The Intersection of Bio and Nano Technologies

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Outline

A. Introduction

(i) Nanotechnology
(ii) Biotechnology
(iii) Nano/Bio Technology Goals

B. Applications of Bio/Nano Technologies[1]

(i) Materials
> Biomimetics
(ii) Electronics/Computers
(iii) Medical

C. Investment in Bio/Nano

D. Summary

E. Classified

[1]http://www.rand.org/publications/MR/MR1307/MR1307.pdf,

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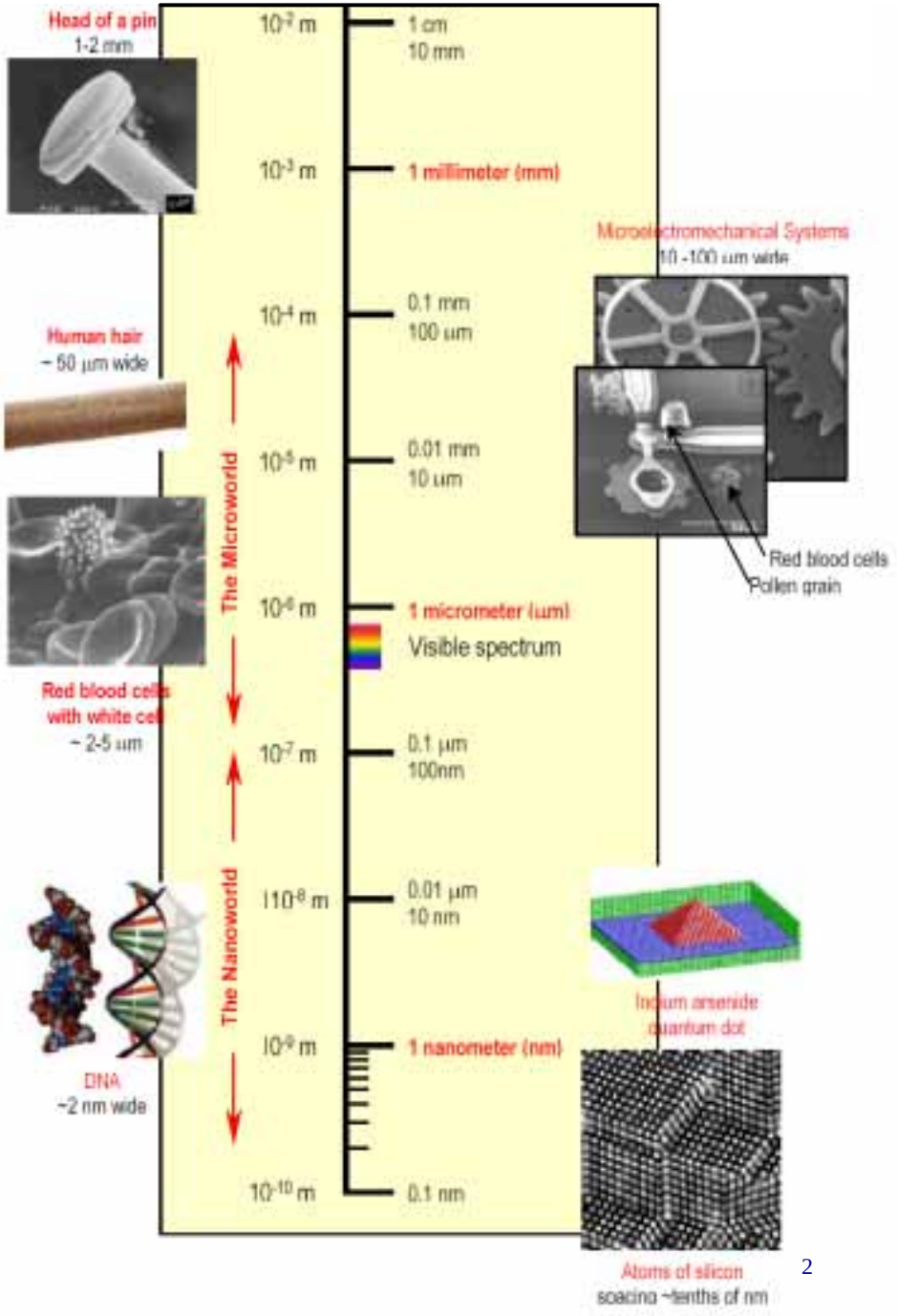
INTRODUCTION: (i) Nanotechnology

Nanotechnology wants to produce nanoscale machines/ components and manufacture at the nanoscale using bottom-up approaches (molecule by molecule)[1].



[1]http://www.cientifica.com/html/docs/NOR_White_Paper.pdf

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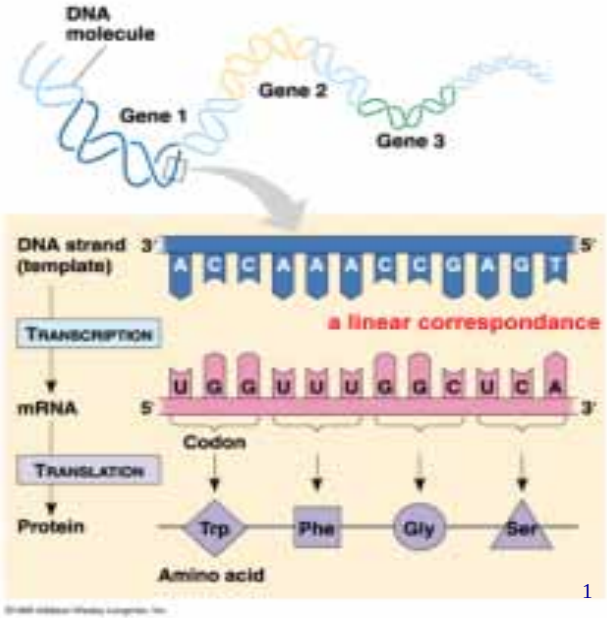
INTRODUCTION (ii) Biotechnology

Cells are ideal "nano factories" and contain enzyme "nano machines".

2



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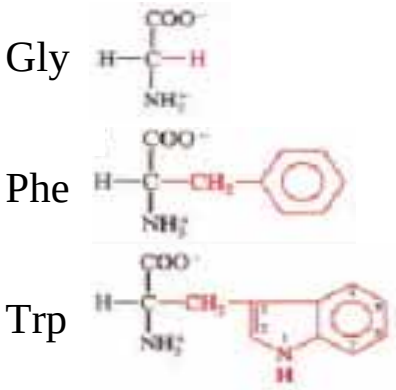

[1]http://fig.cox.miami.edu/~cmallery/150/gene/mol_gen.htm

[2]http://bioch.szote.u-szeged.hu/astrojan/protein2.htm

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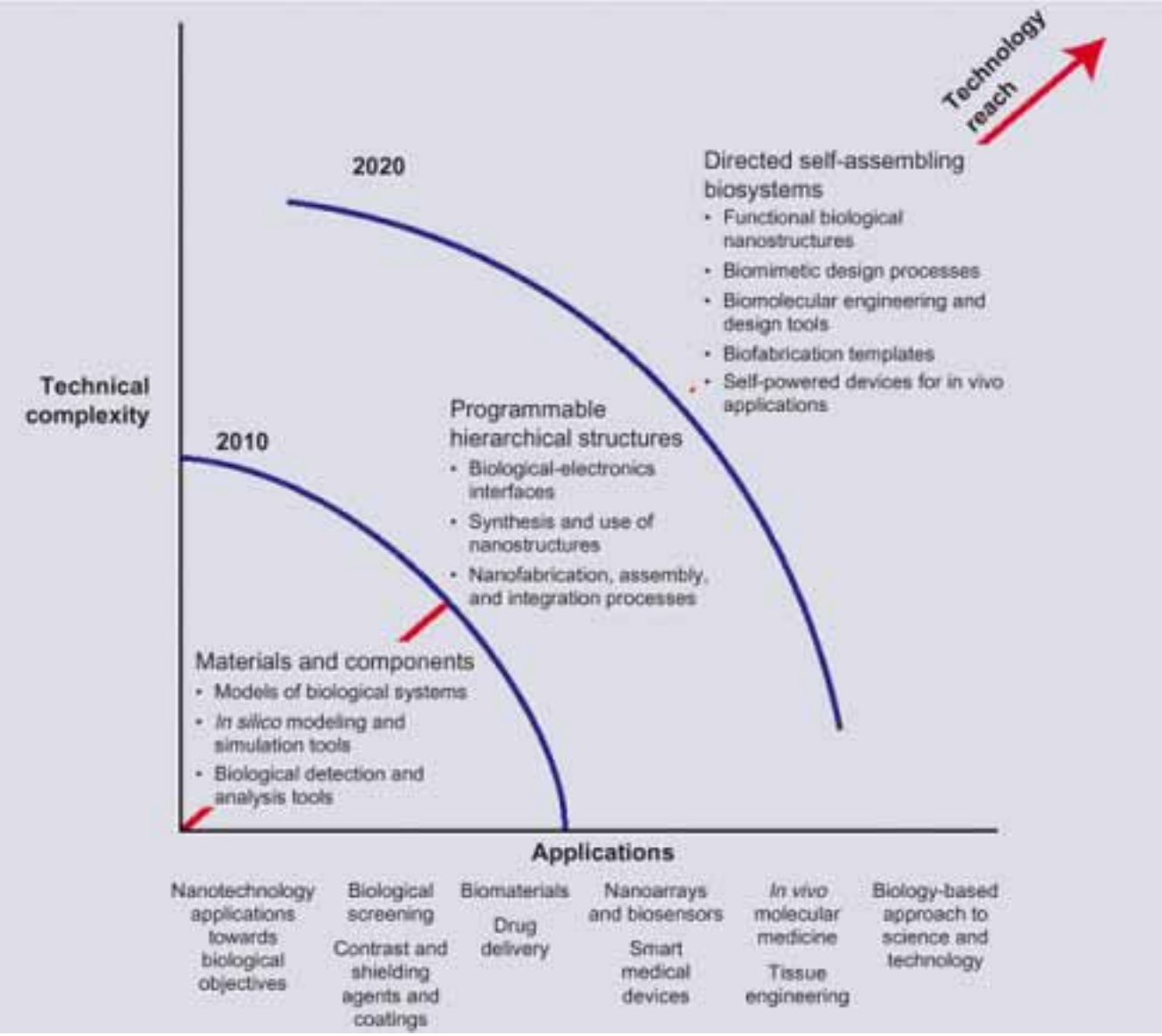
INTRODUCTION (iii) Nano/Bio Goals

Do not believe everything you read!!



Mazzola, L. *Nature Biotechnology*, **21** (2003) pp.1137-1143.

B. Applications of Bio/Nano Technologies

Traditional Materials

- building materials (hard)
- clothing/tents etc. (soft)
- synthetic bone/artificial tissues/organs
  - > enhance strength
  - > reduce weight
  - > increase chemical/heat resistance
  - > alter surface properties

(i) Biomimetics

- study of nature – spider silk, nacre "mother of pearl" is a composite of minerals and organic macromolecules (proteins, lipids, and polysaccharides)
  - often properties of bio materials are superior to human-made materials (if they exist)

[1]Opportunities in Biotechnology for Future Army Applications (2001) Board on Army Science and Technology (http://books.nap.edu/books/0309075556/html/R1.html#pagetop)

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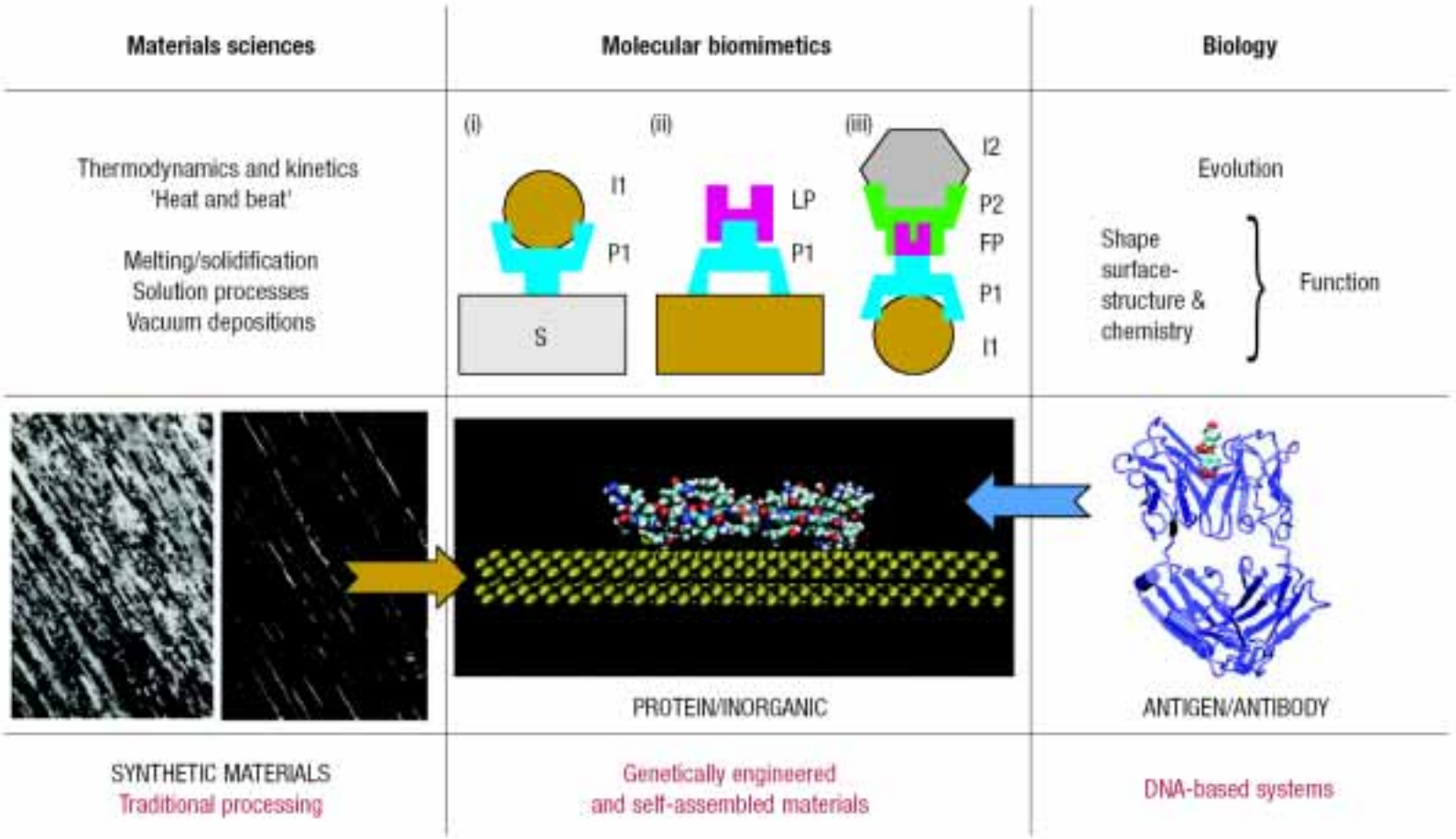
APPLICATIONS (i) Biomimetics: Theory



Sarikaya, M. *et al.*, *Nature Materials*, **2** (2003) pp.577-585.

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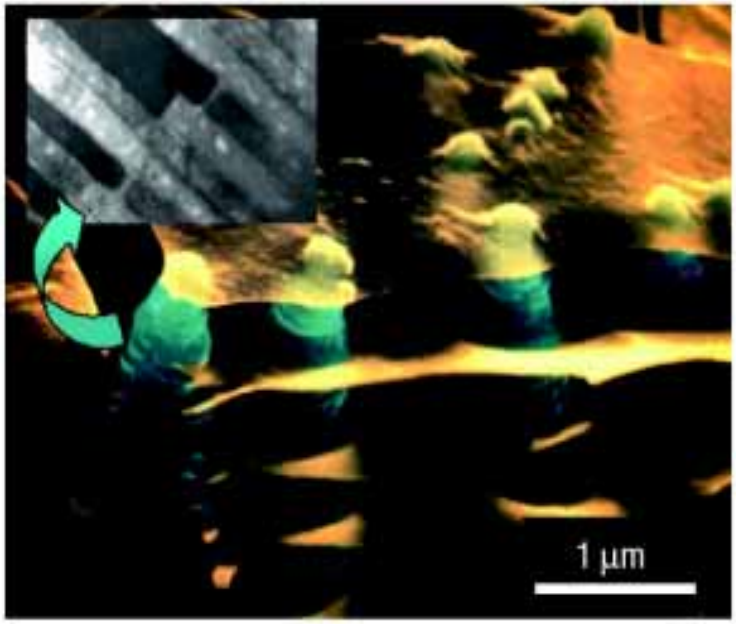
APPLICATIONS (i) Biomimetics:Nacre



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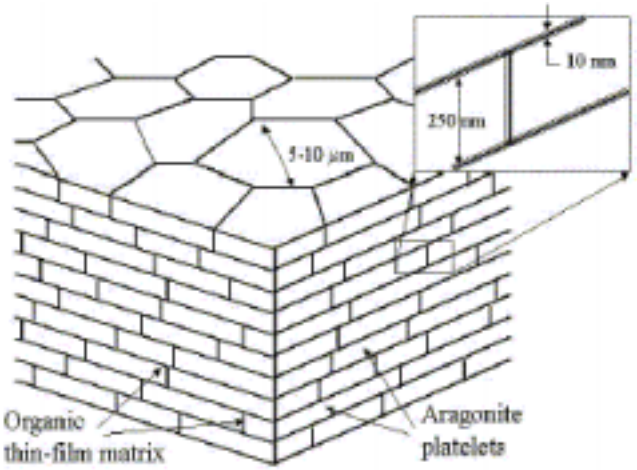

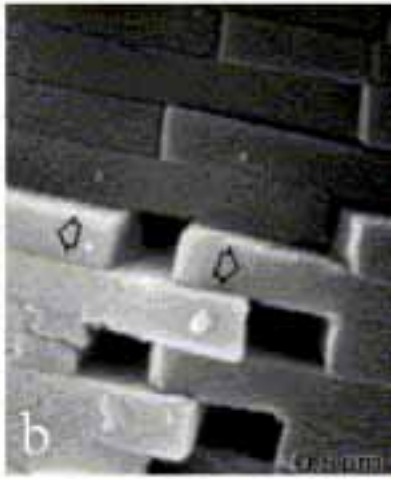

[1]Sarikaya, M. *et al.*, *Nature Materials*, **2** (2003) pp.577-585.

[2]http://www.civil.columbia.edu/em2002/proceedings/papers/595.pdf

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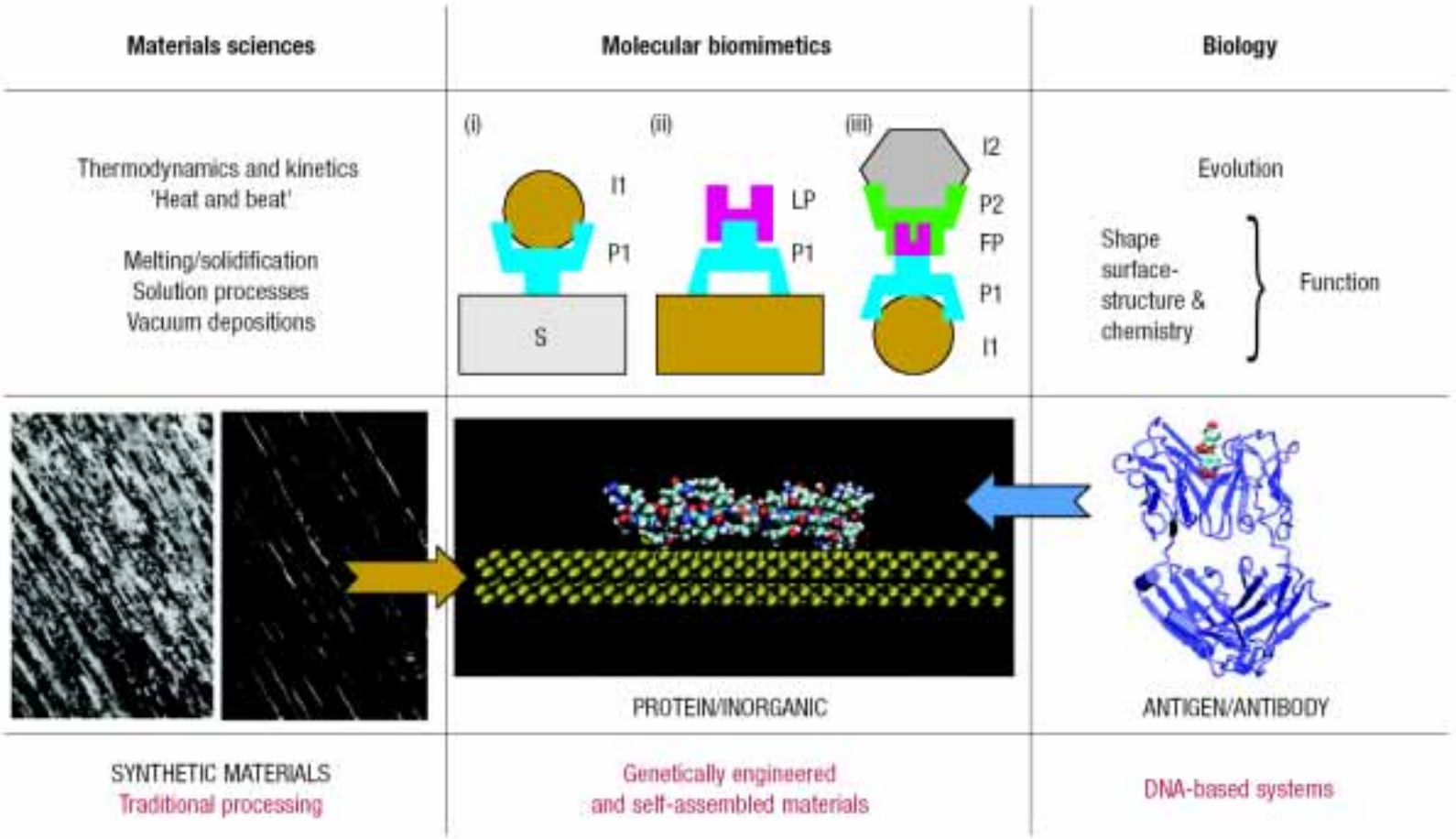
APPLICATIONS (i) Biomimetics: Theory



Sarikaya, M. *et al.*, *Nature Materials*, **2** (2003) pp.577-585.

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APPLICATIONS (i) Biomimetics: Potential Uses[1]

1) Novel ceramics/biocomposites

- personal armour
- munitions
- machine parts

2) Novel biopolymers

- electrical devices (sensors, optoelectronic devices)
- scaffold for organizing nanocrystals
- coatings and novel "wet" adhesives on surfaces
- fibrils related to prions in BSE, new variant Creutzfeld-Jakob

3) Energy generation/use/storage

- novel catalysts to refine fuel
- fuel cells (storage of hydrogen in nanotubes)
- "bacterial" batteries

[1]Opportunities in Biotechnology for Future Army Applications (2001) Board on Army Science and Technology (http://books.nap.edu/books/0309075556/html/R1.html#pagetop)

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APPLICATIONS (ii) Electronics/Computers[1]

Electronics

- top-down approaches to chip manufacturing (photolithography) are expected to approach insurmountable size barriers (limited by wavelength of light)
- bottom-up approaches using self-assembly properties of DNA/proteins
  - > DNA to create nano arrays
  - > DNA to space molecules (carbon nanotubes)
  - > DNA for nano scale movement

Computers

- DNA as a computational device
  - protein-based storage devices (bacteriorhodopsin)

[1]Opportunities in Biotechnology for Future Army Applications (2001) Board on Army Science and Technology (http://books.nap.edu/books/0309075556/html/R1.html#pagetop)

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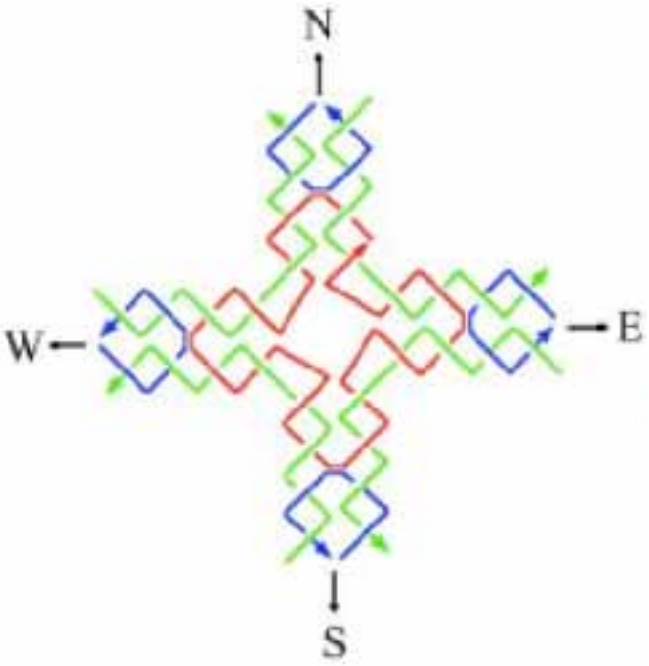
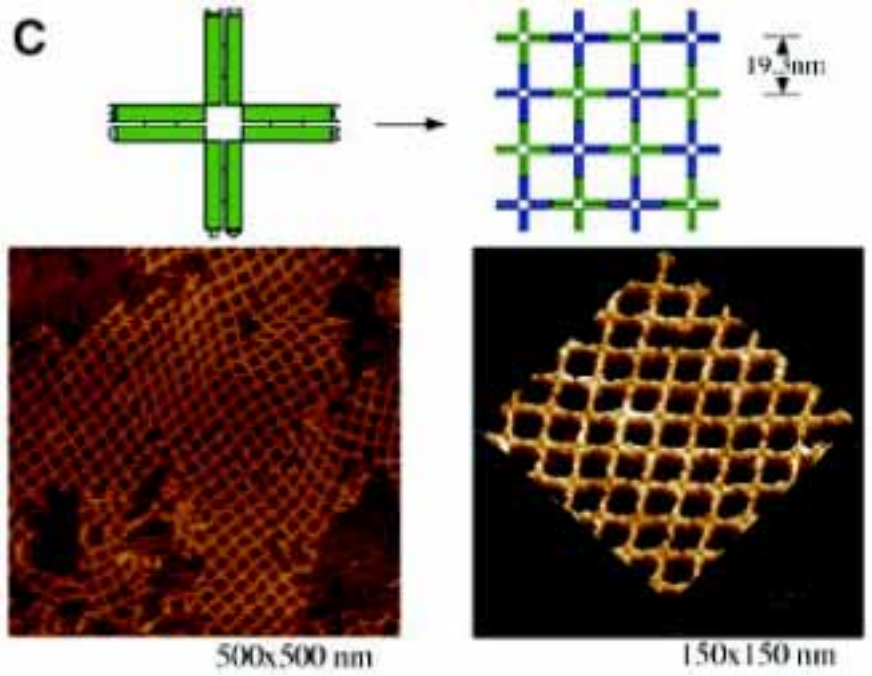
APPLICATIONS (ii) Electronics: Grids





Yan, H. *et al*., *Science*, **301** (2003) pp.1882-1884.

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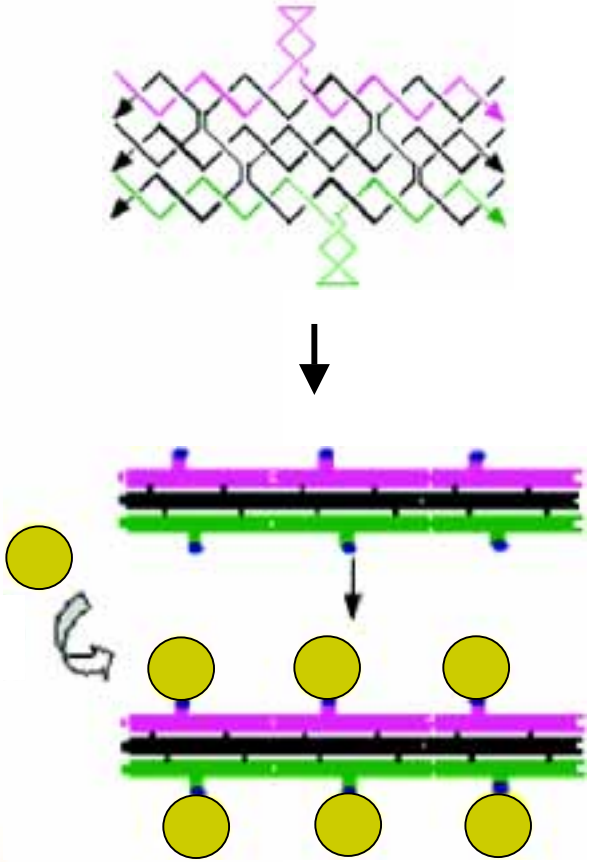
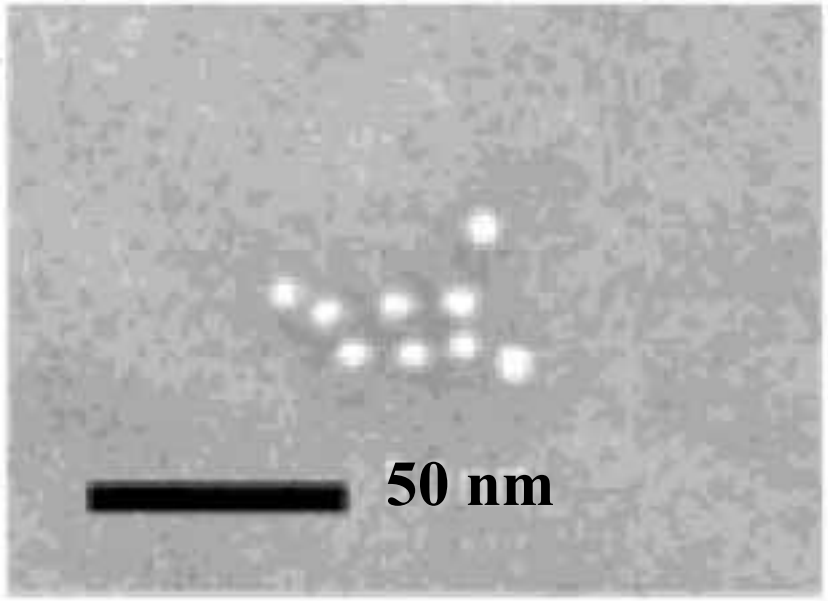
APPLICATIONS (ii) Electronics: Nanometre Scale Spacing





Li, H. *et al*., *J.Am.Chem.Soc*., **126** (2004) pp.418-419.

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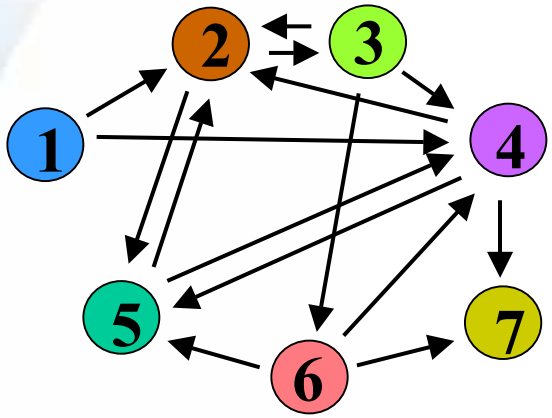
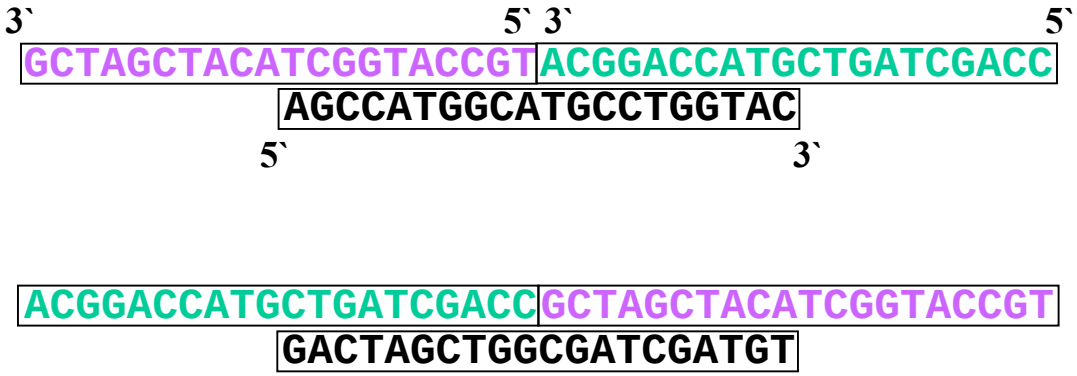
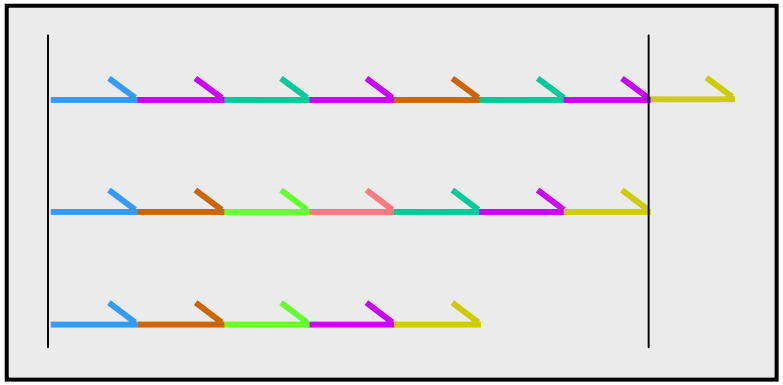
APPLICATIONS (ii) Electronics: DNA Computers[1]







Adelman's group recently solved 20-Variable 3-satisfiablity problem on a DNA Computer (over 1 million possible solutions)[2]

[1]Adelman, L.M. *Science* **266** (1994) pp.1021-1024.

[2]http://www.usc.edu/dept/molecular-science/SAT20.pdf

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APPLICATIONS (ii) Electronics: Potential Uses

1) Electronic components (potential to leap-frog current technologies)

- cheaper, lighter, faster
  - > computers
  - > guidance systems
  - > satellites
  - > photography
  - > lasers
  - > nanoscale sensors (bacteria/viruses)
- traditional computer industry is fighting back
  - > sub 100 nm spacing

2) Computing/Storage

- parallel DNA computing
  - > code breaking
  - > flight paths
- information storage
  - > bacteriorhodopsin
  - > DNA

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APPLICATIONS (iii) Medicine

Fighting Disease

- Drug Development
  - > combinatorial chemistry
  - > DNA/Protein arrays
  - > drug delivery/targeting systems
- Gene replacement
  - > cloning
  - > gene delivery/targeting systems
- Disease recognition
  - > bio machines to monitor/deliver medicines
  - > lab-on-a-chip
- Organ healing/transplants
  - > synthetic tissues/matrices
  - > synthetic bone

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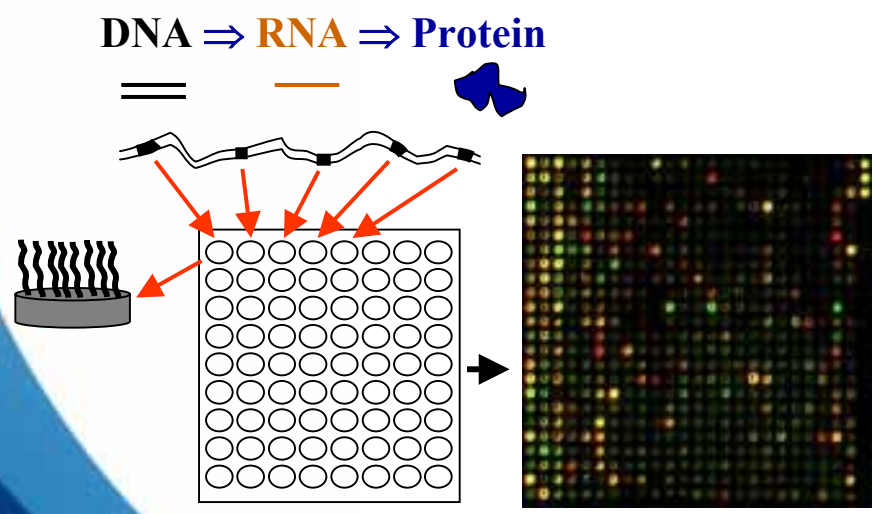
APPLICATIONS (iii) Medicine: Drug Development[1]

Combinatorial Chemistry

- combinatorial chemistry and screen for activity using ultra-high-throughput screening
  - > 100,000 compounds/day
  - > 50,000 toxic chemicals/year

DNA/Protein Arrays

- sequencing of genome and DNA arrays allow for the identification of cell-specific gene expression pattern for ALL genes



Identify targets in *specific* cell types - weapons?
> skeletal muscles (movement)
> smooth muscles (involuntary contractions)
> cardiac muscles (heart)

[1]Wheelis, M., *Biotechnology and Biochemical Weapons*, The Nonproliferation Review/Spring, 2002

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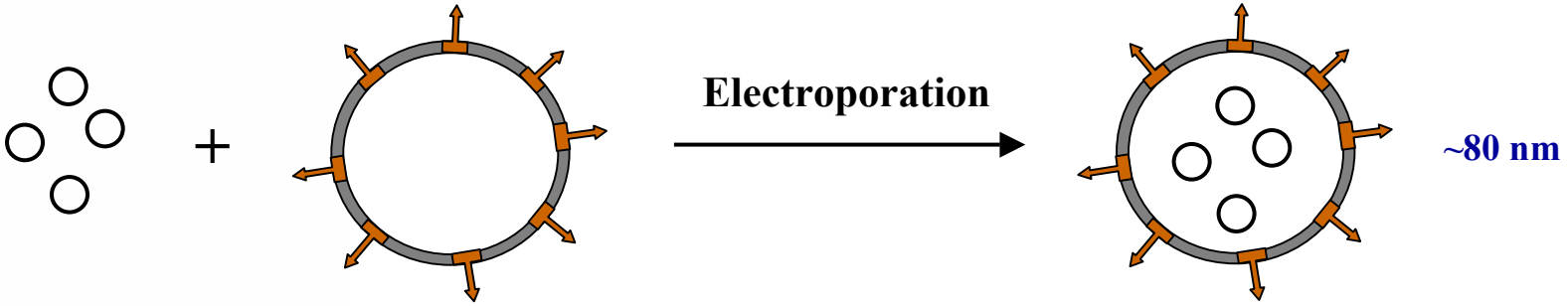
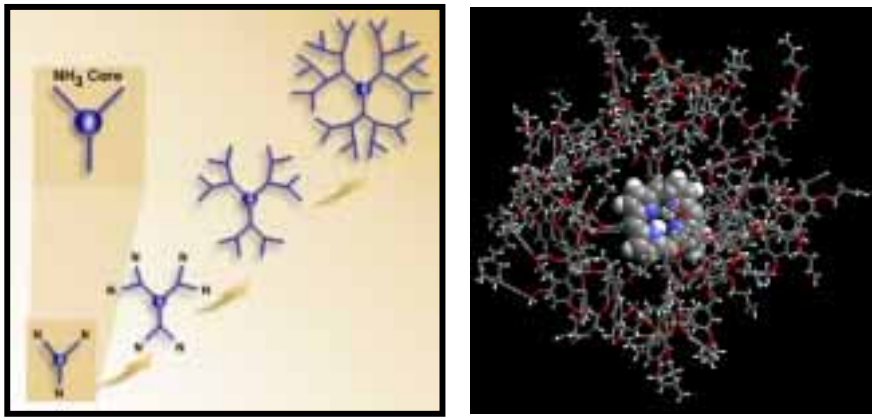
APPLICATIONS (iii) Medicine: Drug Delivery

Yeast-Derived Nanoparticles[1]



Dendrimers



[1]Yamada, T., *et al.*, *Nature Biotechnology* **21** (2003) pp.885-890.

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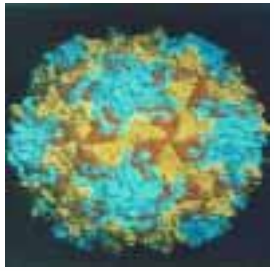
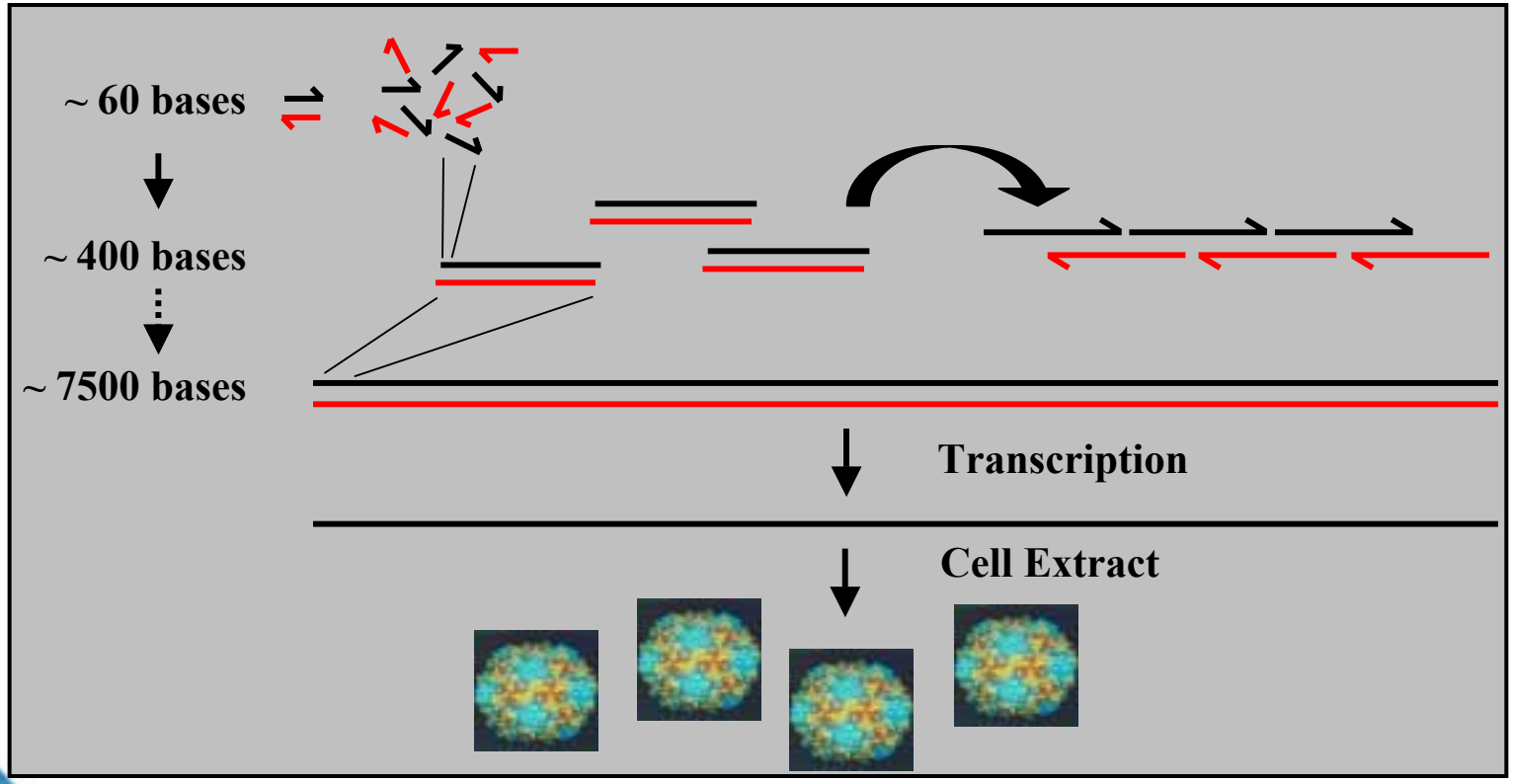
APPLICATIONS (iii) Medicine: Cloning - Polio



> small, non-enveloped, one copy of + sense, single-stranded RNA genome of 7.5 kilobases (small)
> sequence available at NCBI website (http://www.ncbi.nlm.nih.gov/genomes/VIRUSES/viruses.html)



Cello, J., Paul, A.V. and Wimmer, E. (2002) *Science* **297,** pp.1016-1018.

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APPLICATIONS (iii) Medicine: Polio DNA

1 ttaaaacagc tctgggggttg tacccacccc agaggcccac gtggcggcta gtactccggt 61 attgcggtac ccttgtacgc ctgttttata ctcccttccc gtaacttaga cgcacaaaac 121 caagttcaat agaaggggct acaaaccagt accaccacga acaagcactt ctgtttcccc 181 ggtgatgtcg tatagactgc ttgcgtggtt gaaagcgacg gatccgttat ccgcttatgt 241 acttcgagaa gcccagtacc acctcggaat cttcgatgcg ttgcgctcag cactcaaccc 301 cagagtgtag cttaggctga tgagtctgga catcctctac cggtgacggt ggtccaggct 361 gcgttggcgg cctacctatg gctaacgcca tgggacgcta gttgtgaaca aggtgtgaag 421 agcctattga gctacataag aatcctccgg cccctgaatg cggctaatcc caacctcgga 481 gcaggtggtc acaaaccagt gattggcctg tcgtaacgcg caagtccgtg gcggaaccga 541 ctactttggg tgtccgtgtt tccttttatt ttattgtggc tgcttatggt gacaatcaca 601 gattgttatc ataaagcgaa ttggattggc catccggtga aagtgagact cattatctat 661 ctgtttgctg gatccgctcc attgagtgtg tttactctaa gtacaatttc aacagttatt 721 tcaatcagac aattgtatca taatgggtgc tcaggtttca tcacagaaag tgggcgcaca 781 tgaaaactca aatagagcgt atggtggttc taccattaat tacaccacca ttaattatta 841 tagagattca 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APPLICATIONS (iii) Medicine: Cloning - Polio

- production of poliovirus required 3 years/$300,000 funding from Defense Advanced Research Projects Agency (DARPA)

- currently 1734 reference viral sequences at NCBI
  - > Variola virus (smallpox) 185,578
  - > Marburg Virus 19,112
  - > Ebola Virus 18,959

- problems if virus requires viral proteins for replication (smallpox/Marburg/Ebola require viral proteins for viral genome replication) but with DNA sequence can make protein(s)

- Venter's group synthesized φX174 bacteriophage (5,386 base pairs) using overlapping oligos in 2 weeks[1]

[1]Smith, H.O., *et al.*, (2003) *PNAS* **100**, pp.15440-15445

APPLICATIONS (iii) Medicine: Possible Uses

1) Drug discovery
- new toxic drugs (combinatorial chemistry)
- new drug targets (genomics, DNA arrays)

2) Drug delivery
- viral vectors
- dendrimers, liposomes

3) Gene replacement (cloning)
- manufacture existing microbes (polio)
- manufacture novel microbes (Venter)
- alter existing microbes (antibiotic/vaccine resistant, antimaterials, evade immune system etc.)

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INVESTMENT (i) Country Spending

Table 2 Global government funding in nanotechnology [1]

Country	Funding level ($ million/year unless indicated otherwise)
Japan	$810 (2003)
US	$774 (2003)
European Union	$1.2 billion/4 years
Germany	$118 (2003)
United Kingdom	$90 (2003)
France	$50 (2003)
Australia	$93 (2003)
Korea	$1.2 billion/10 years
Taiwan	$110/6 years
China	$280
Switzerland	$45/3 years
Canada	$80/5 years
India	$15/3 years

Canadian Investment

1) National Institute of Nanotechnology
   > located at the University of Alberta (2005)

2) Also numerous labs within National Research Council and Department of National Defence[2]
   > The Institute for National Measurement Standards (INMS)
   > Materials and Component Technologies at the Institute for Microstructureal Sciences (IMS)
   > Polymer Nanocomposites at the Industrial Materials Institute (IMI)

[1]DeFrancesco, F. *Nature Biotechnology*, **21** (2003) pp.1127-1129

[2]http://www.nrc-cnrc.gc.ca/nanotech/projects_e.html

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Summary

Bio/Nano Technologies (Disruptive)

1) Medicine

- drug delivery
- cloning

2) Electronics/Nanoscale Fabrication

- potential for huge impact – current knowledge/needs will drive market

3) Materials

- high potential for nanomaterials, but time required for impact of bio

4) Computers

- immediate potential limited for DNA computers
- potential for information storage (bacteriorhodopsin)


DEFENCE
R&D
DÉFENSE