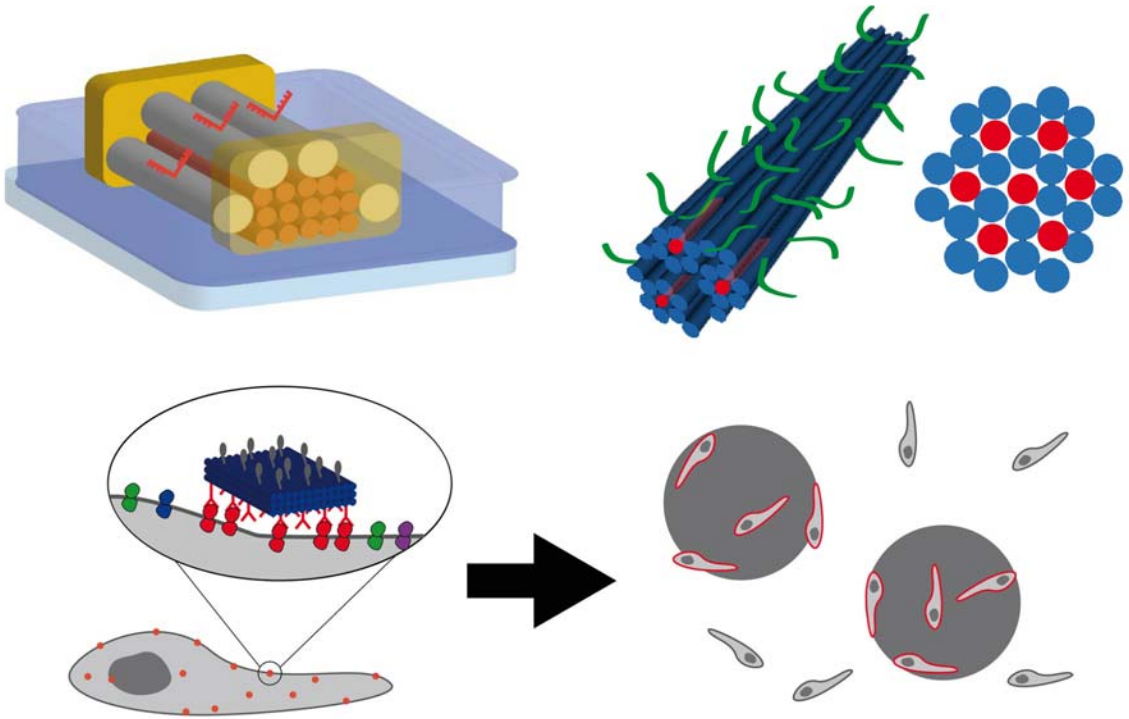
DNA Nanodevices for Diagnostic, Therapeutic and Biological Tools

DNA-Nanosysteme für diagnostische, therapeutische und biologische Werkzeuge

Dr. David M Smith
24. April 2013



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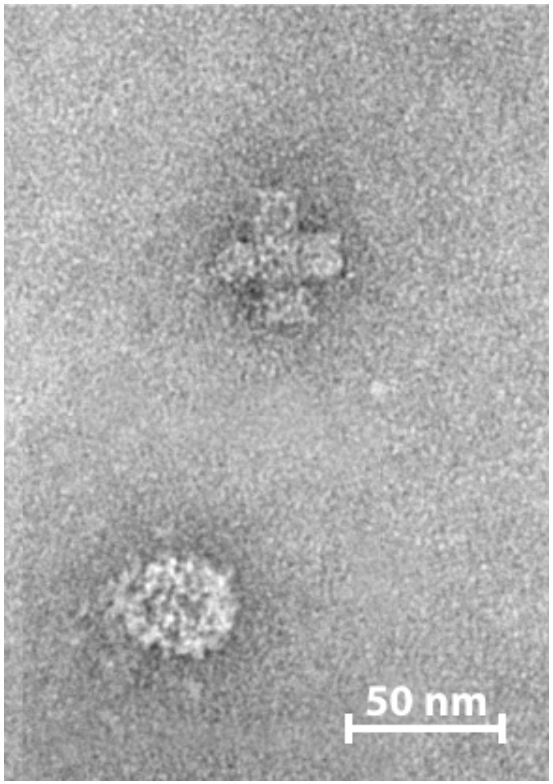
Nanoscale cell interactions

DNA origami nanostructure

Douglas *et al.*, Nature

Tomato bushy stunt virus

Alberts *et al.*, The Cell



Björn Högberg

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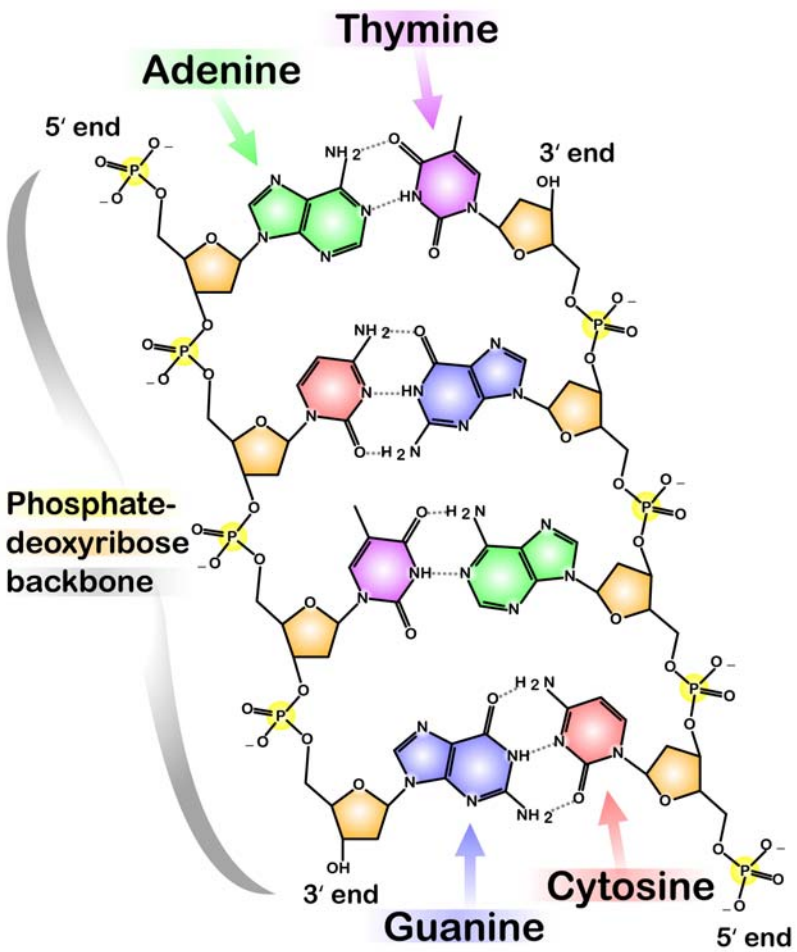
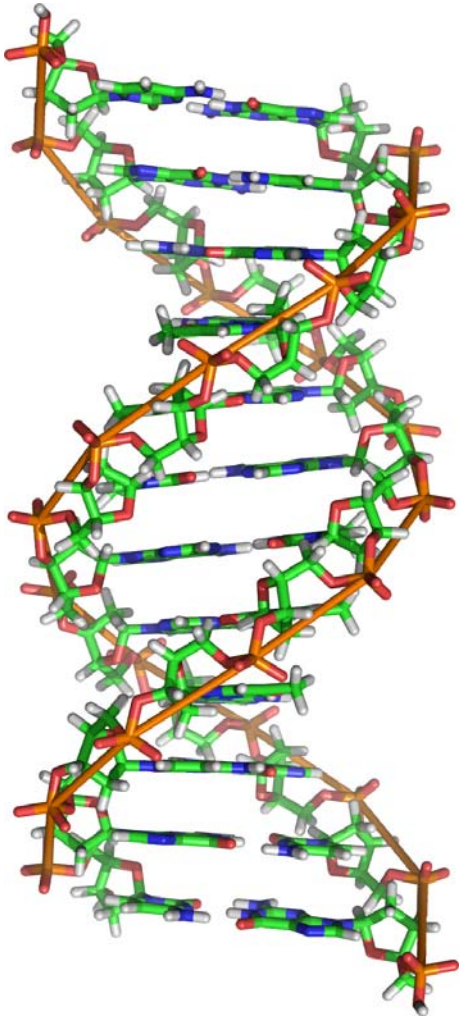
DNA: Molecular structure





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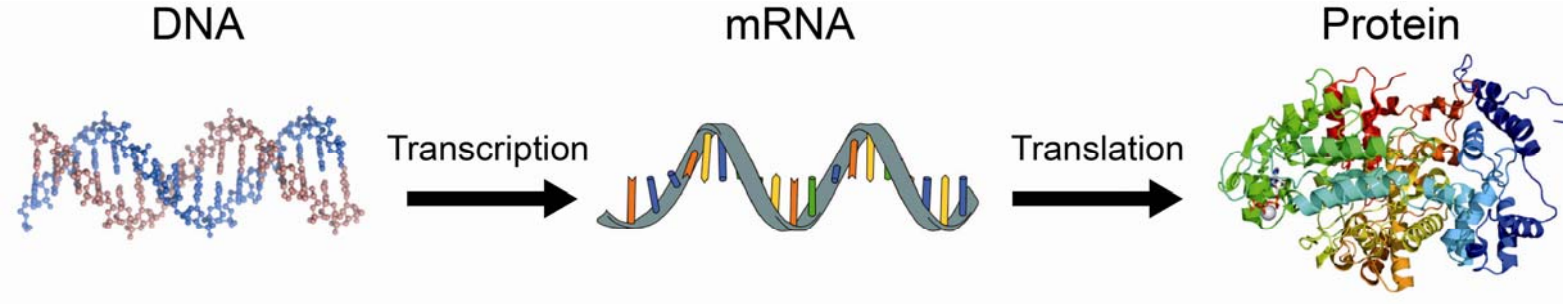
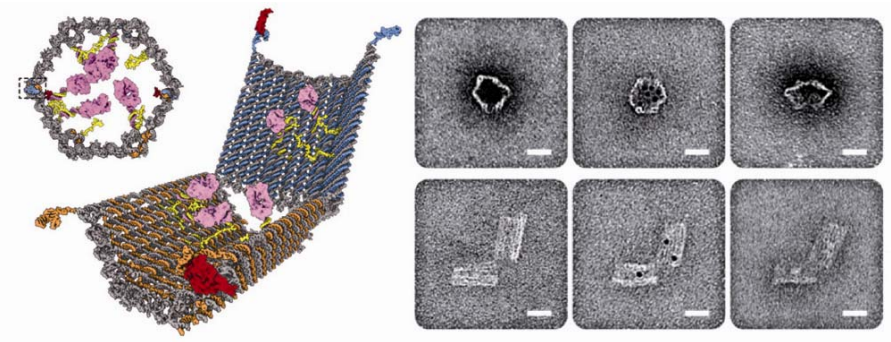
DNA self-assembly

Classic view: DNA is a blueprint



DNA Nanotechnology: Programmed molecular self-assembly

(Chen *et al.*, Nature, 1991)



(Douglas et al., Science, 2012)

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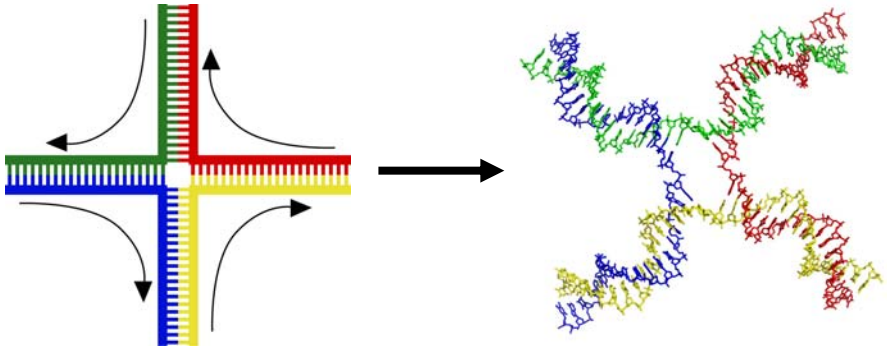
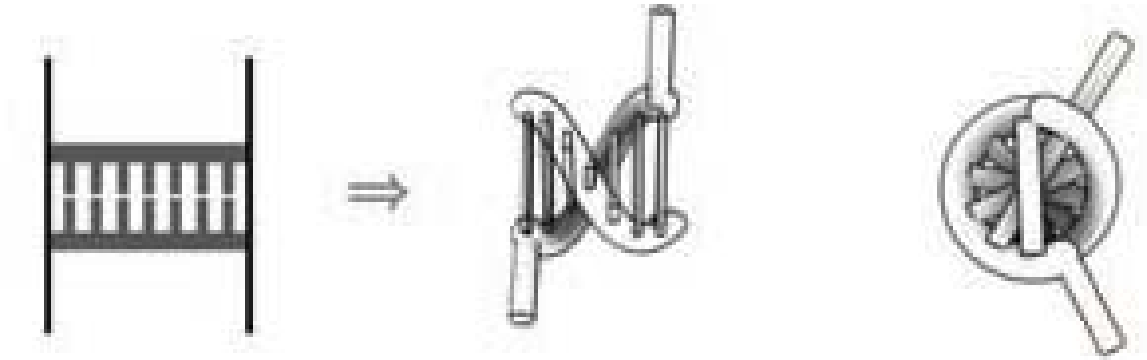
The basis: branched DNA junctions

Holliday Junction

- Mobile: genetic recombination
- Static: branched DNA architectures



Helical twist ➔ Branches in 3 dimensions



(Dietz et al., Science, 2009)

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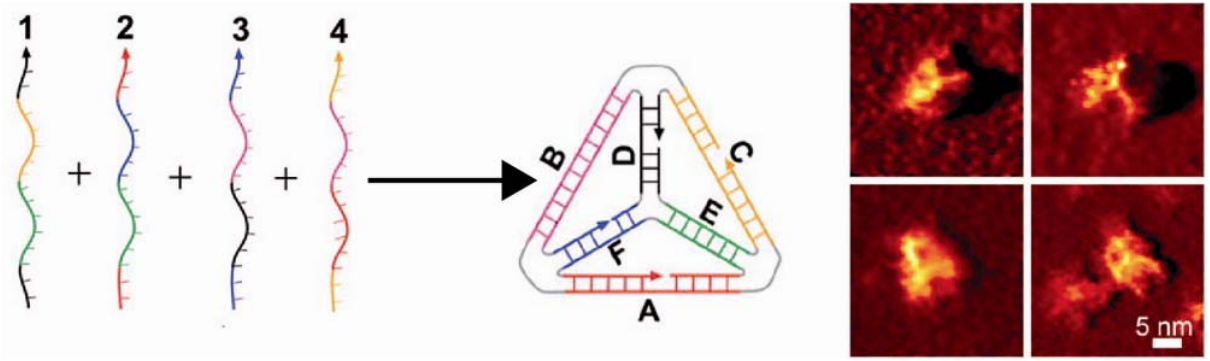
First steps: wireframe lattices and cages

2d surfaces

Simple wireframe structures

(Chen *et al.*, Nature, 1991)



(Goodman *et al.*, Science, 2005)

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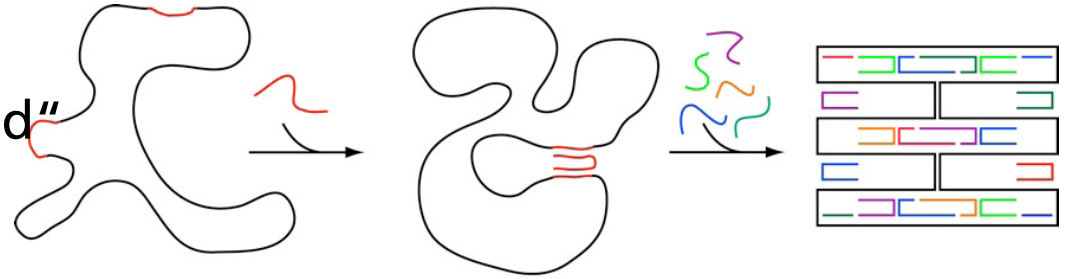
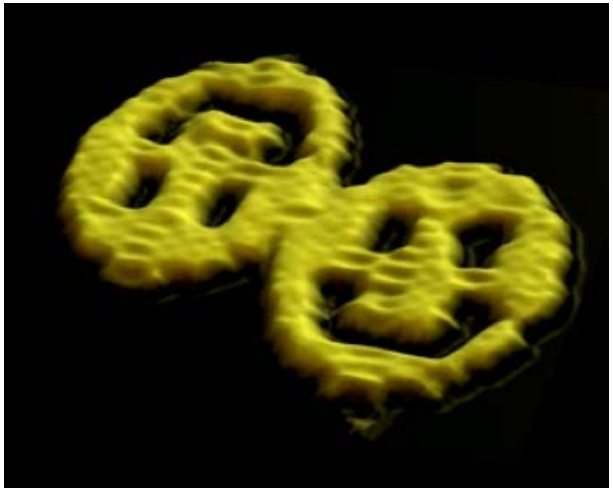
Adding complexity through “DNA origami”

Scaffolded DNA origami

- Long single-stranded “scaffold”
- Short “staple“ strands





(Rothemund, Nature 2006)

(Dietz *et al.*, Science 2009)

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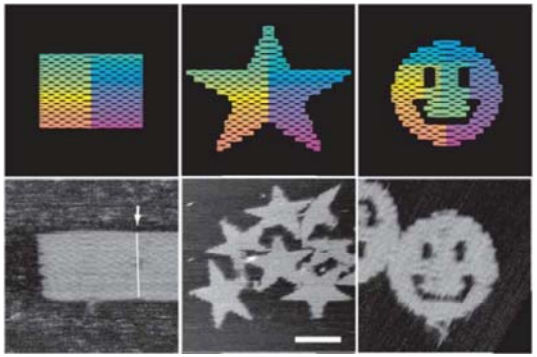
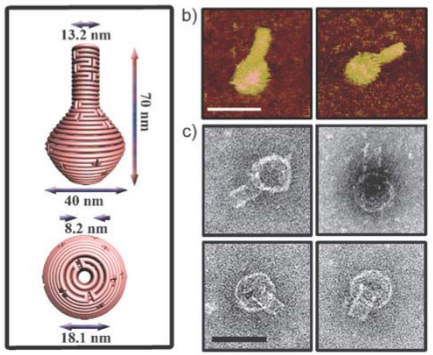
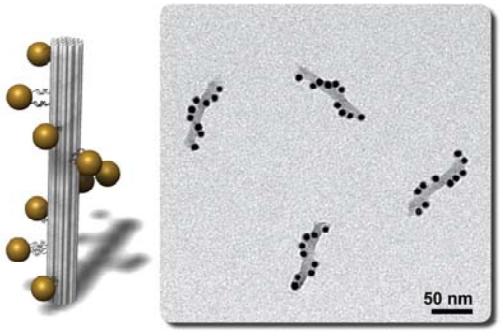
Complex 2D, 3D and composite structures



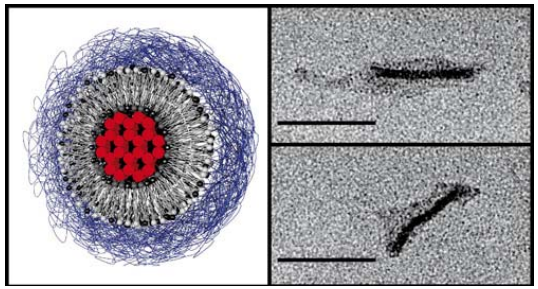
(Rothemund, Nature 2006)



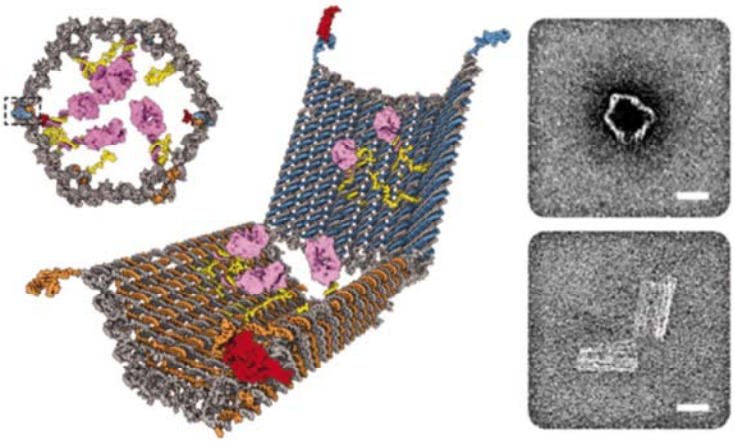
(Han *et al.*, Science 2011)



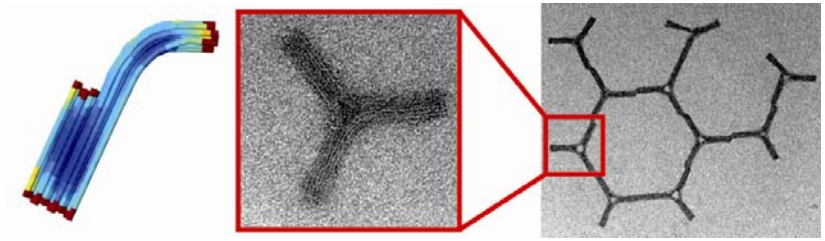
(Kuzyk *et al.*, Nature, 2012)



(Smith *et al.*, Nanomedicine, 2013)



(Douglas *et al.*, Science, 2012)



(Images courtesy of S. Kempter)

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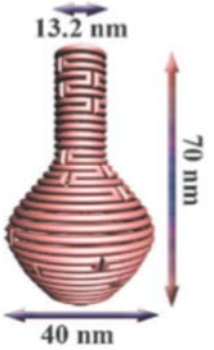
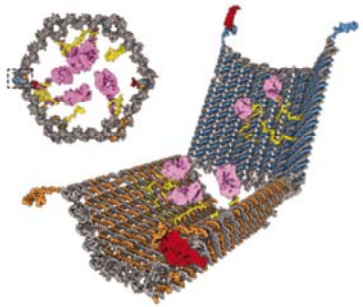
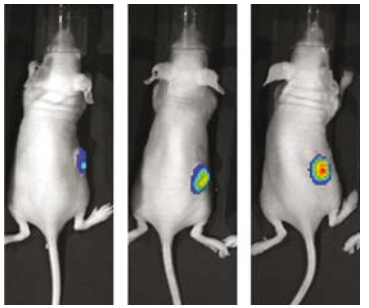
A new material for biomedicine

- Programmable nanomaterial
- Nanometer-precise features
- Advanced functionalities
- Scalable one-pot production
- Biocompatible







(Lee *et al.*, Nat. Nanotech., 2012)

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DNA Nanodevices at Fraunhofer IZI

- Diagnostic tools
  - Nanostructured elements for biosensors
- Therapeutic agents
  - Targeted drug carriers
- Biological tools
  - Coupling system for bead-based cell sorting

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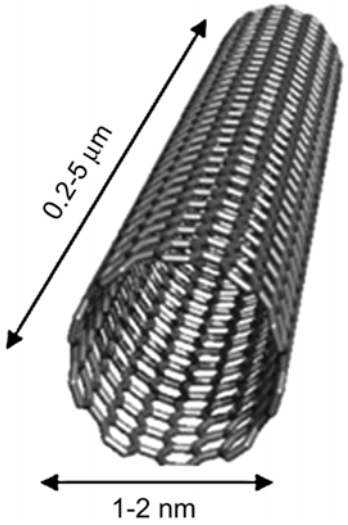
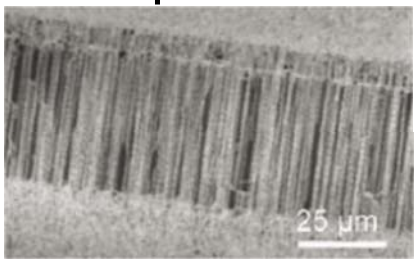
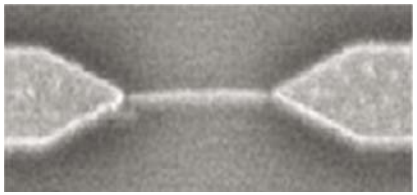
Diagnostics: nanostructured biosensor components

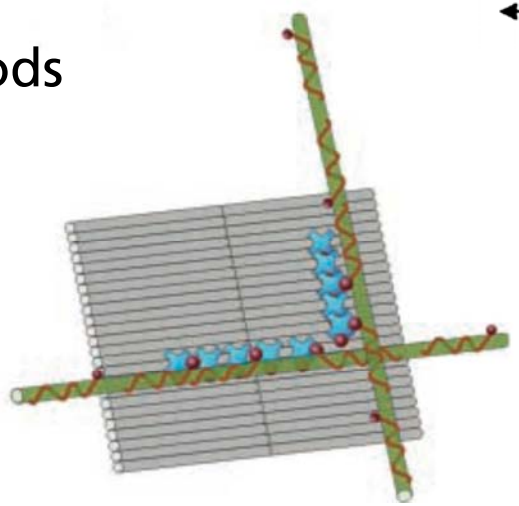
- Motivation: Next-generation biosensors

- Single-walled carbon nanotubes
  - Exceptional properties for ultra-sensitive biosensors
  - Alignment & ordering necessary for optimization
  - Bottom-up self-assembly methods









(Eskelinen *et al.*, Small, 2011)

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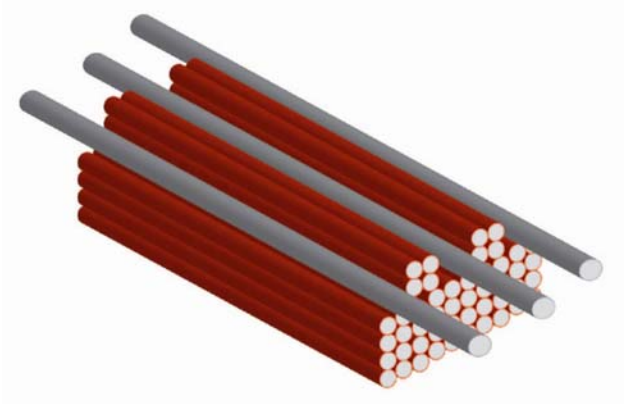
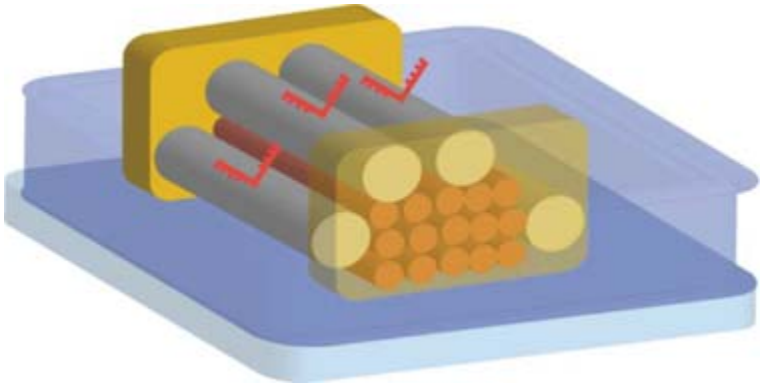
DNA-based templating of biosensor components

- Optimization of topology via rapid-prototyping of DNA substrates
  - Automated “DNA Brick” assembly
- Development and optimization of SWNT-nanotemplate attachment
  - Priority: retain electrical properties of nanotubes
- Corollary: modular DNA-carbon nanotube components for delivery, thermal-based therapy, etc.





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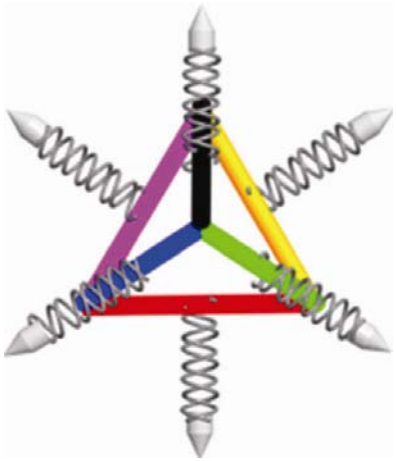
Therapeutics: targeted drug delivery

- Motivation: Paul Ehrlich's "Magic bullet"
  - Targeting/recognition
  - Specific release/action
  - Multiple functions

- Delivery of small nucleotides
  - RNAi therapies
  - Common platform for cancer & other disease therapies



(Lee *et al.*, Nat. Nanotech., 2012)

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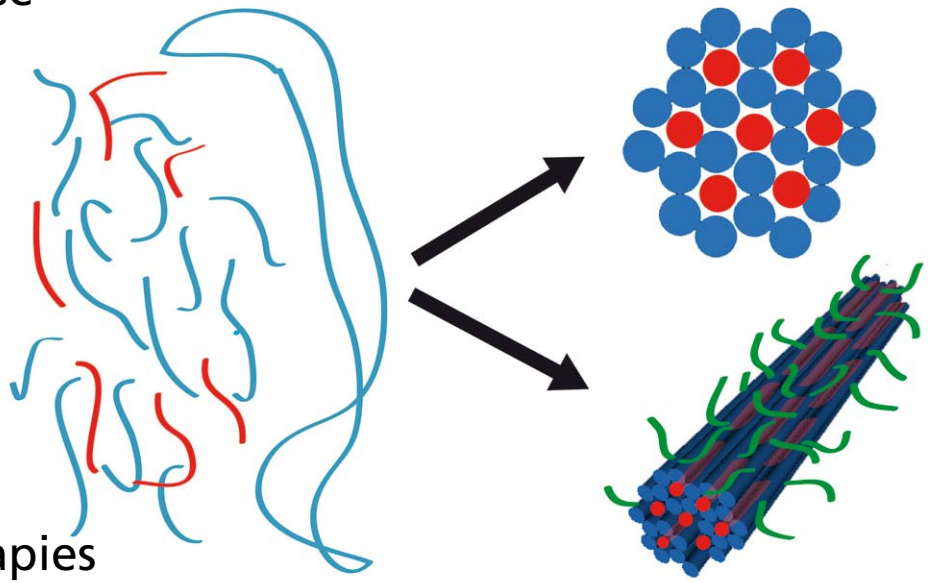
DNA-based carriers for small nucleotides

- Loading on embedment principle
  - Molecular symmetries of DNA/RNA/etc. for high packing
  - Tunable degradation-based release
- Multiple functionalities
  - Targeting/recognition
  - Uptake/cell penetration
  - Protection & biostability
- Multi-stage & multi-component therapies
  - Targeted thermal-based therapies
- In conjunction with RIBOLUTION



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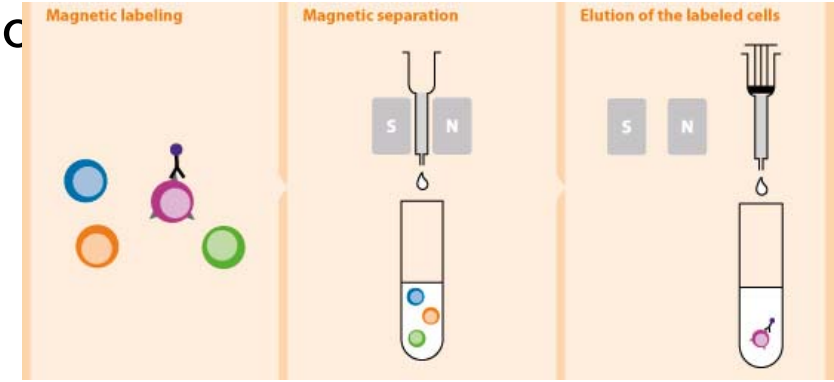
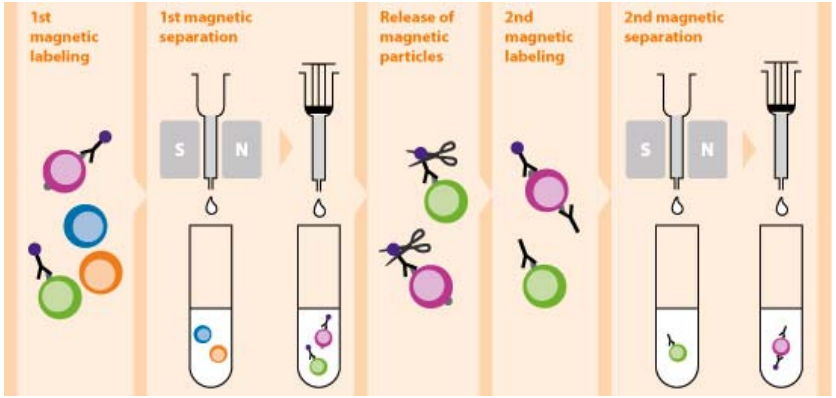
Tools: bead-based sorting of cell populations

- Motivation: Recognition and sorting o
  diverse cell populations



- Bead-based sorting (e.g., MACS)
  - Simple, straightforward, universal
  - Single marker or multiple steps
  - “AND-gate” recognition



(Miltenyi biotech)

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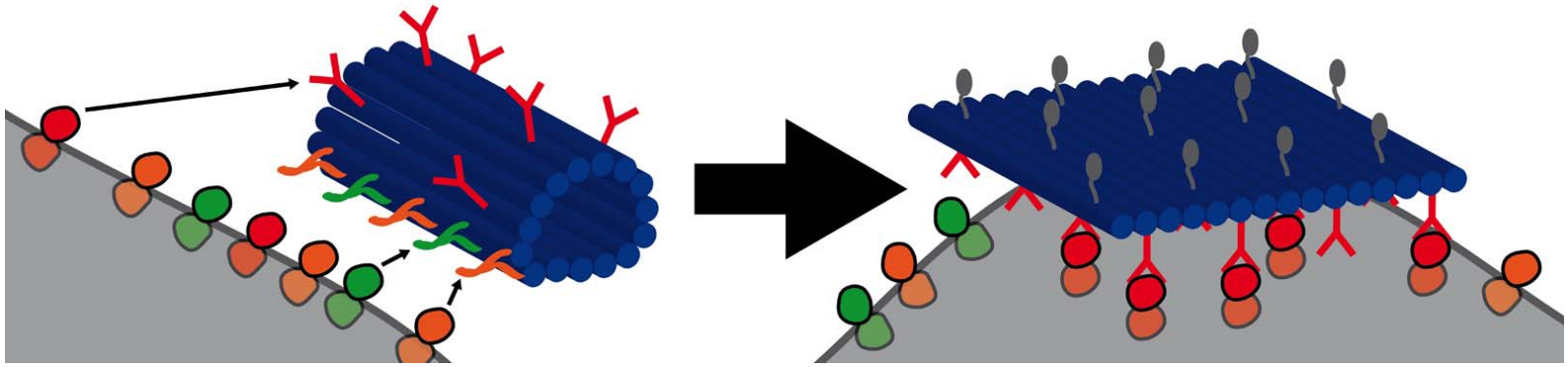
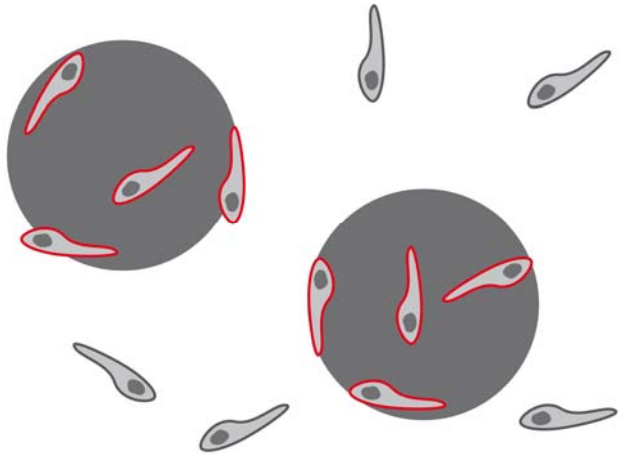
“AND-gated” recognition and mechanical coupling



- Recognition of multiple surface markers
  - Antibody binding to surface
  - Molecular “locks”
- Coupling into bead-based separation
  - “AND-gated” exposure of attachment points



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Market view

- DNA nanosystems: open but emerging industry presence

- Global biosensor market (Industry Experts analysis)
  - Estimated at $8.5 billion in 2012
  - Doubling of volume ($16.8 billion) by 2018

- Global drug delivery market estimations (Cientifica analysis)
  - Estimated $136 billion by 2021
  - 60% nanocarriers

- Cell sorting/separation market
  - Major presence in Germany (Miltenyi, Partec, Pluriselect)

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Closing points

- DNA is a programmable material which can be used to create precise nanometer-sized shapes beyond any other currently available technique

- We aim to use this technology to generate devices for aiding in diagnostic/therapeutic application and biological research

- Corollary projects
  - Immunomodulation, cancer vaccines, DNA vaccines, cancer marker analysis, optical systems

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Credits

- Fraunhofer IZI
  - Christoph Schneider M.Sc.
  - AG Nanotechnologie (Kuhlmeier)
  - Abteilungs- & Institutsleitung
- Partners
  - Yale MB&B (AG Prof. Regan)
  - LMU (AG Prof. Liedl)
  - Uni-Köln (AG Prof. Neundorf)
  - Ben-Gurion (AG Eyal Nir)
- LMU München
  - Prof. Tim Liedl
  - Christian Engst M.Sc (FhI EMFT)
- Funding
  - Fraunhofer Attract

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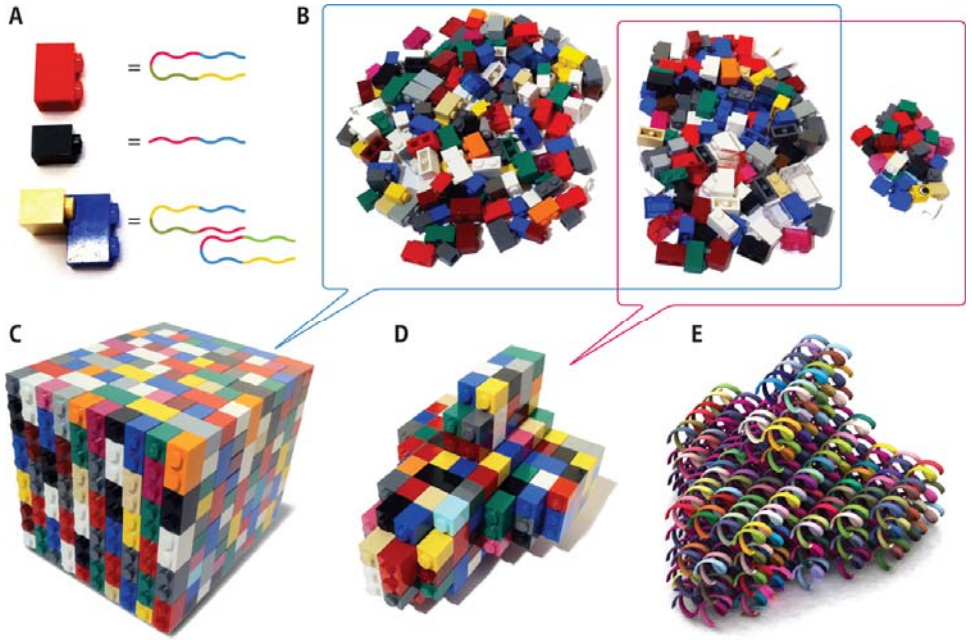
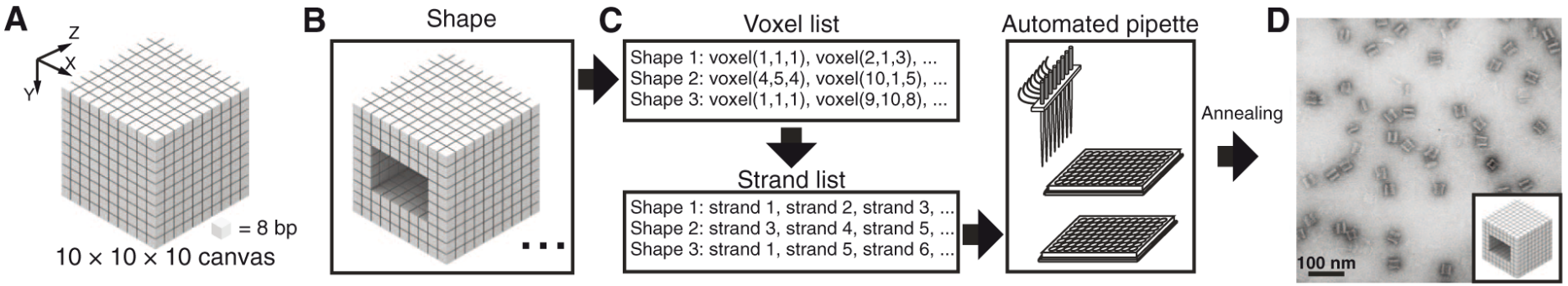
DNA Bricks

LEGO-like DNA bricks

- Rapid prototyping
- Short synthetic strands
- Sculpting by carving
- **Adaptable 2D/3D canvas**
- Automation of workflow



(Gothelf, Science, 2012)



(Wei *et* al., Nature, 2012; Ke *et al.*, Science, 2012)

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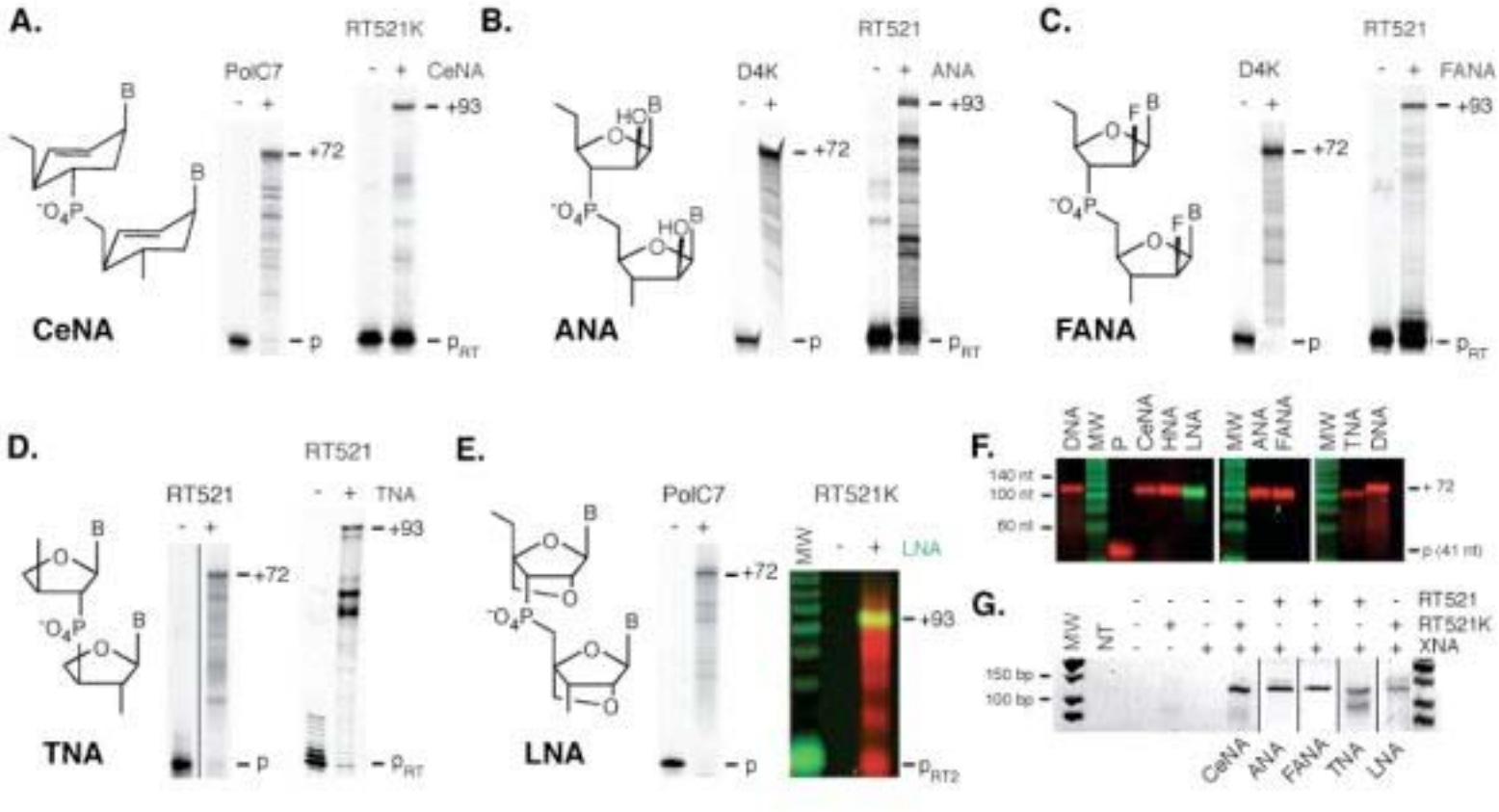
Future: engineered “xeno”-nucleic acids

Pinheiro *et* al.: “Synthetic Genetic Polymers Capable of Heredity and Evolution”



(Pinheiro *et al.*, Science, 2012)

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