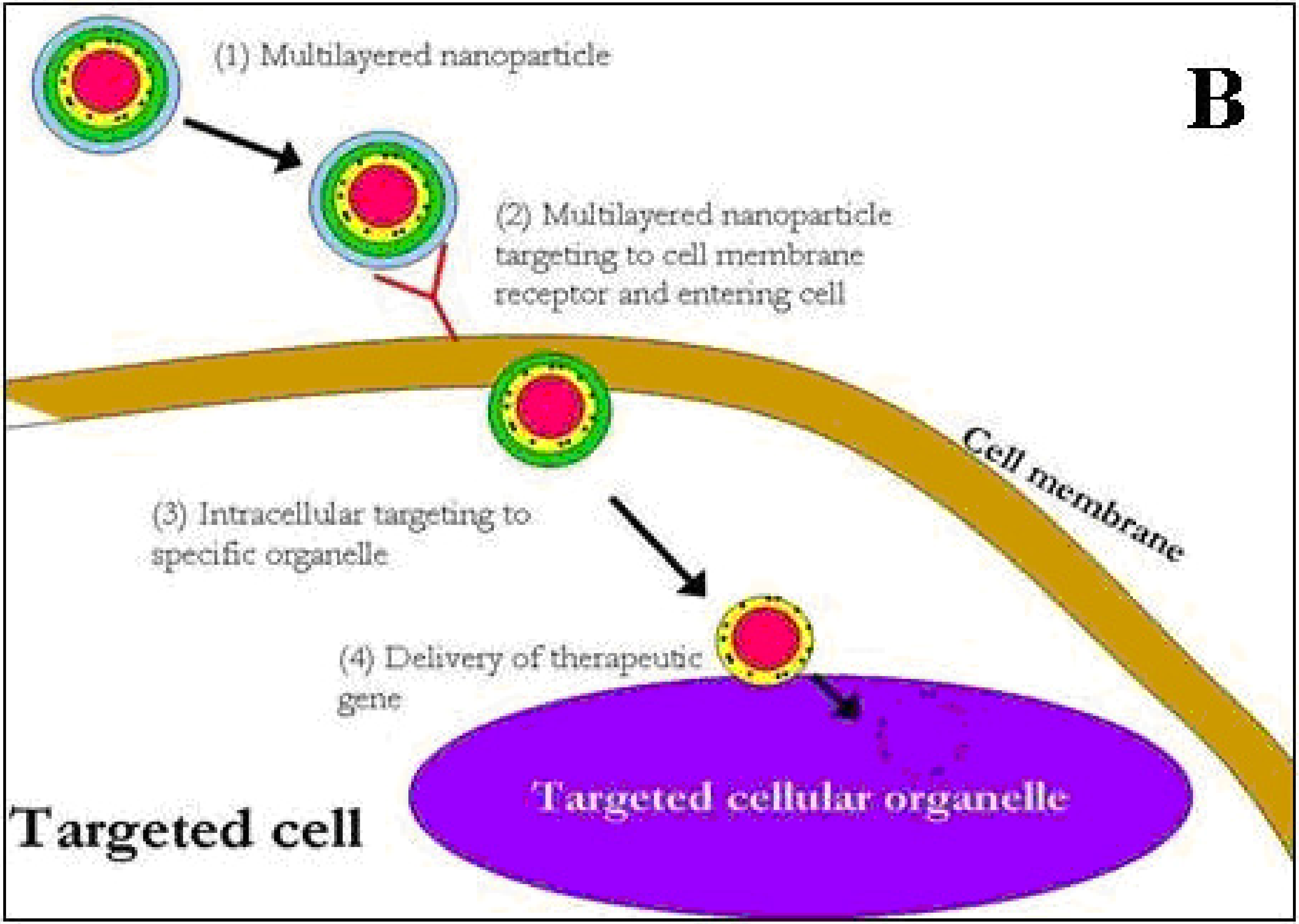
To use, de-layer nanoparticle one layer at a time



Leary and Prow, PCT (USA and Europe) Patent pending 2005

The Multi-Step Drug/Gene Delivery Process in Nanomedical Systems



The Challenge: Optimal Drug Delivery to the Right Cells without the "Side Effects"

A very tough problem that has been grossly underestimated by most research groups!

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One Solution to the Problem of Targeted Drug Delivery

“Nanofactories”

Don’t try to guess the proper amount of drug for each cell. Manufacture it to the needs of that specific cell. With upstream biomolecular switches and feedback control, it doesn’t matter how many nanoparticles are able to successfully target to a rare cell in-vivo. The total output of therapeutic genes from all targeted nanoparticles will self regulate to the proper dose for that cell.

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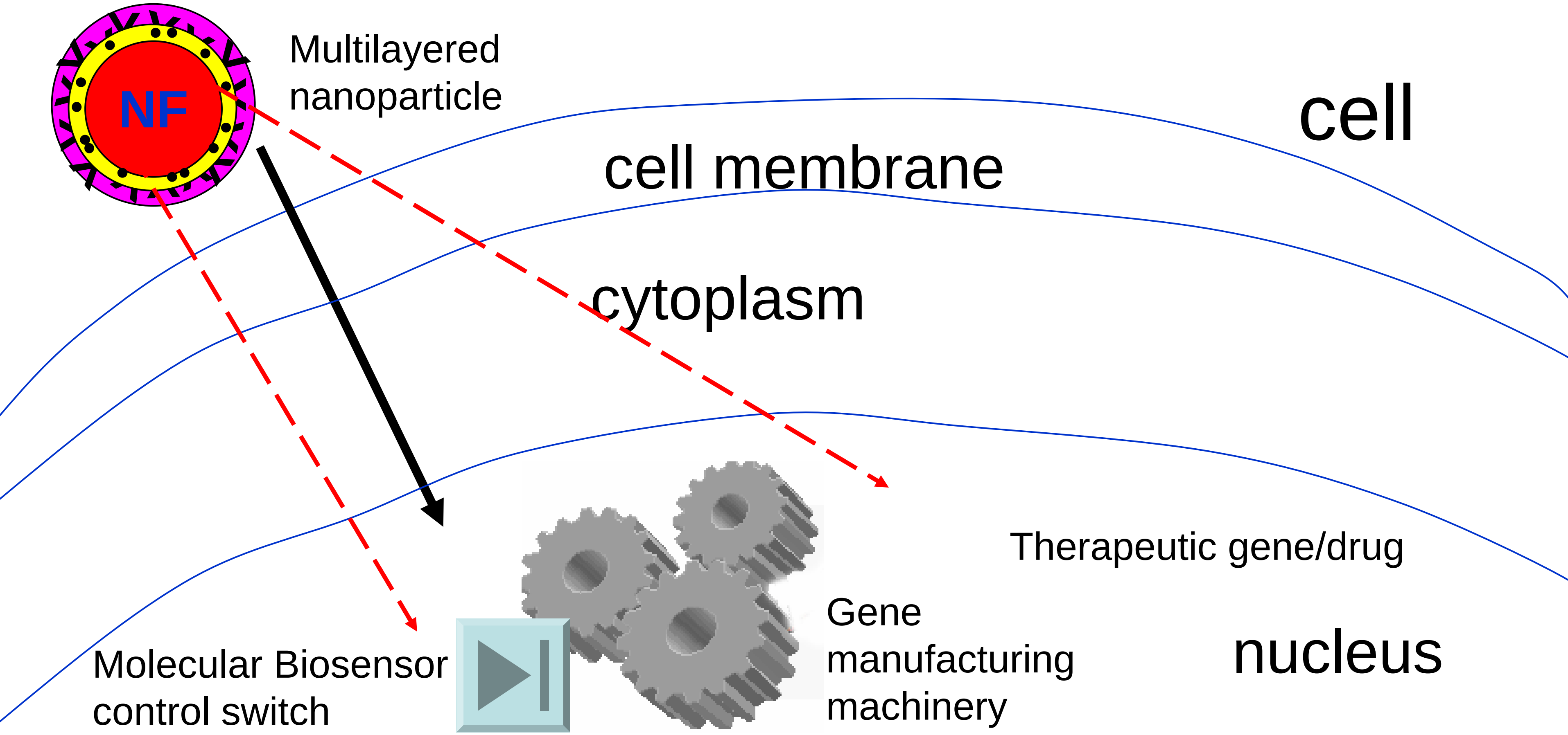
Concept of nanoparticle-based "nanofactories" (NF) manufacturing therapeutic genes inside living cells for single cell treatments



The nanoparticle delivery system delivers the therapeutic gene template which uses the host cell machinery and local materials to manufacture therapeutic gene sequences that are expressed under biosensor-controlled delivery.

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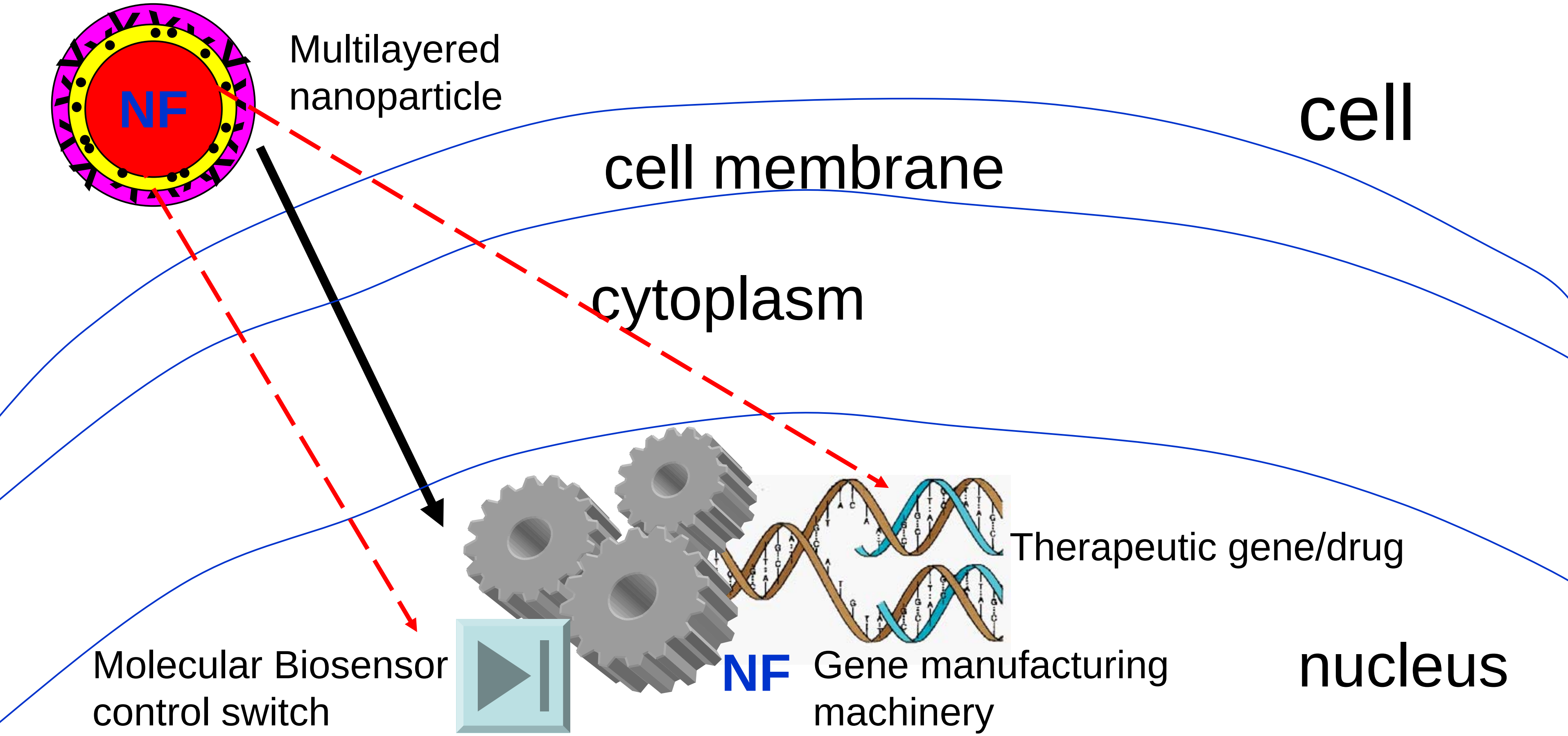

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References

Prow, T.W., Rose, W.A., Wang, N., Reece, L.M., Lvov, Y., Leary, J.F. "Biosensor-Controlled Gene Therapy/Drug Delivery with Nanoparticles for Nanomedicine" Proc. of SPIE 5692: 199 – 208, 2005.

Overview of Readings