Biomimetics and Bio-Inspiration

- Bio-inspiration has always been a part of humanity’s technological pursuits
- When do we copy nature versus just get inspiration from nature?
NanoBio History: So What’s Different Now?

Bio Timeline

- 1973: “Modern” Era Begins
- 1975: Alsilomar Conference
- 1976: First Biotech Company
- 1978: Smith & Nathans win Nobel Prize
- 1985: Mullis publishes PCR paper
- 1981: Binning and Rohrer win Nobel Prize
- 1985: Binning, Quate, and Gerber invent AFM
- 1986: Binning and Rohrer win Nobel Prize
- 1989: First commercial AFM

Info Timeline

- Intel 4004
- 1971

Nano Timeline
NanoBio History:
So What’s Different Now?

1985
Democratization Happened…

What Henry Ford did for automobiles, PCR and AFM did for biotechnology and nanotechnology, respectively and independently.

Economics $\alpha$ scope of adoption = N (collective of researchers)
A “Wisdom of Crowds” effect for the entire research area
Bionanotechnology Future

(Self-Assembled) Structures

- Diagnostics – medical and human performance
- Nano-Manufacturing – self-assembly and directed assembly, but, defect/error tolerance, design tools, thermodynamics are plotting against you
- “Non-obvious” and “non-sexy” areas, i.e., tribology

Au/Pd NPs

RF in

RF out
NanoDiagnostics Impact

[Analyte] vs. Time
Sensor Chip for Flexible Detection

Independently incorporate many distinct receptors and nanowires with excellent reproducibility!

Biology has evolved the ability to synthesize inorganic materials
- The master of “ambient conditions” materials science
- Proteins control the nucleation and growth of inorganic structures from nano- to macroscopic scales
Silica in Biology

Biosilicification - formation of amorphous silica (diatoms, sponges, mollusks)

Diatoms

Silaffin Protein

Marine Glass Sponge (T. aurantia) Spicules

Silicatein α Protein


Morse et al., PNAS. (1998) 95:6234
Formation of Biosilica

$$\text{H}_2\text{N-SSKKSGSYSGSKGSKRRIIL-COOH}$$

$\text{R5 peptide}$

$\text{Silaffin peptide}$

$+ \text{Silicic acid (TMOS)}$

Silica formation under ambient conditions: room temperature, neutral pH

2 μm
Peptide Binder Library

COBALT OXIDE
Co-12 HYPTLPLGSSTY
Co-14 QYKHHHPQKAH
Co-17 QLLPLTPSLLQA
Co-18 CFSQLNALPLIL
Co-9 KLHSSPHTPLVQ

CARBON NANOTUBES
CN-1 HSSWYWAFNNKT
CN-2 HTSWYWAFNTKT
CN-3 YTHVLPFPSS
CN-4 HAWVDIRPIHS

IRON OXIDE
Fe-1 LPDSHHYKSDDH
Fe-2 QHMQQFQTQGIQ
Fe-4 SLYSNPTVPYSY
Fe-7 LPGSHQYQQLL
Fe-8 QHTQISWPQVR
Fe-10 QQLPKNGCLPAV

SILICA
Si-3 KPHHHHTHHMYT
Si-8 KPSHHHHHTGAN
Si-7 APPGHHHHWHOHH
Si-1 MSPHPHRHHHT
Si-4 MSASSYASFSWS

GOLD
Au3 AYSGAFPPMPF
Flg1 DYKDDDDK

GADOLINIUM
Gd-1 TTFHYANQVHR
Gd-2 AETVESCLAKSH
Gd-3 LPYGTNSHRAPV
Gd-6 SLASYLQSWLGS
Gd-7 TKNMLSLPVGPG
Gd-8 EDNLAVERSQIM

GERMANIA
Ge-8 SLKMPHPWPHLLP
Ge-34 TGHQSPGAYAAH
Ge-10 SFLYSYTPRPL
Ge-18 HATGTHGLSLSH

TIN OXIDE
Sn2-1 KNAGQYPSSALM
Sn4-1 SPSSAHTPPT
Sn4-2 TPTLTRSMSSLLF
Sn4-3 STLTSSTSSLVA

COBALT PLATINUM
CoPt KYHLHSHPLHK
CoPt KTHSLHSPSHK
CoPt HLHSPLHHPHK
CoPt KLHSSPHTPLVQ

SULFHYDRYL


Positively charged
Aromatic, hydrophobic
Hydroxyl
Sulfhydryl
Negatively charged
Addressable Biomolecular Domains on Nanoparticle Surfaces

Bi-Functional Biotemplate

M+ Binds to M1

Binds to M2

Biotemplate Coated Nanoparticle

Site-Specific Deposition of Nanoparticles

Monodispersed NPs

Pd

Ni

4200 particles /μm²

70 particles /μm²

Advanced Materials 2006, 18, 1988
Controlling Nanomaterial Properties

Clay Binding Domain  Metal Binding/Bioactive Peptide

Bifunctional Biotemplate

Peptide-functionalized Clays

S2 Peptide

→ Antimicrobial

→ Magnetic

(Drummy, Vaia & Naik Submitted)
Bio-Functionalized Nanomaterials

- Labeling
- Gene regulation
- Light harvesting
- BFNs
- Catalysis
- Actuation
- Assembly
- Sensing
Colorimetric Response of Biofunctionalized Nanoparticles

Molecular Target Assays
3 Part Design

UNAGGREGATED
Au nanoparticles

AGGREGATED
Au nanoparticle

OLIGONUCLEOTIDES

APTAMER ("Glue")

Hybridization
4°C overnight

ANALYTE
("Disruptor")
We must continue to:

- Lead innovative, integrated, and multidisciplinary R&D

Example: **Tailored ISR & Effects Delivery**

Cross-Domain, Multi-Directorate, Integrated Effects

- Seamless Air, Space and Cyber Enterprise
  - USAF’s S&T Response to the Global “Daunting Challenge” of Counter-Terrorism: *foundational to AF2T2EA4*
  - Exploits/Extends USAF Core Competencies of Global Reach and Persistence
  - Staring & Cross-Phenomenology integration yielding “Total SA”
  - Continuous Sensing through Effects Delivery

**Global Access**

“Episodic” - Synoptic

**Regional, Persistent, High Altitude Surveillance**

**Continuous “Forensics”**

Tailored Effects

- Hunter / Killer Wolf Pack
- Urban
- Mountains & Caves
- Foliage
- Predator
- Small UAV
- micro UAV
- Joint STARS
- Global Hawk
- SBR
- SBIRS
- Near SPACE
- SensorCraft
- HSI
- U-2
- AAA Sites
Bio-X STT
Urban Environment Game Changers

- Taggants
- Small UAVs
- Biotronics
- Bio G&C
Program Vision

BIOLOGY DEVICE

Strain gauge on Polyimide film
Rigid metal support

Characterize
Understand
Emulate

BIOLOGY

DEVICE

Strain gauge on Polyimide film
Rigid metal support
Lateral Line System

Superficial Neuromast

- Cupula
- Hair Cells

Canal Neuromast

- Protection
- High pass filter
- Amplification

BioSense
Bio-Sensory Structure Emulation

DARPA

C. Liu/C. Coombs
Spider flow and vibration tracking
Wake tracking in seals

Dehnhardt, Mauck, Hanke & Bleckmann, Science 292 (2001)
Artificial Hair Sensor

C. Liu
Device Improvement via Cupula

Hydrogel cupula is assembled to the hair to increase sensor sensitivity.

Bi-sectional hair with rubbery base is designed to improve device robustness.
Bionanotechnology: Technology Impact

Bio-Functionalized Nanomaterials (BFN)

Labeling
Gene regulation
Light harvesting
BFNs
Sensing
Assembly
Catalysis
Actuation

\[
\text{OH} + \text{H}_2 \xrightarrow{\text{BFNs}} \text{OH}
\]
Cognition Impact

External Physiological Effects (TMS & tDCS)

“COGNITION”

Diet

Cognitive/Physiological Loop

Molecular Aspects

AF Training

EFFECT: Cognition Enhancement, e.g., Accelerated Learning

mTOR: molecular role in moving memory from short-term to long-term
Molecular Targets of Opportunity: Cognition

Stress, Sleep Deprivation & Cognitive function

Enhanced Molecular Signatures
Orexin
S6K-P
Stress hormones

Molecular Signatures
Orexin
S6K+/- P
Stress hormones

Rodent Models: Molecular and Neuro-Behavioral

+ leucine

+ cognitive marker
Nano in Biology: Nanoshells / Nanoparticles

Nanoshells exhibit a unique electromagnetic resonance response

VS.
Academic partners are telling us which areas of the brain are important in a given task – i.e., visual acuity.

We can safely stimulate those regions of the brain via TMS or TDCS in RHP.

We can directly measure warfighter improvement via Live, Virtual, Constructed (LVC) environment of RHA.

Revolutionize pilot training and effectiveness via recent advances in neuroscience and cognition!
Study Methodology

TMS Treatment

• Subjects
  – 20 healthy volunteers (age 18-35)
  – Medical/Neurological Evaluation
  – Subjects with metal in the head, neurological disorder, seizure risk, history of seizures will be excluded

• Task
  – Difficult Surveillance and Reconnaissance (SAR) Task
    • Target vehicles among similar distracter non-target vehicles
    • Three levels of search difficulty – vary # of targets and distracters
    • Accuracy and reaction time data will be recorded
Parting Thoughts
(truth in advertising)

“The not so good…”

• Bio-based approaches can be very expensive (good plug for bio-inspiration)

• Bio-based approaches can be very slow (but that is not always a bad thing)

• Response & signal transduction: What’s your ROC curve look like? (know your engineering brethren)

“And now the good…”

• Great lessons in the non-obvious

• Mastery of the ambient

• Truly unique surfactants for materials control
ACKNOWLEDGMENTS

Materials and Manufacturing Directorate  
(R. Naik, Bio RL)

Human Effectiveness Directorate

Bio-X STT

Air Force Office of Scientific Research

DARPA
Insects Sensing Using OBPs

bee antennae, 400X

ASP1 has large hydrophobic binding pocket similar to pheromone binding proteins from other insects.
Biomimetic Sniffer

From Biology...

Goal: Genetic engineering of Odor Binding Protein (OBP) for chemical agent detection.

Specific Objectives: Clone OBPs from insects into systems that would allow genetic manipulation, screen against target compounds and incorporate into solid state device.

Approach: Develop a genetic screen for identifying OBP variants that bind to a specific chemical ligand using a molecular biology and computational approach. Develop a biomimetic sensor that can detect chemical signatures.

Benefits:
- Sense, and ID chemical threats/signatures.
- Hybrid, multifunctional, sensors: Low-cost, distributed, omni-present lightweight sensors.

....to sensor platforms.
Quartz Tuning Fork (QTF) Sensor

Benefits:
• Inexpensive.
• Highly selective.
• Tunable.
• Robust.

Quartz tuning fork
• Inexpensive
• Used in watches
• High quality factor of 90,000
• Low power consumption

Sensor fabrication
• Using photolithography, bridge the forks with a polymer
• Polymer has a protein-binding functional group
• Immerse the tuning fork in a solution of OBPs
• OBPs are now attached to the polymer wire
• Expose the QTF to air
• As material bind to the OBPs, the tension of the polymer wire changes, which changes the frequency of the QTF

Tuning fork vibrates at a highly defined frequency

(Bio) Polymer Fiber with Asp1
Functionalize CNTs with engineered biomolecules

Insect Odor Sensing Mechanism

nanomaterials (sensitivity) + biomolecules (selectivity) = chemosensor

CNT Binding Domain

TNT Binding Domain

Bifunctional Biotemplate

Biomimetic Chemosensor
Sensor Chip for Flexible Detection

Independently incorporate many distinct receptors and nanowires with excellent reproducibility!

NanoBio History:
So What’s Different Now?

Fig. 1. Number of articles on nano science and engineering, based on the presence of the string “nano*” in article titles, abstracts, and keywords in the ISI Web of Science database. Data provided by David Wojick; figure prepared by Luis Bettencourt.

4 “Groups” in Synthetic Biology

1. Biologists – test current understanding of natural biological systems

2. Chemists – an extension of synthetic chemistry

3. ‘Re-writers’ – Genomes encoding natural biological systems can be ‘re-written’, producing engineered surrogates that might usefully supplant some natural biological systems

4. Engineers – biology is a technology with an emphasis on development of foundational technologies to make the design and construction easier

In vivo circuits: Riboswitch Strategy

SWITCH/SENSOR
Identification/recognition elements that are coupled to genetic control

REPORTER
Development of pathway/reporter system (optical and redox-based assays)

INTEGRATION
Packaging of genetic switches and reporter assay for device integration
Riboswitch Mode of Action: Modularity

Engineer Synthetic Riboswitch triggered by small molecule

Cell-Based Sentinel

CELL LYSATES

Positive Control 0-8hrs

Riboswitch Off 0-8hrs

Riboswitch On 0-8hrs

43
Cell-Based Sentinel Data
Autodock4* Results: Riboswitch Binding Pocket

Critical role of cytosine and uracil at positions 22 and 24


Software - Autodock4 (Scripps Research Institute)
Riboswitch Mode of Action: Remote Activation

Engineer Synthetic Riboswitch triggered by small molecule or external field

“Off” state with extensive pairing

f ~ GHz
Response of PFN Sensor

Response Time

Absorbance at 614 nm

Time (min)

Flg Domain Effect

PFNs  Pt^{2+}  Pd^{4+}  Co^{2+}  Pb^{2+}  Hg^{2+}

Flg-A3

A3

Phage Peptide Display (PD)

Low voltage TEM image of M13 phage selected for binding to Co/Pt nanoparticles
**Peptide Functionalized NPs**

**Detection Limit**

<table>
<thead>
<tr>
<th>Recognition element</th>
<th>Metal ion</th>
<th>Conc.</th>
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</thead>
<tbody>
<tr>
<td>Mirkin</td>
<td>DNA</td>
<td>Hg$^{2+}$</td>
</tr>
<tr>
<td>Chang</td>
<td>DNAzyme</td>
<td>Pb$^{2+}$</td>
</tr>
<tr>
<td>Lu</td>
<td>mercapto</td>
<td>Hg$^{2+}$</td>
</tr>
</tbody>
</table>

**Peptide Functionalized NPs**

<table>
<thead>
<tr>
<th>PFN + [M+]</th>
<th>Absorbance (nm)</th>
<th>Metal ion Conc. (nM)</th>
<th>Metal ion Conc. (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFNs</td>
<td>539</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pt$^{2+}$</td>
<td>542</td>
<td>22.6 ± 0.1</td>
<td>4.5 ± 0.1</td>
</tr>
<tr>
<td>Pd$^{4+}$</td>
<td>617</td>
<td>31.0 ± 11.0</td>
<td>3.3 ± 1.2</td>
</tr>
<tr>
<td>Co$^{2+}$</td>
<td>593</td>
<td>191.4 ± 52.7</td>
<td>11.3 ± 3.1</td>
</tr>
<tr>
<td>Pb$^{2+}$</td>
<td>614</td>
<td>242.0 ± 8.6</td>
<td>50.2 ± 1.8</td>
</tr>
<tr>
<td>Hg$^{2+}$</td>
<td>580</td>
<td>26.4 ± 11.3</td>
<td>5.3 ± 2.2</td>
</tr>
</tbody>
</table>