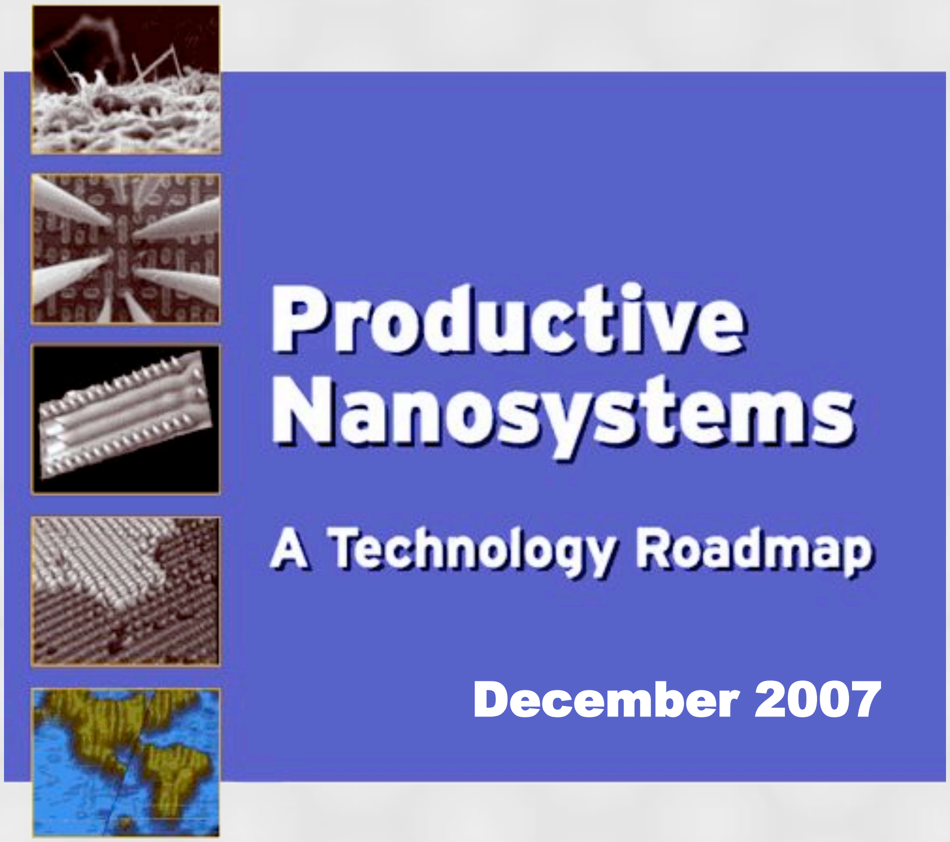
Protein Engineering

Challenges and applications for composite nanosystems

Eric Drexler

RosettaCon 2008

nanorex



Leadership:

Battelle Memorial Institute

Hosting National Labs:

Oak Ridge

Brookhaven

Pacific Northwest

Organized by:

Battelle

Sponsors:

The Waitt Family Foundation — Helping Good People Do Great Things

Foresight Nanotech Institute — Advancing Beneficial Nanotechnology

Sun microsystems

Zyvex Labs

nanorex

Synchrona

Hosting National Labs:

Oak Ridge National Laboratory

Brookhaven National Laboratory

Pacific Northwest National Laboratory

Roadmap partners:

Bio

EPRI

Nano Business Alliance

SPIE

NSTI

semi

SME

Modular molecular systems

Useful parts that don’t fit

Putting it together: composite systems

Protein–DNA complementarity

Applications and challenges

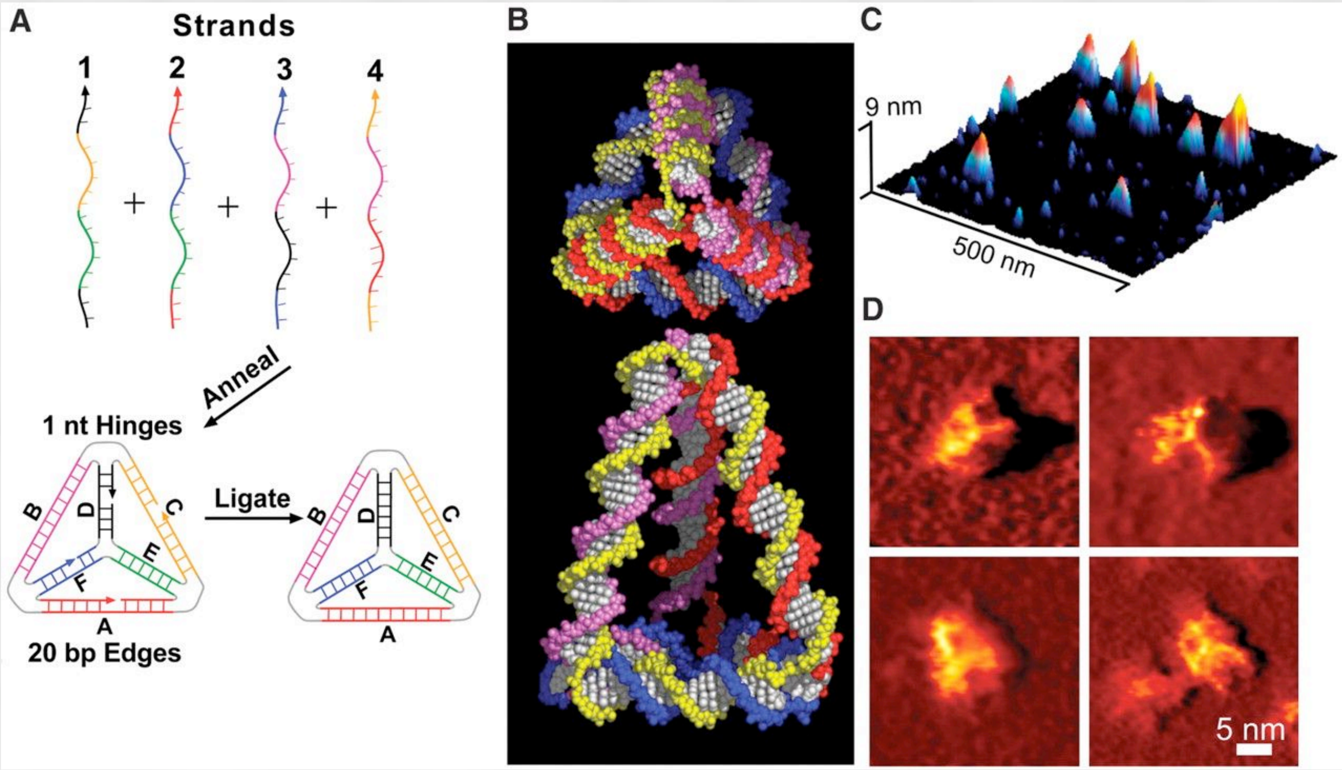
Modular Molecular Composite Nanosystems:

	DNA	Protein	Specialized
Limitations	narrow range of functions, limited binding	small structures, difficult design, slow production	non-modular, seldom much design freedom
Strengths	large structures, easy design, fast production	broad range of functions, versatile binding	unlimited range of materials and functions
Natural roles	structural frames, large-scale pattern organization	assembly interfaces, precise alignment, diverse functions	catalytic, optical, mechanical, electronic...

Integrate components to build systems:

- **3D, atomically precise scaffold, easily re-configured**
- **100s to 1000s of parts in addressable locations**

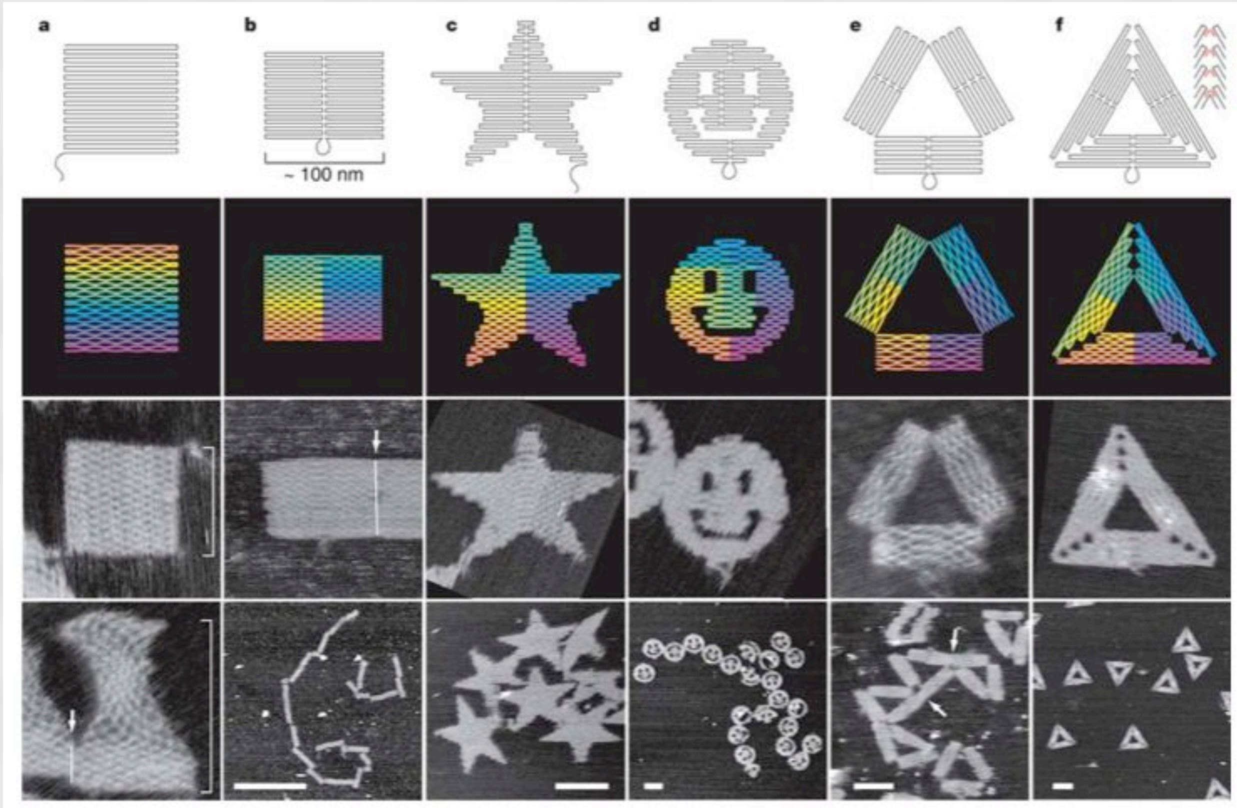
“Rapid chiral assembly of rigid DNA building blocks for molecular nanofabrication”



R. P. Goodman *et al., Science* **310**, 1661 -1665 (2005)

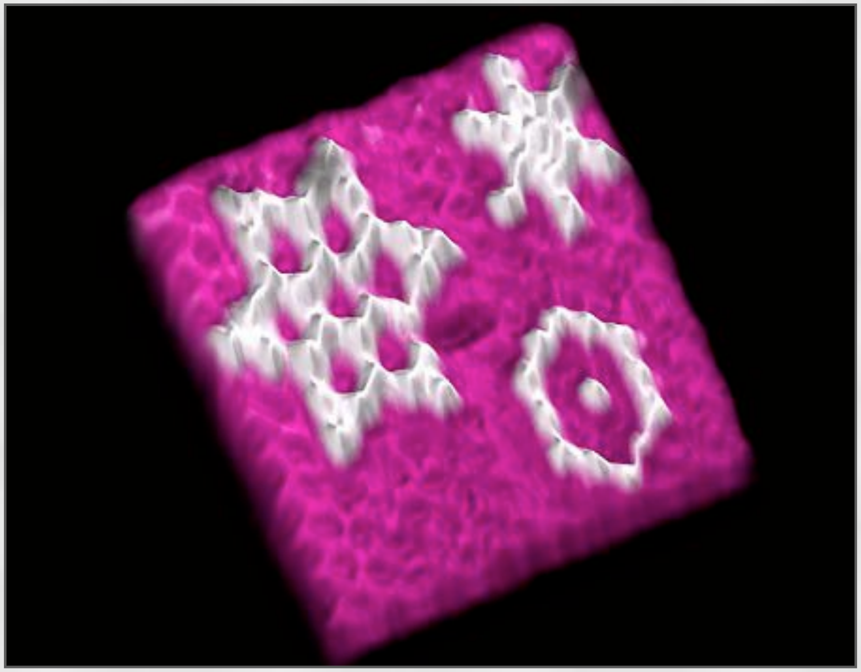
Published by AAAS

~ 1/2 million atoms per structure

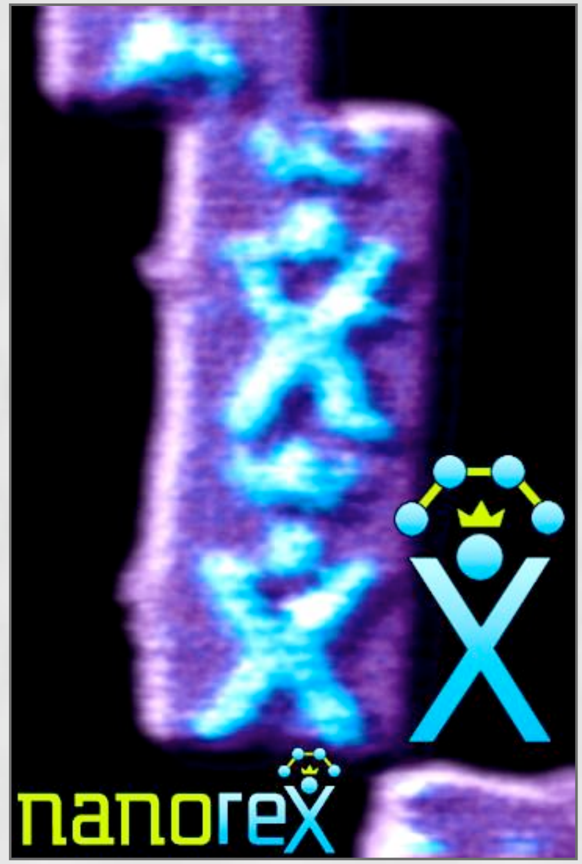


Rothemund P.W.K., “Folding DNA to create nanoscale shapes and patterns.” *Nature*, 440:297–302 (2006).

Fast, routine, reliable

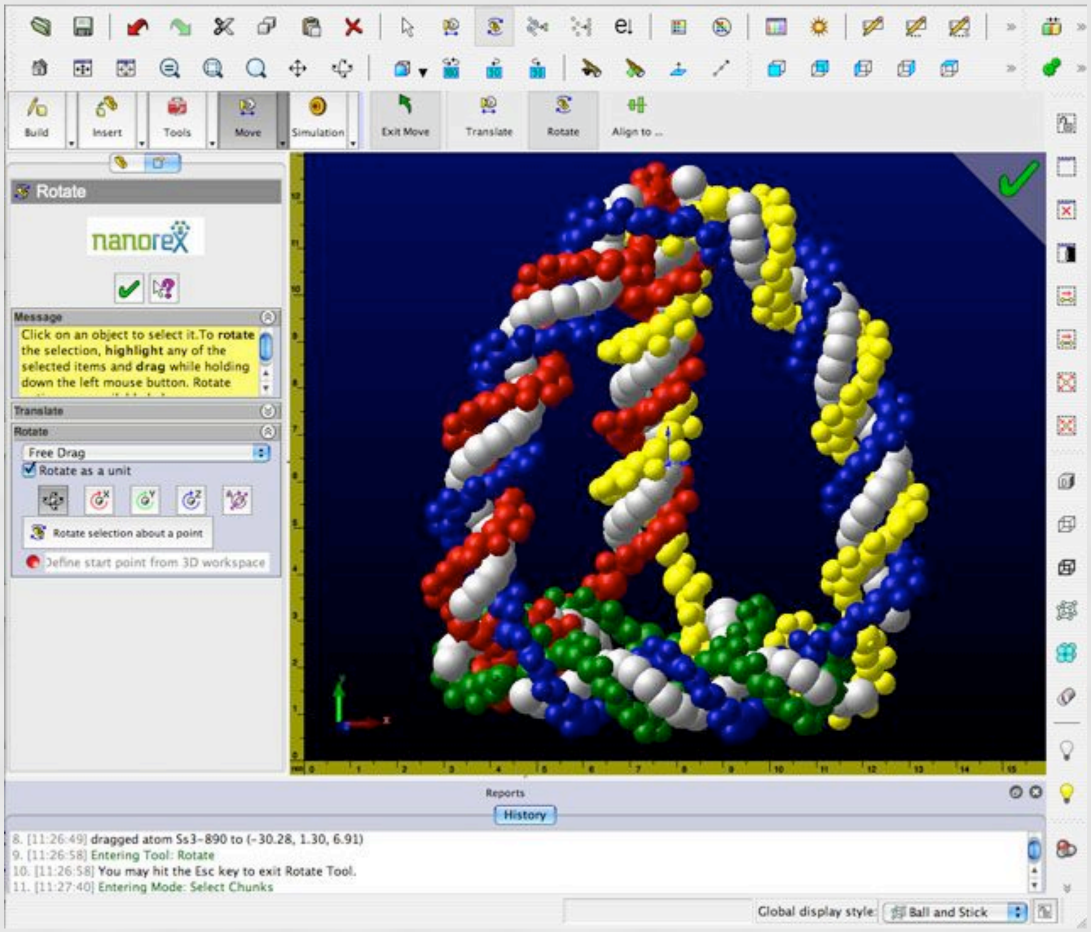


Paul Rothemund (2005).



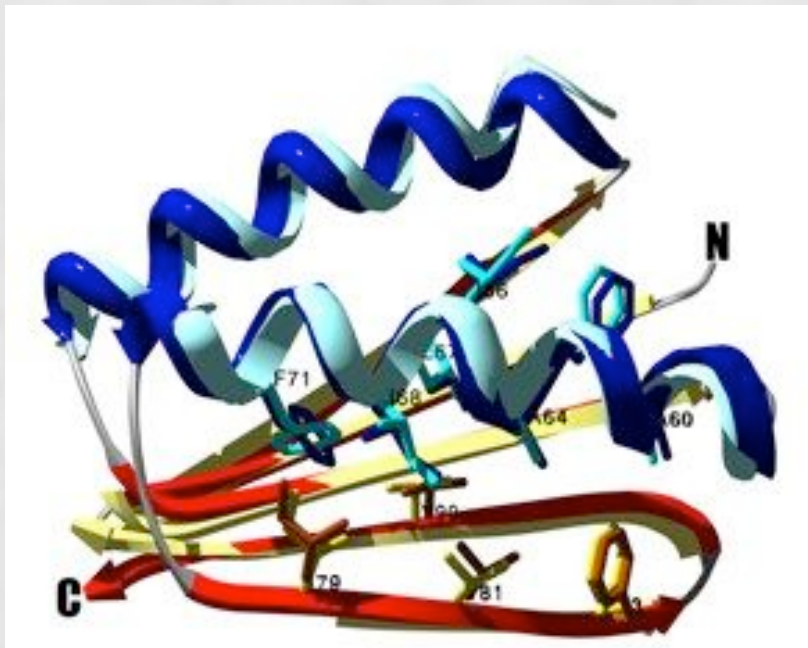
Mark and Erika Sims,
21–25 August (2006)

NanoEngineer-1 (July 2008, v.1.1.1)



Computer-aided design for molecular systems,
open-source software from Nanorex

“Design of a Novel Globular Protein Fold with Atomic-Level Accuracy”



Kuhlman *et al., Science* **302:**1364–68 (2003)

“RosettaDesign server for protein design”

www.rosettadesign.med.unc.edu

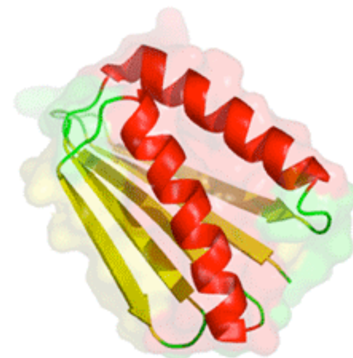
http://rosettadesign.med.unc.edu/index.html

RosettaDesign

Welcome to the RosettaDesign web server.

RosettaDesign identifies low energy sequences for specified protein backbones, and has been used previously to stabilize proteins and create new protein structures.

Please login to begin using RosettaDesign.



Liu and Kuhlman, *Nucleic Acids Res*
34:W235–W238 (2006)

Modular molecular systems

Useful parts that don’t fit

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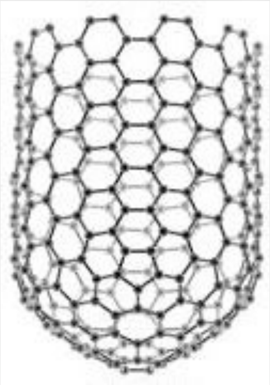
Applications and challenges

Specialized functional structures:

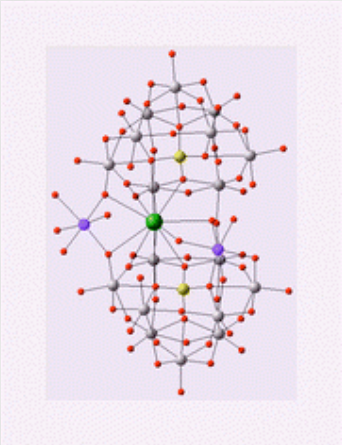
(atomically precise parts)

Porphyrins

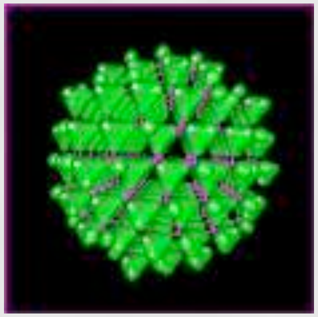
electronic, chemical,
biological, structural,
electronic, optical,
optoelectronic,
electromechanical,
electrochemical...



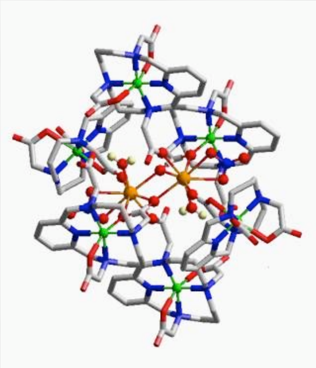
Nanotube segments



Metal-oxide clusters



Quantum dots



Metal complexes

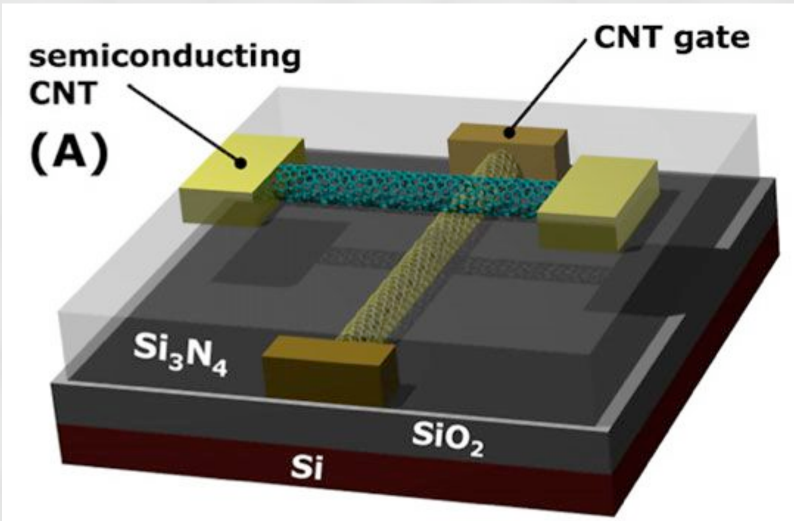
Have components for:

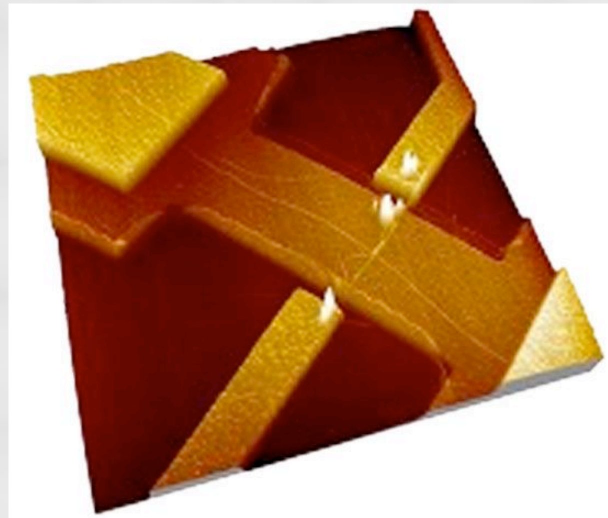
- molecular sensing
- photovoltaic energy conversion
- photochemistry
- efficient light emission
- plasmonic devices
- molecular electronics
- carbon nanotubes (lots of functions)

Abundant parts, but no way to assemble them to build complex systems

— Need circuit boards and sockets! —

“A carbon nanotube gated carbon nanotube transistor with 5 ps gate delay”





J Svensson *et al.* Nanotechnology **19**:1–6 (2008)

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Rosetta*DNA*

Rosetta*Design*

Rosetta*Surface*

Rosetta

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DNA origami strand, at 7.5 kilobases,
could encode ~ 10 medium-size proteins,
but...

Information densities:

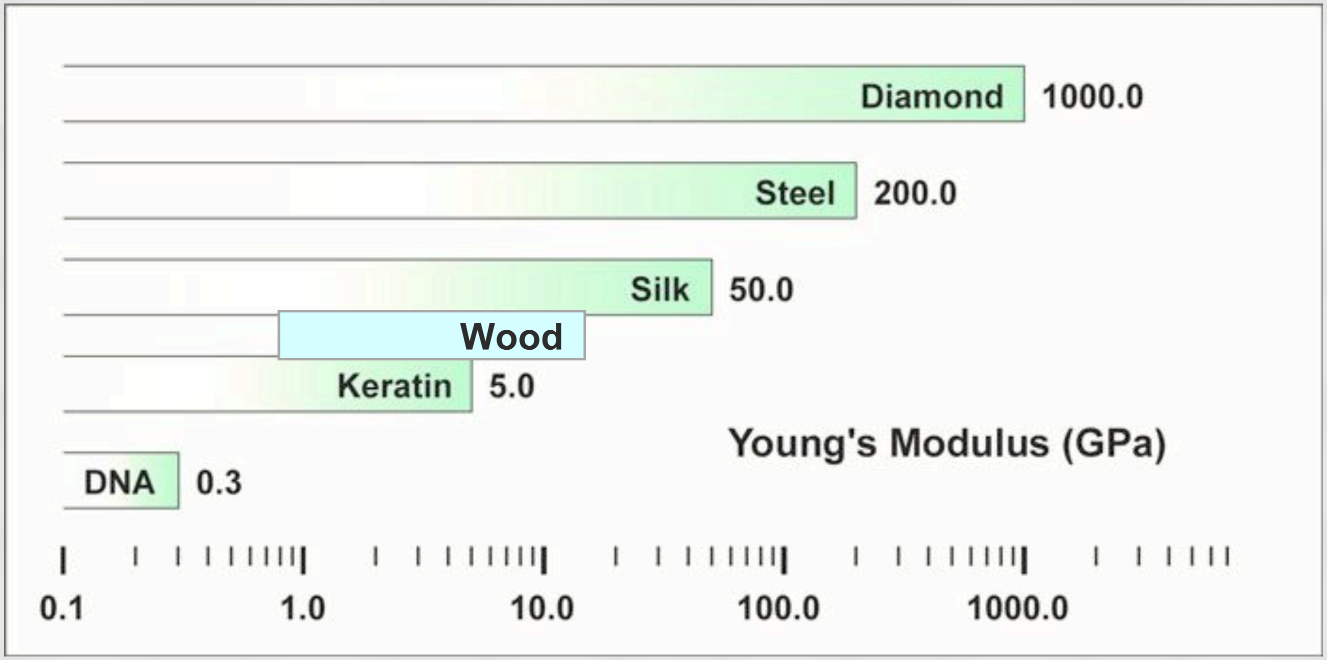
DNA ≈ 2 bits/nm^3

Protein ≈ 40 bits/nm^3

Pentium < 10^{-4} ***(in the structure, data is less dense!)***

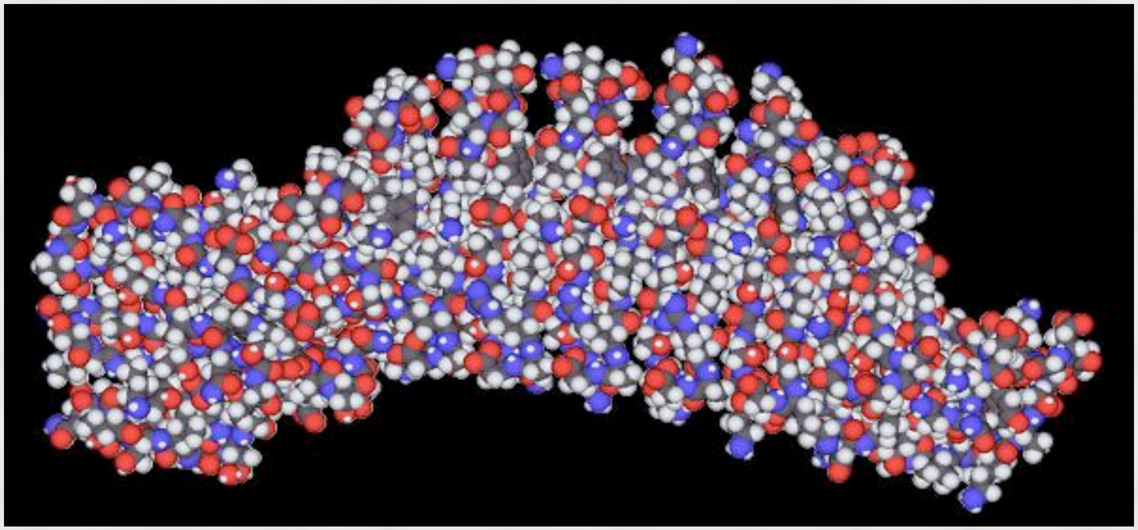
Information density **is part of the reason why proteins are designed to bind DNA, and not** ***vice versa.***
Functional diversity is not enough.

Values of Young's modulus for several biomolecular and inorganic materials



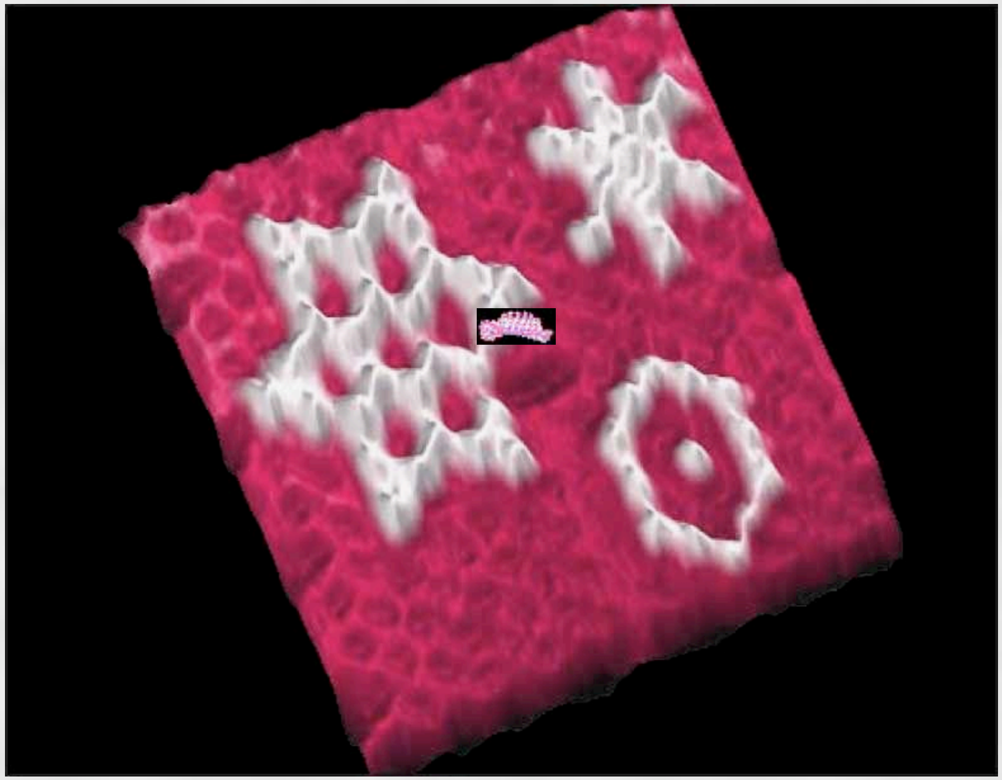
Protein advantage: 10 to 100 x modulus of DNA
=> 1/10 to 1/100 as much area within
the r.m.s thermal fluctuation radius

De novo protein, 329 residues (almost all beta-sheet)
length = 11 nm



"Crystal structure of OspA mutant" (PDB 2oy7)
Makabe, K., Biancalana, M., Yan, S., Gawlak, G., Koide, A., Koide, S. ***(2008, to be published)***

DNA origami, 7.5 kilobases,
length, width = 100 nm



Paul Rothemund, *Nature* 440:297 (2006)

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Composite-system applications:

- **Biomedical sensoring & targeting using boolean logic and counting**
- **"Nanochips in microsockets" for general purpose digital systems** ***(a major yield/reliability challenge)***
- **Epitaxial macromolecular crystals on nanolithographic patterns: stacked RAM cells for petabit chips** ***(a lesser yield/reliability challenge)***
- **Workbenches for nanoscience** ***(must work sometimes...)***

High-payoff directions:

- Improving methodologies for interface design, for proteins, DNA, crystals, nanostructures…
- Rules defining combinatorial design domains: "protein origami" (or "protein Legos")
- Improved physical *and chemical* stability:
  - – design rules, restricted set of amino acids, non-aqueous environments (*eg,* ionic liquids)
- Creative cheating: unnatural amino acids, organic crosslinkers, template components…
- Integrated, multi-material, multi-scale modeling, design, and data analysis

- Additional promise + a broader community + a unified message = Vast Funding

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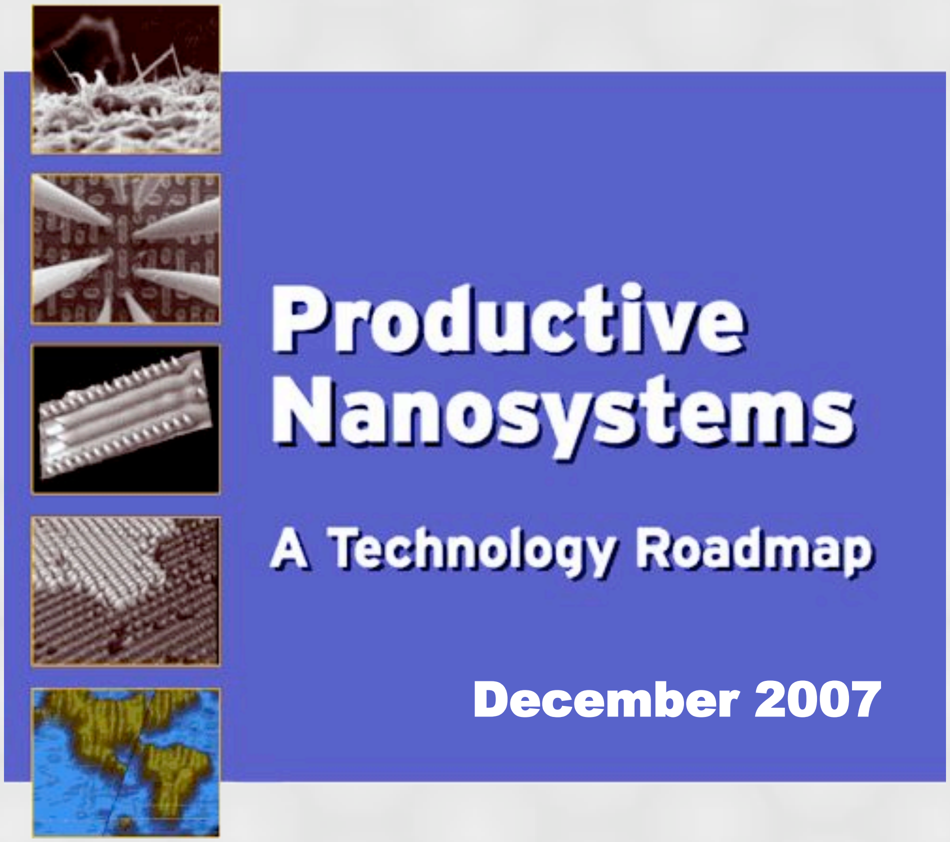

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PDFs posted at www.e-drexler.com