Self-assembly of Microsystems
EDMI Micro-724

EPFL, September 2025

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University of Washington

- Founded November 4, 1861
- Public research university
  - Campuses in Seattle, Tacoma, Bothell
- University community*
  - Instructional faculty: 5,800
  - Staff: 16,000 (+18,000 health workers)
  - Student enrollment:
    - 52,000
    - Undergraduate: 35,000
- Research*
  - Budget: $1.7B grants and contracts (total UW budget $6B)
  - Since 1969, among top 5 US institutions in research funding
  - Since 1992, 4 Nobel Prize winners
  - Ranked #8 overall / #2 among public institutions by US News & World Report

* FY 2024 numbers

INSTITUTE FOR NANO-ENGINEERED SYSTEMS

- Institute founded in 2016
  - Focus areas
    - Integrated photonics
    - Scalable nanomanufacturing
    - Augmented humanity
  - NanoES nano.uw.edu

- Partner institutes
  - Clean Energy Institute (CEI)
  - Institute for Protein Design (IPD)
  - Molecular Engineering and Sciences (MolES)

- Member, NSF National Nanotechnology Coordinated Infrastructure
  - Washington Nanofabrication Facility [wnf.uw.edu](wnf.uw.edu)
  - Molecular Analysis Facility moles.washington.edu/facilities/molecular-analysis-facility/

National Nanotechnology Coordinated Infrastructure

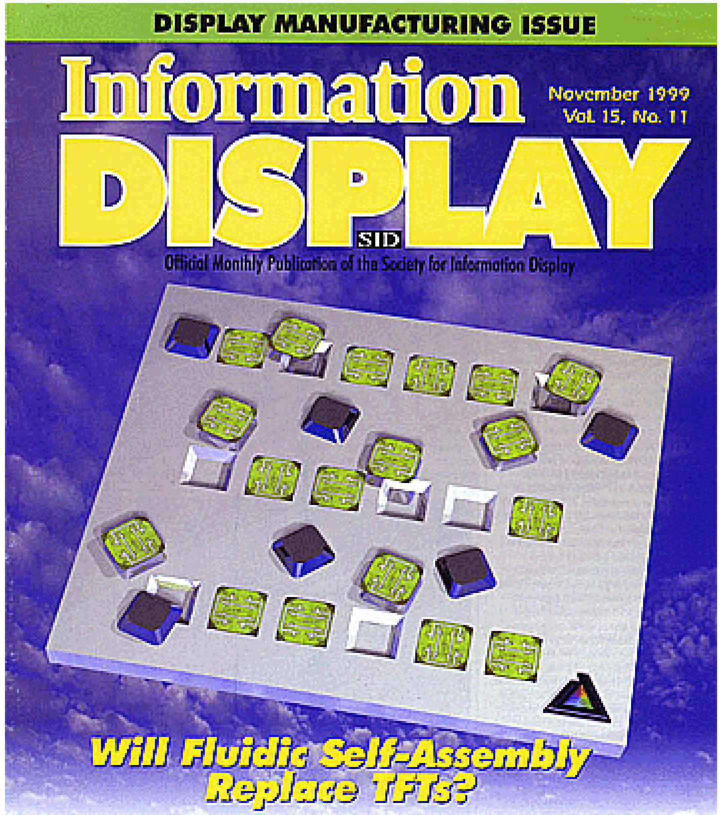
- NNCI sites provide researchers from academia, small and large companies, and government with access to university user facilities with leading-edge fabrication and characterization tools, instrumentation, and expertise within all disciplines of nanoscale science, engineering and technology.
- 16 sites, 29 facilities, 2000 tools, more than 1 million user hours in 2021
- Supported by the US National Science Foundation with $160M

nnci.net

Part I:
Self-assembly Basics

Motivation; overview; history; examples

Selfassembly of Microcomponents (~30 years ago)



DISPLAY MANUFACTURING ISSUE

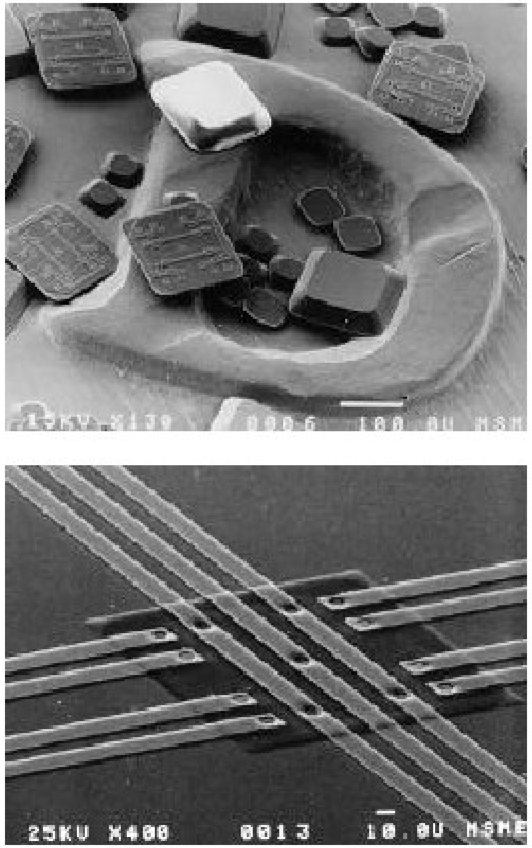
Information DISPLAY

November 1999
Vol. 15, No. 11

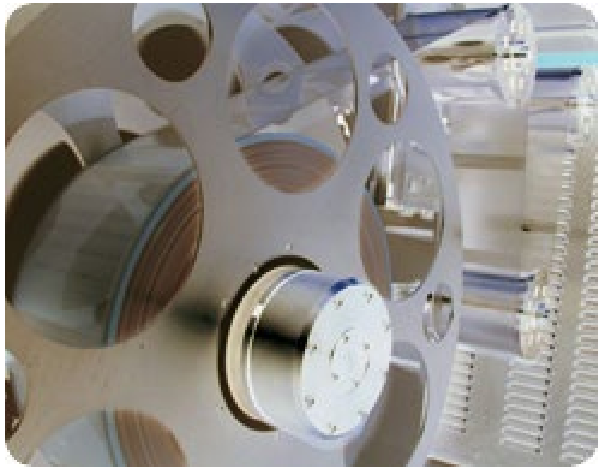
SID

Official Monthly Publication of the Society for Information Display

Will Fluidic Self-Assembly Replace TFTs?

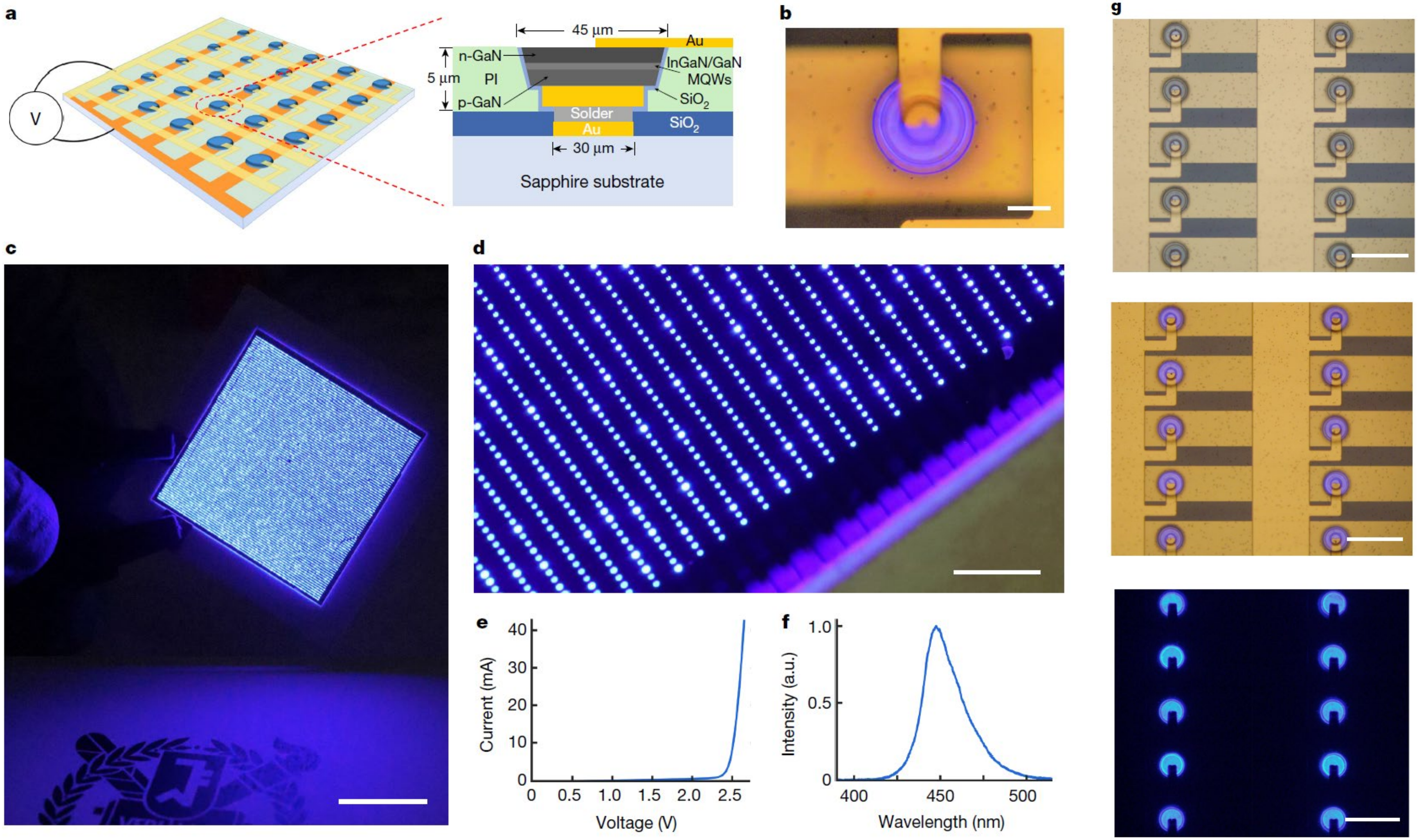


“Nanoblocks”: fluidic agitation and assembly by gravity and shape matching
(Yeh, Smith *IEEE MEMS* 1994)



Assembly of RFID tags at 2M/hr (Alien Technology)

Selfassembly of Microcomponents (now)



FSA of microLED displays (Lee et al. *Nature* 2023)

What Is Self-assembly?

Is it …

- chemistry?
- materials science?
- nanotechnology?
- tossing components into a box, shaking it, and hoping that after some time, the assembled product appears?

What Is Self-assembly?

- “The autonomous and spontaneous organization of components into patterns and structures” – George Whitesides
- “The science of things that put themselves together” – John Pelesko
- “A scalable manufacturing method for heterogeneous integrated microsystems”

Why Study Self-assembly?

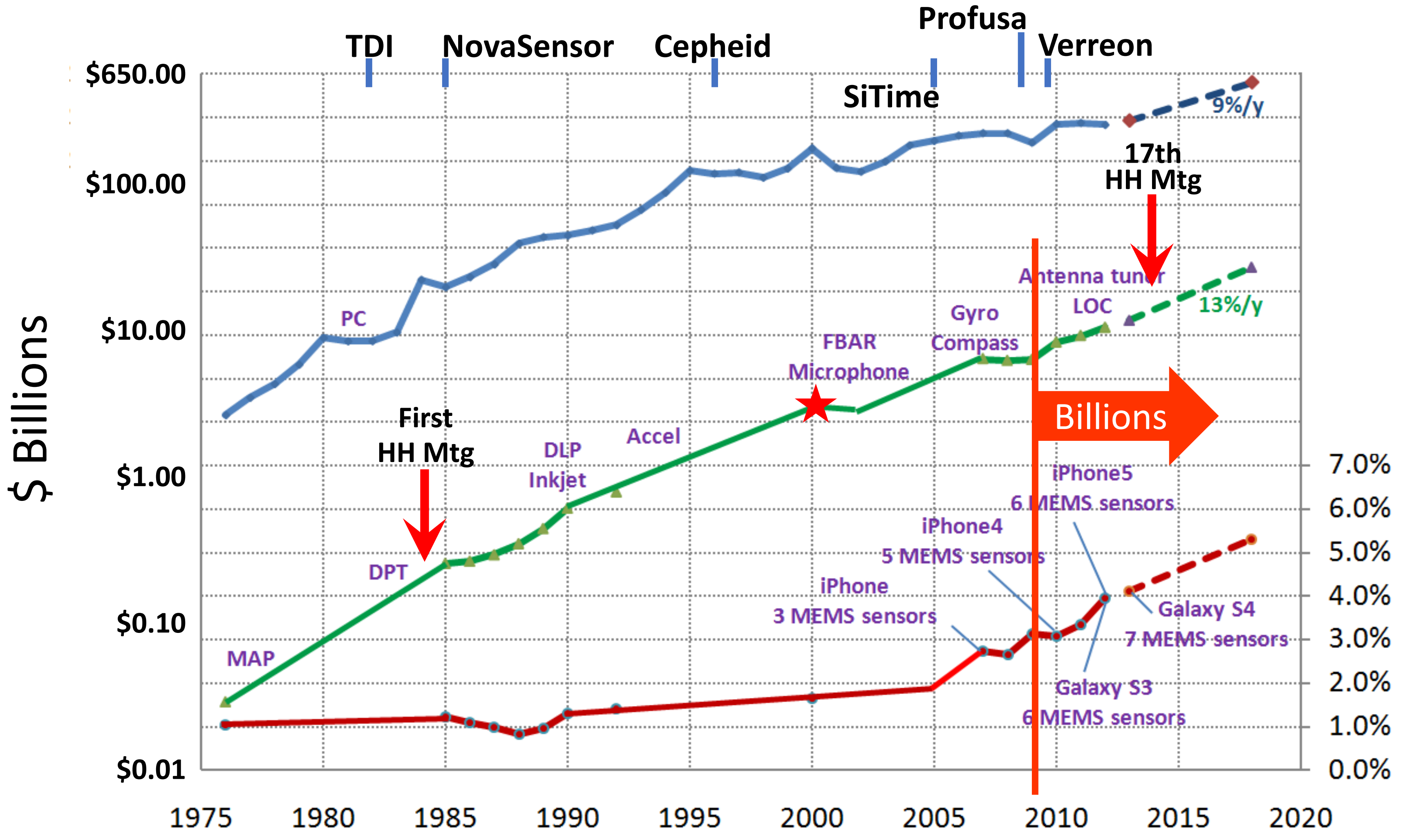
- Because it occurs frequently in nature (organic and inorganic).
- Because it is a concept that is equally interesting for mathematicians, chemists, computer scientists, biologists, electrical engineers, and others.
- Because it may hold enormous potential for the development of novel manufacturing techniques, especially at small scales.

Why Is Self-assembly Important?

- Microfabrication is, for the most part, a parallel manufacturing technology
  - Key to success of VLSI electronics
- Packaging is a bottleneck as it requires sequential processing steps
- This is an increasing problem, esp. for a new generation of hybrid integrated microsystems
  - The trend to microLED displays has created additional opportunities
- Unlike pick-and-place, self-assembly is a parallel manufacturing technology
  - Enabler of complex heterogeneous microsystems

Global SEMI and MEMS (Component) Markets

Blue: SEMI, Green: MEMS, Red: MEMS/SEMI (right axis)

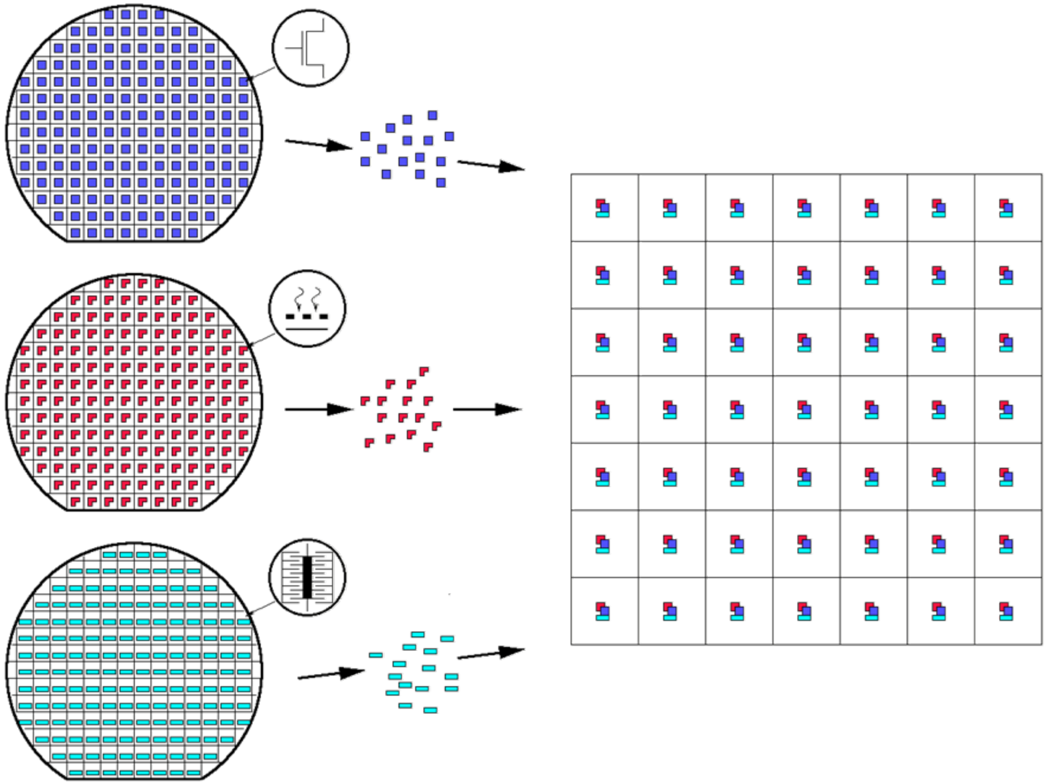


Janusz Bryzek, 2013

Slide courtesy of Kurt Petersen (Hilton Head 2014)

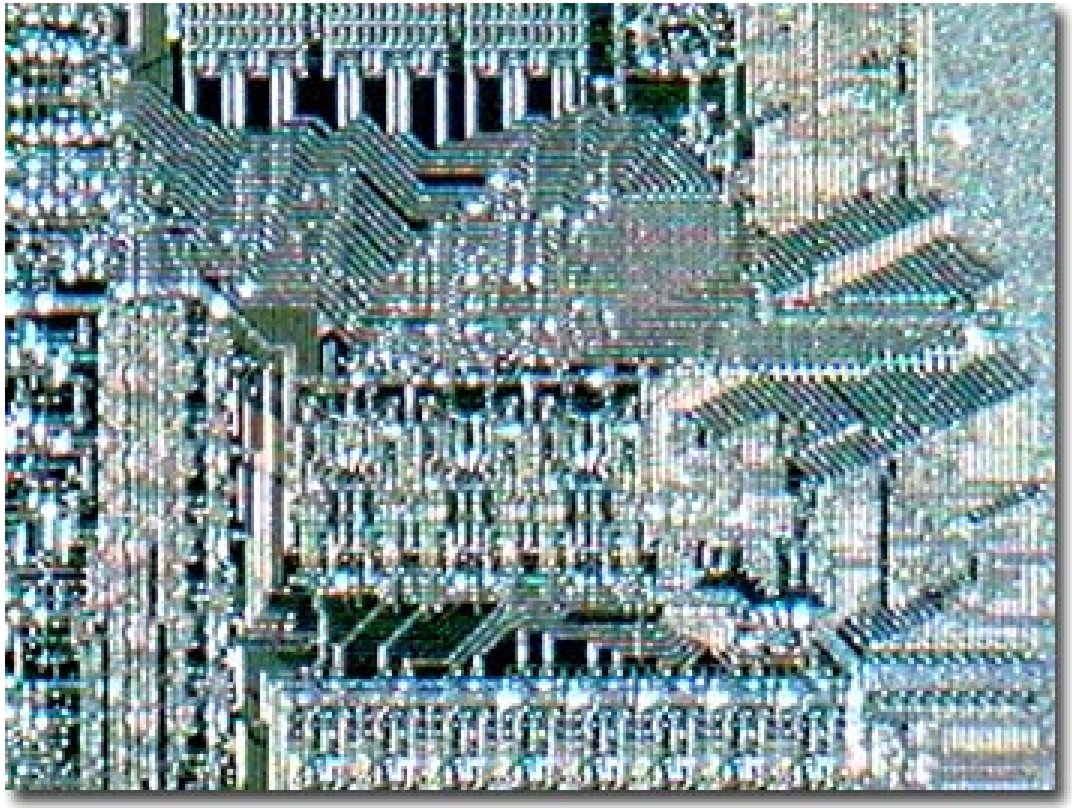
Micro-assembly

- Very large numbers of very small components
- Independent parallel fabrication of components
- Fabrication at high density, assembly at lower density
- Hybrid systems built from standard components



Enabling technology for complex heterogeneous microsystems

Circuit City



Integrated circuit, microscopic view

City landscape, macroscopic view

Key Features of Self-assembly

1. Structured particles (components)
   - The basic building blocks that form an assembly; their structure ultimately determines the assembly product.
2. Binding force
   - Holding the particles together.
3. Environment
   - Controlled conditions that provide the framework for physical interactions and lead to reproducible results.
4. Driving force
   - Provides the energy to keep the assembly going; typically, it has a stochastic nature (e.g., vibration, oscillation, noise, heat, …).

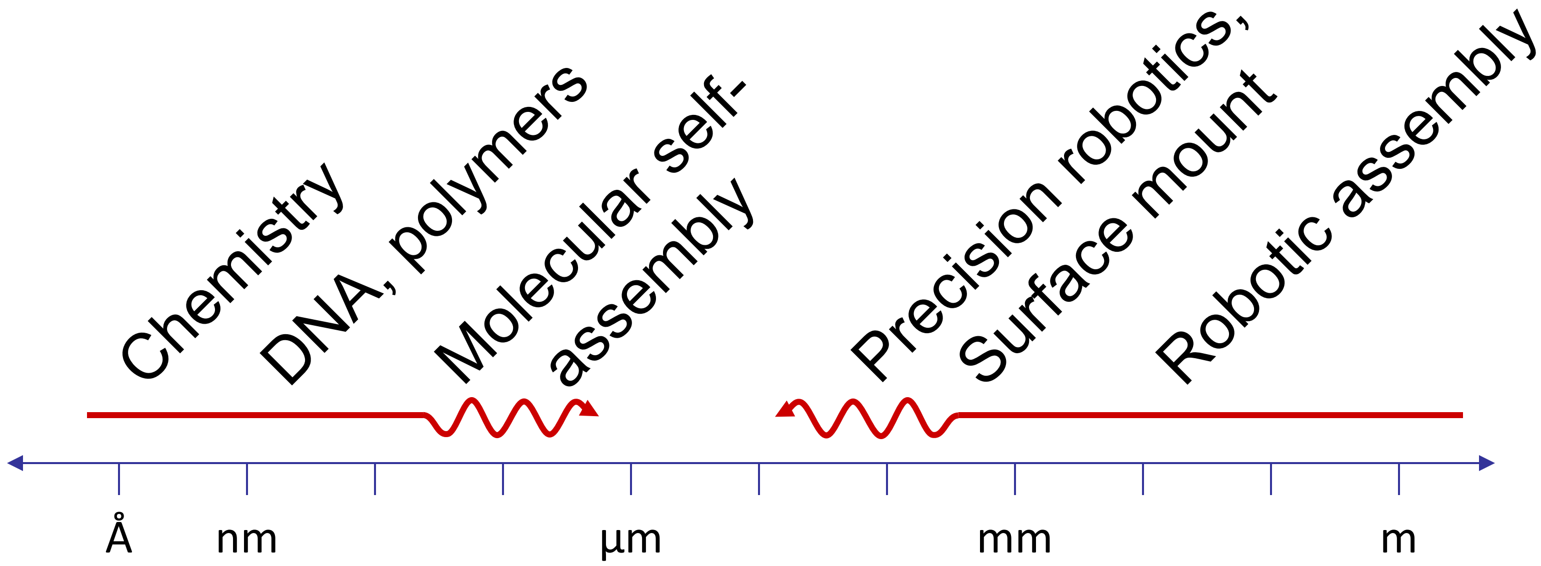
Other Features of Self-assembly

- Is there anything missing?
  - Reduction of entropy
  - Parallelism
  - Performance metrics (time, yield)
  - …

Motivation

In the micro range (approx. 0.1 μm – 100 μm) there exists a “no-man’s-land” for engineered assembly

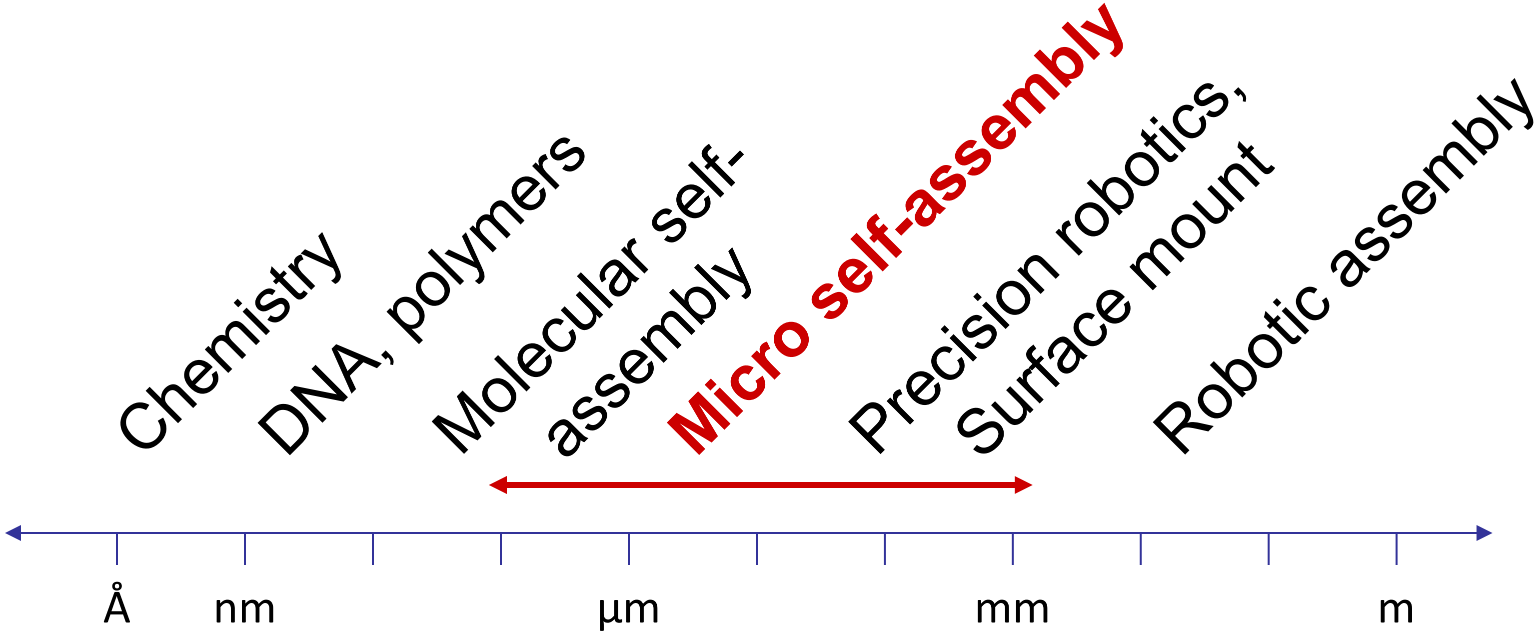
- Conventional robots get very expensive
- Chemical synthesis cannot produce non-periodic or heterogeneous assemblies



Motivation

Goals:

- High volume, flexible manufacturing
- Complex hybrid microsystem integration



Chemistry

DNA, polymers

Molecular self-assembly

Micro self-assembly

Precision robotics, Surface mount

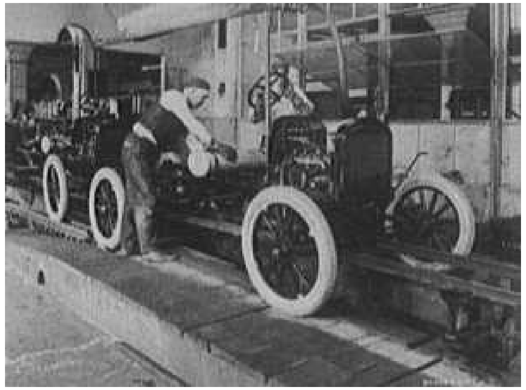
Robotic assembly

Å nm µm mm m

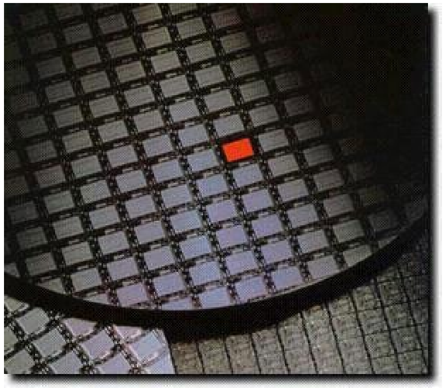
Motivation

Self-assembly offers a paradigm shift in the manufacture of complex, heterogeneous microsystems that integrate sensing, actuation, computation, and communication.

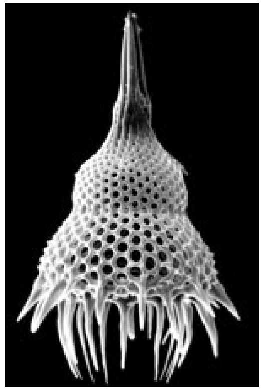
“0D”
manual labor



“1D”
conveyor belt



“2D”
VLSI



“3D”
self-assembly in nature
Radiolarium l. maritalis

Landmarks in Self-assembly

1930s Turing develops the theory of universal computation

1950s von Neumann develops theory of automata replication

1953 Watson & Crick discover the structure of DNA

1955 Fraenkel-Conrat & Williams self-assemble the tobacco mosaic virus in a test tube

1957 Penrose & Penrose construct a simple self-replicating system

1961 Wang develops "Wang tiles" demonstrating the equivalence of tiling problems and computation

Landmarks in Self-assembly

1991 Seeman & Chen self-assemble a cube from DNA

1991 Cohn, Kim & Pisano create self-assembling electrical networks

1993 Yeh & Smith file patent on fluidic self-assembly (FSA)

1994 Adleman launches field of DNA computation by using DNA to solve a Hamiltonian path problem

1994 Shimoyama & Miura's group model milli-scale self-assembly with chemical reaction kinetics

1996 Shimoyama & Miura's group demonstrates micro-scale self-assembly using surface tension

Landmarks in Self-assembly

2000 Whitesides's group self-assembles 3D electrical networks from millimeter-scale polyhedra

2003 Böhringer's group modulates surface energy to achieve programmable self-assembly

2004 Shih adapts the methods of Seeman to self-assemble a DNA octahedron

2004 Winfree & Rothemund self-assemble a Sierpinski triangle from DNA

2006 Rothemund folds DNA origami

… see lectures by Juergen, Francesc, and Massimo

Taxonomy of Assembly

- Serial assembly
  - One or more components (identical or different) assembled one-by-one
  - Manual, tele-operated, or autonomous
  - Common technique in manufacturing: pick-and-place
- Parallel assembly
  - Multiple components (identical or different) assembled simultaneously, or in multiple batches
  - Common techniques in manufacturing and nature:
    - synthesis (chemistry)
    - growth (biology)

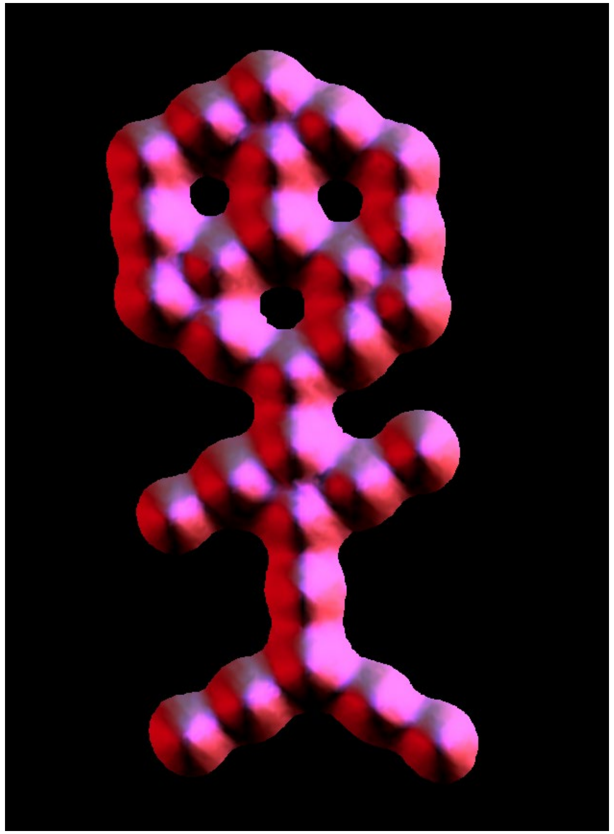
Taxonomy of Assembly

- Parallel assembly
  - Deterministic: order of assembly and destination of components is uniquely determined in advance
  - Stochastic: order of assembly or destination of components is determined in part by a random process

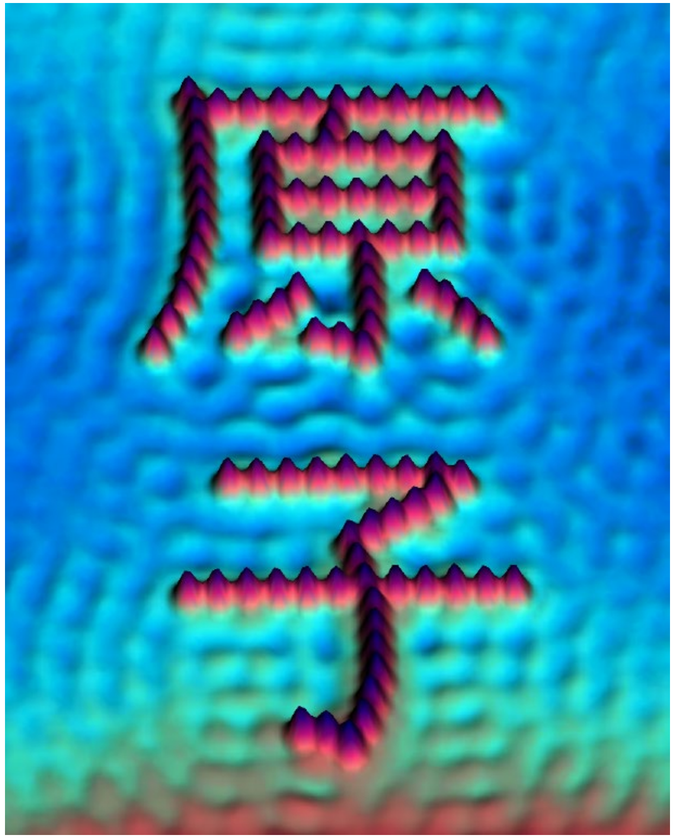
- Compare with
  - Motion planning (robotics)
  - Annealing (chemistry, materials science)

Example: Serial, Deterministic Nano-assembly by STM

Carbon Monoxide on Platinum (111)
[Zeppenfeld & Eigler]

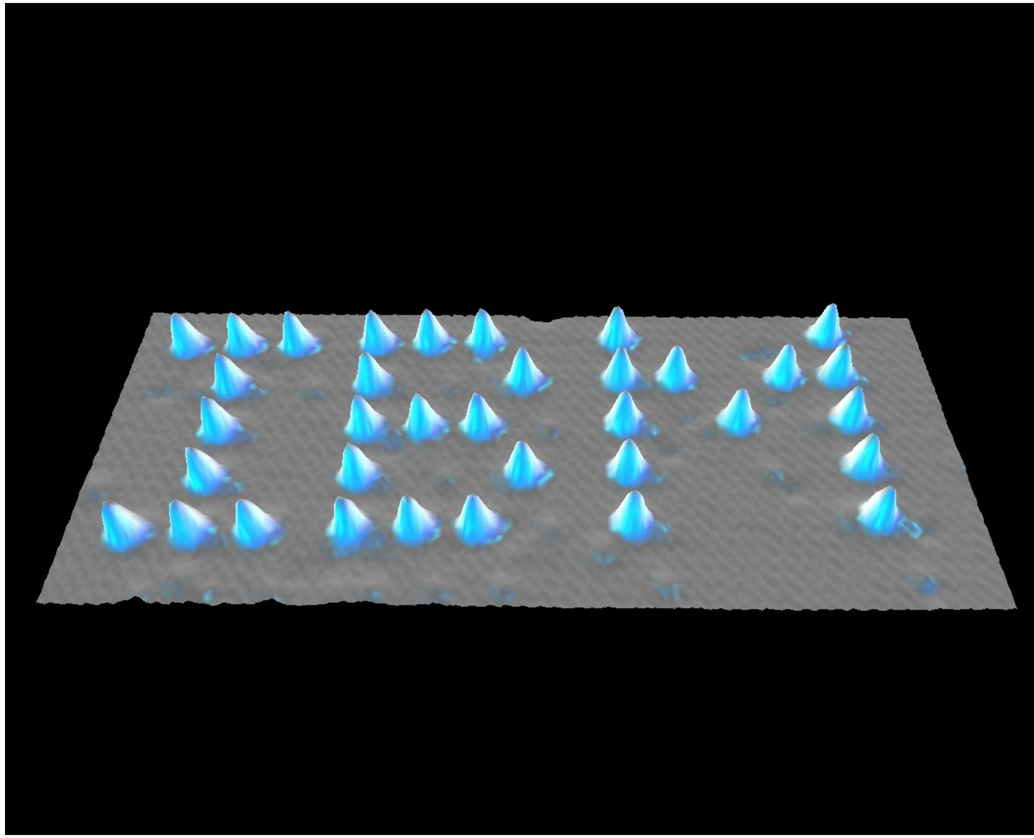


Iron on Copper (111)
[Lutz & Eigler]



Xenon on Nickel (110)

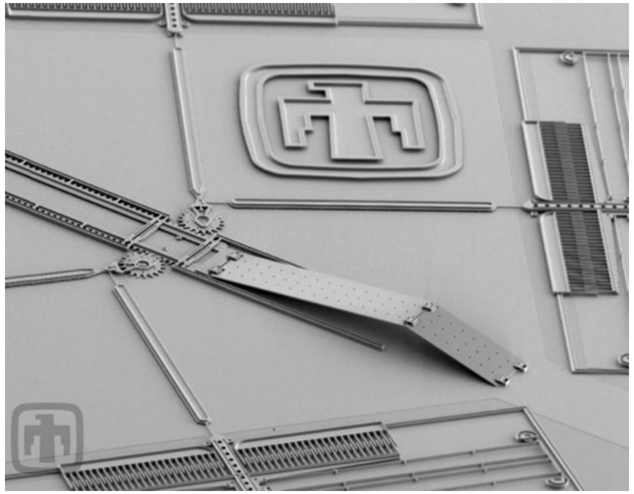
[Eigler, Schweizer ‘89]



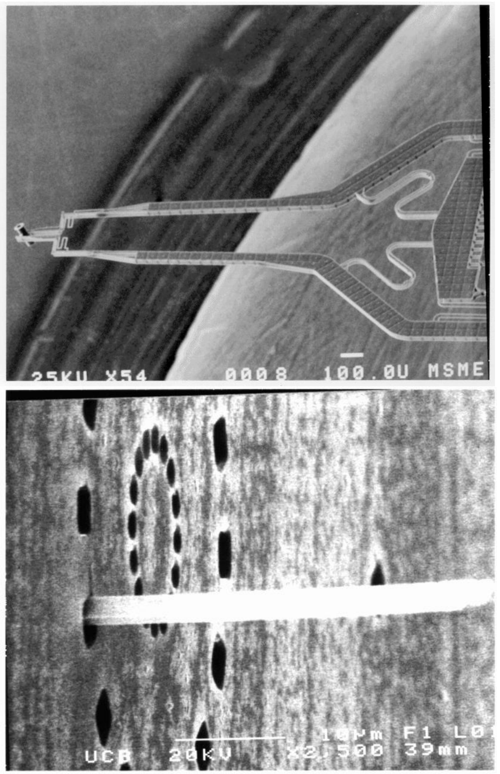
Examples: Deterministic Parallel Assembly

- Self-assembling 3D structures
  - "micro origami"
  - [Pister et al. '92], [Syms et al. '95, '98], [Fujita et al. '96]
- Flip-chip, wafer-to-wafer transfer
  - Combine devices from two (or more) wafers
  - [Cohn & Howe '97], [Singh et al. '97]
- Microgripper arrays
  - Parallel pick-and-place
  - [Keller & Howe '97]

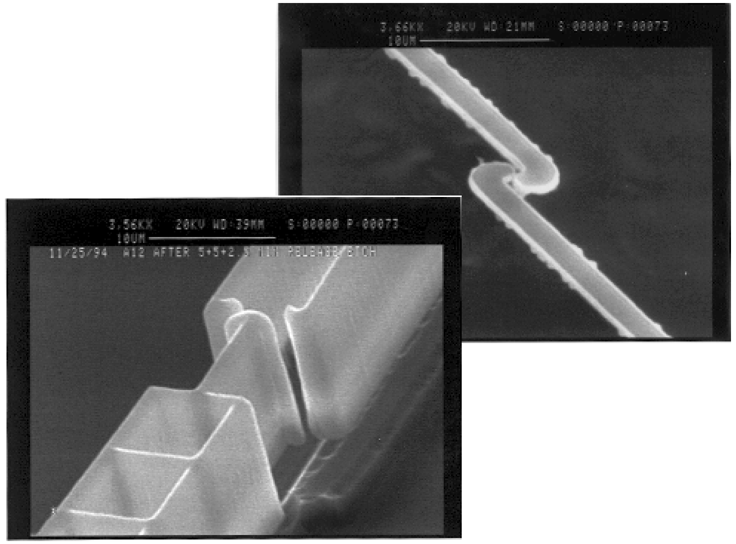
Deterministic Parallel Assembly



Self-deploying Micromirror Assembly. Sandia National Labs, Albuquerque '98



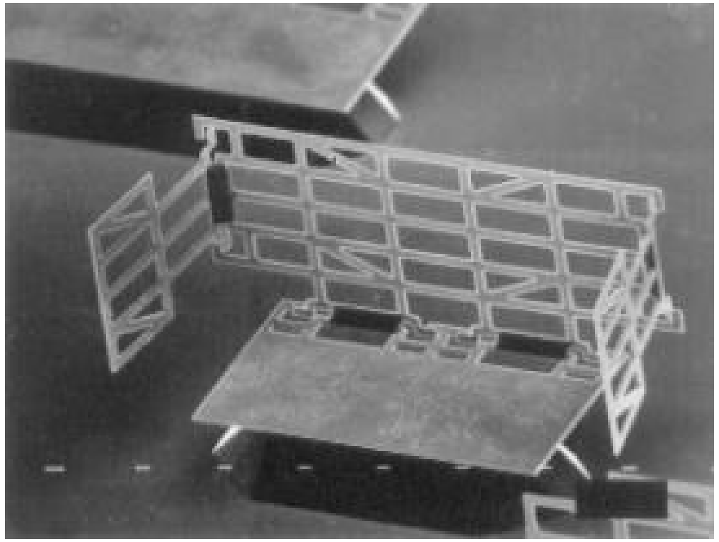
Micro-tweezer in HexSil technology. Keller, Howe, UC Berkeley '98

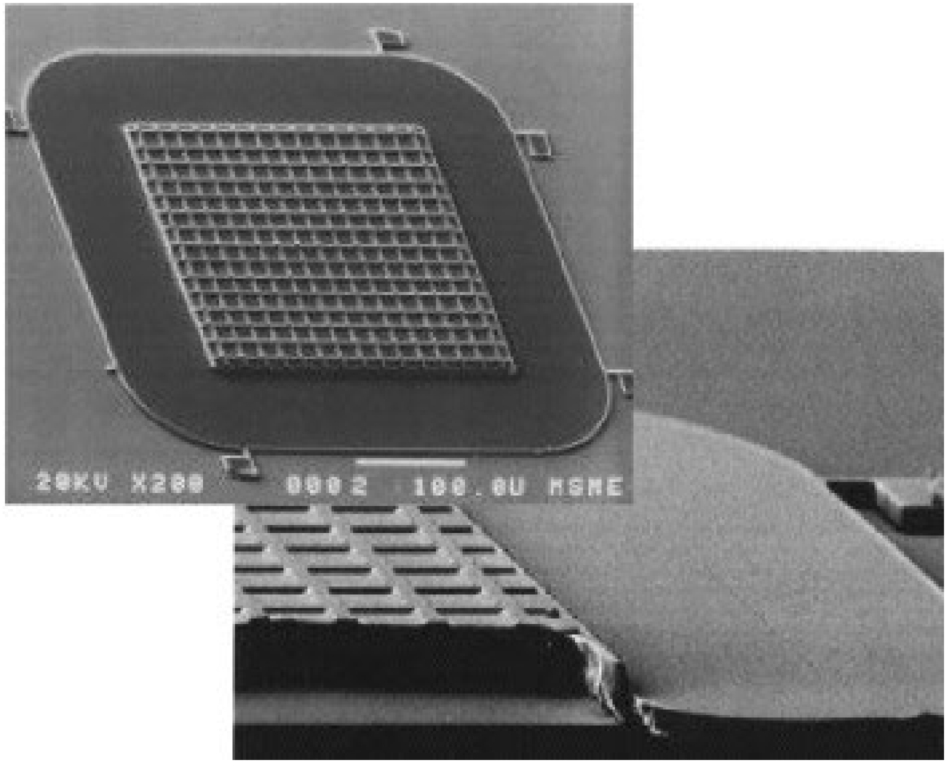


Micro snap fasteners. Böhringer, Prasad, Donald, MacDonald, Cornell University '95

Deterministic Parallel Assembly

<u>Solder reflow assembly.</u>
R. Syms, Imperial
College, London, '95



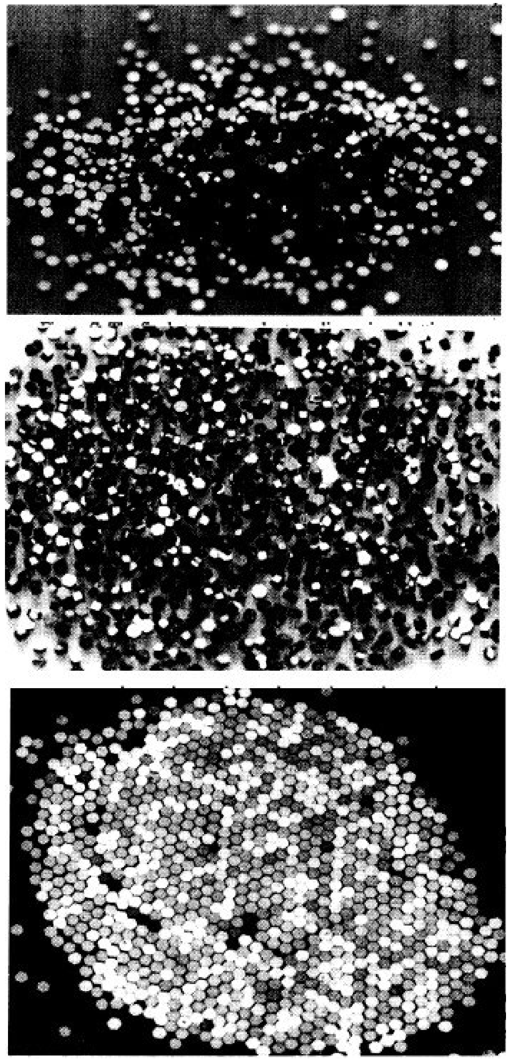


<u>Flip-chip assembly and hermetic sealing.</u> Cohn, Liang, Howe, Pisano, UC Berkeley, '97

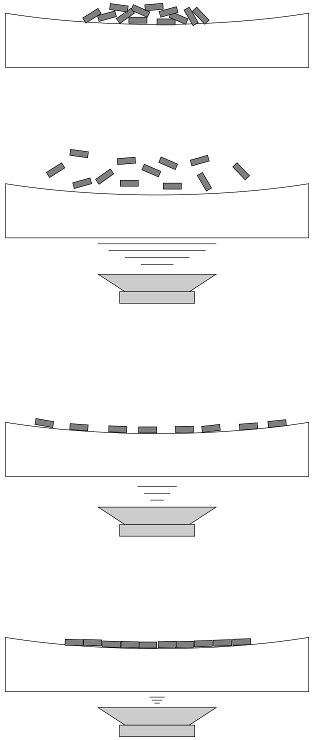
Examples: Stochastic Parallel Assembly

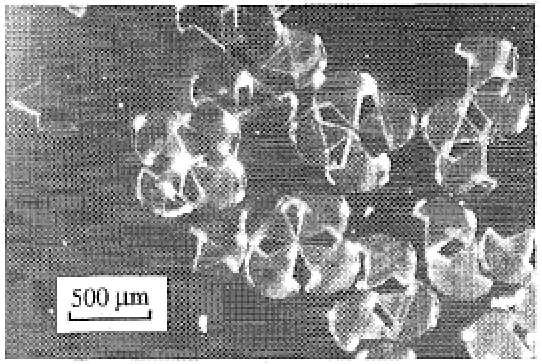
- Shape matching
  - Early work: hexagon packing [Cohn et al. ‘91], fluidic self-assembly [Yeh, Smith ‘94], [Hosokawa et al. ‘96]
  - Lock-and-key assemblies [Rothemund ‘00…], [Fang, Böhringer ‘06]
- Capillary force driven
  - 3D circuits [Gracias et al. ‘00], adaptive optics [Srinivasan et al. ‘02], [Jacobs et al. ‘02], programmable assembly [Xiong et al. ‘03]
- DNA origami
  - [Rothemund ‘06]

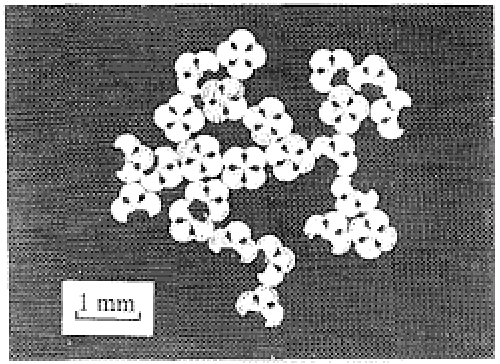
Stochastic Parallel Assembly



Cohn, Kim, Pisano ’91

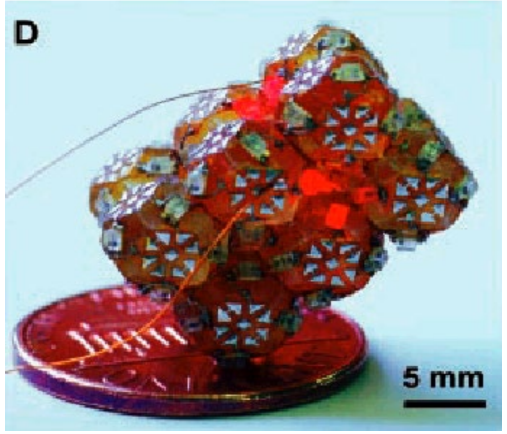




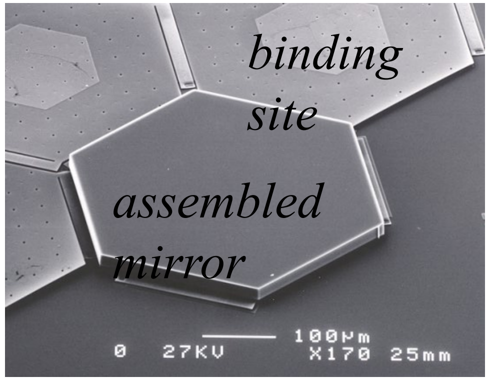


Hosokawa,
Shimoyama, Miura ‘96

Capillary Force Driven Self-Assembly



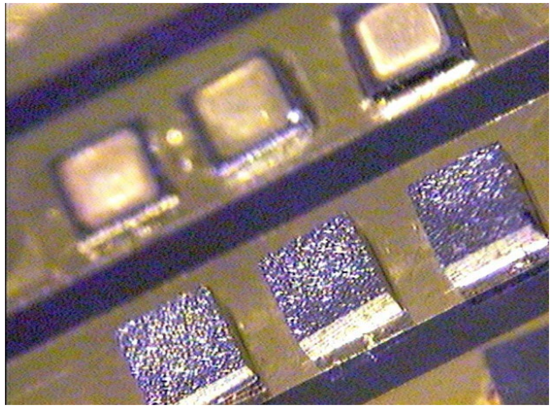
3d circuit
Gracias et al.,
Science ‘00



Srinivasan et al.,
IEEE Quantum El. ‘02

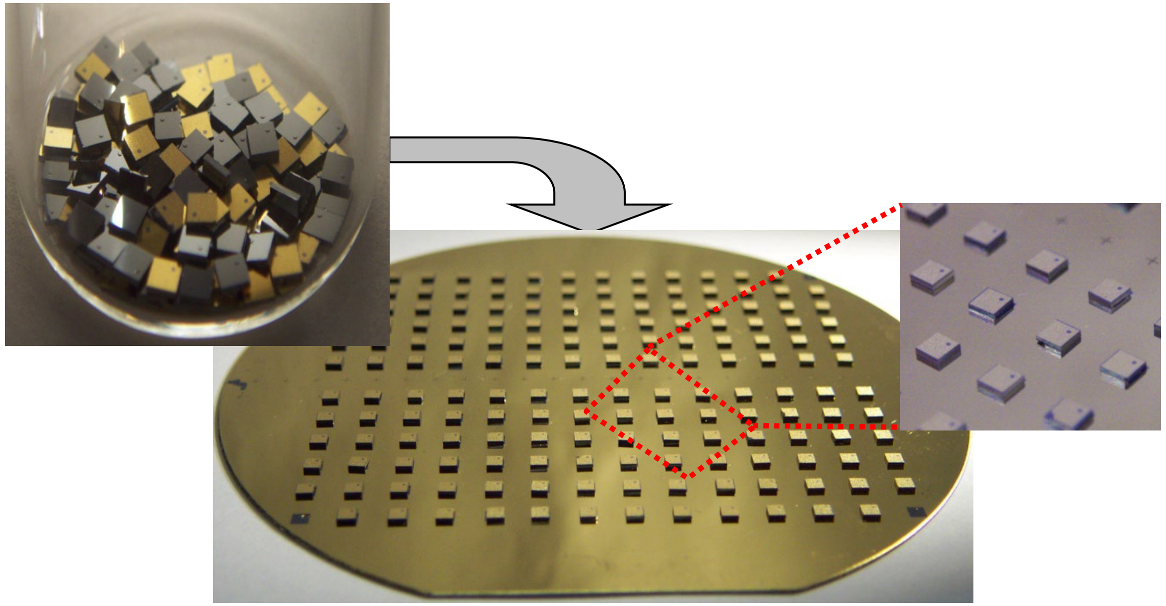
Flexible display
Jacobs et al.,
Science ‘02

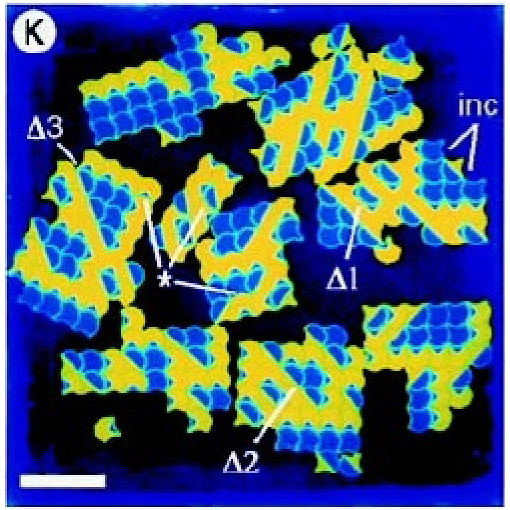
Multi-batch
Xiong et al.
JMEMS ‘03



Lock-and-key Self-Assembly

Fang et al.
JMEMS ‘06

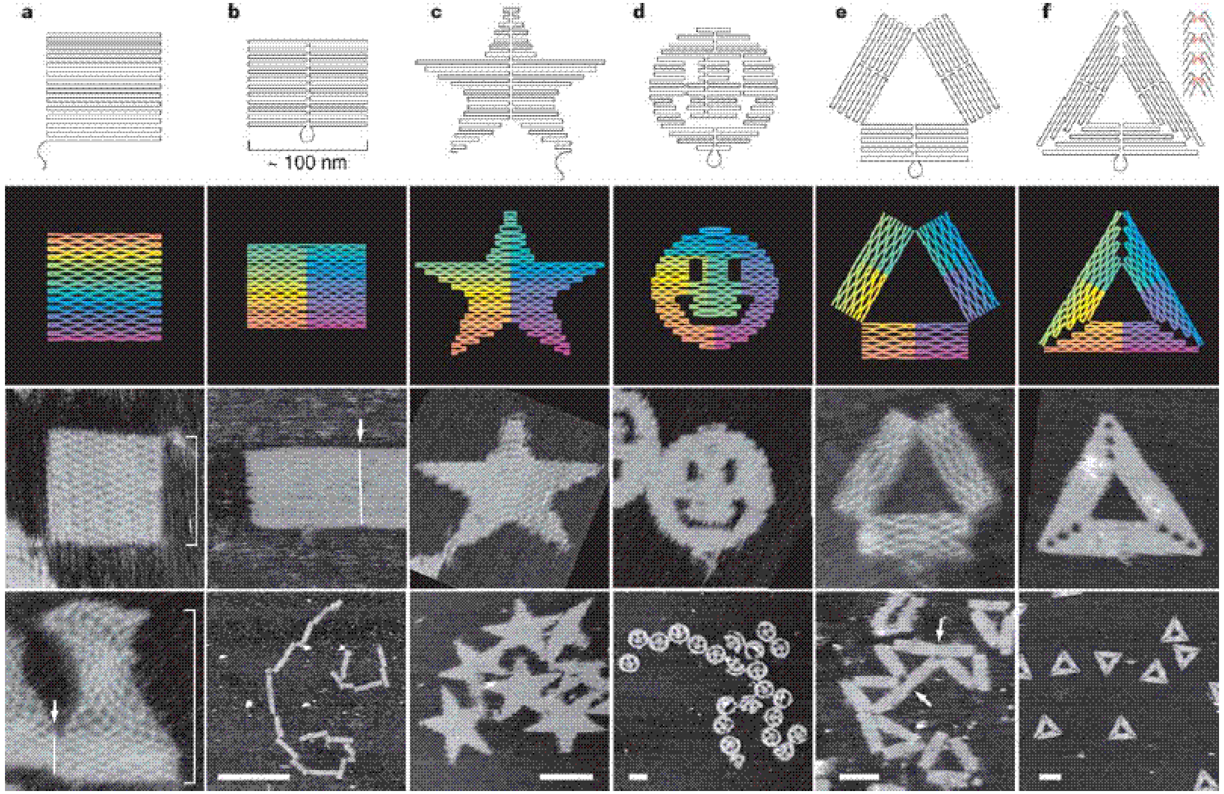




Logic assembly
Rothemund *PNAS* ‘00

Nano Self-Assembly Systems

DNA Origami
P. Rothemund
Nature ‘06

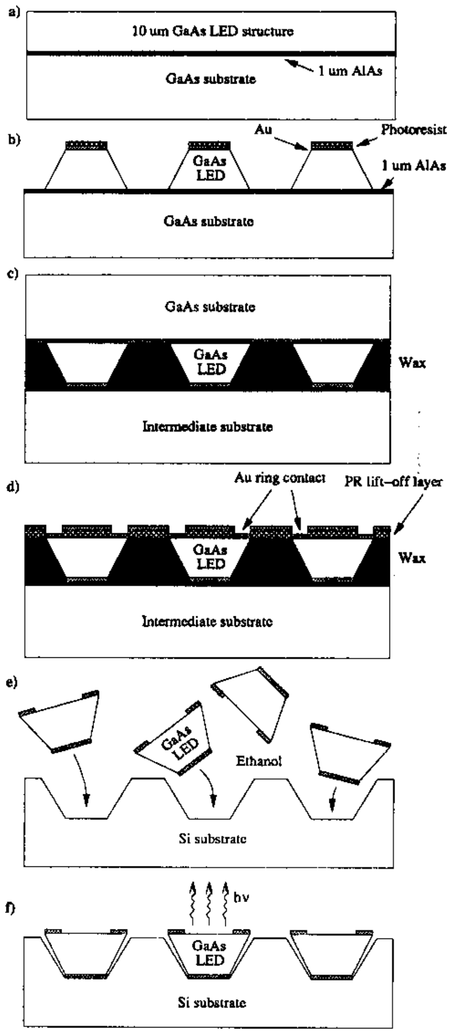


Also see work by Winfree, Dwyer, Reif, Seeman, and many others

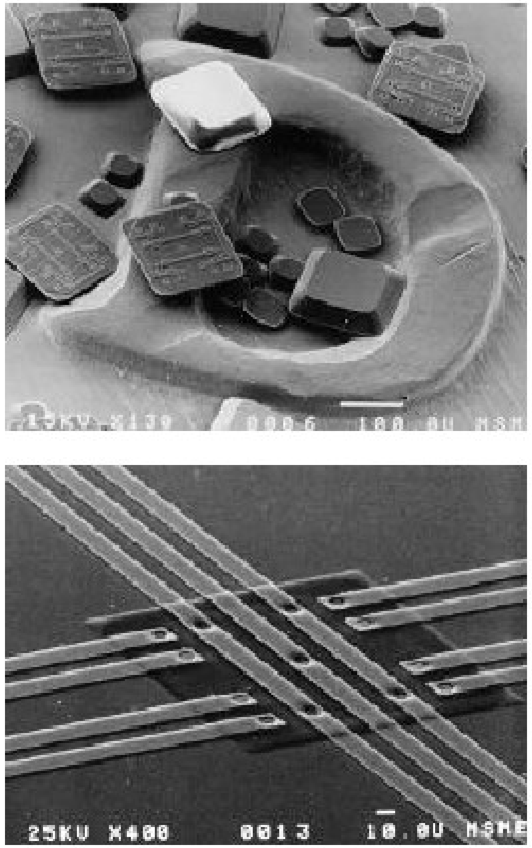
Template Driven Assembly

Fluidic self-assembly (FSA)

- H.-J. J. Yeh, J. S. Smith, “Fluidic Self-assembly of Microstructures and its Application to the Integration of GaAs on Si”, *IEEE MEMS*, 1994
    - Goal: integrate GaAs components onto Si substrate
    - Anisotropic wet etching in Si forms pyramid-stump shaped holes
    - GaAs components with (almost) matching shapes self-assembly
    - Subsequent formation of electrical connections
    - Extension to molded plastic substrates
- Patented in 1996: Smith, Yeh, Method for fabricating self-aligned microstructures, US Patent 5,545,291.



Fluidic Self-assembly (FSA)



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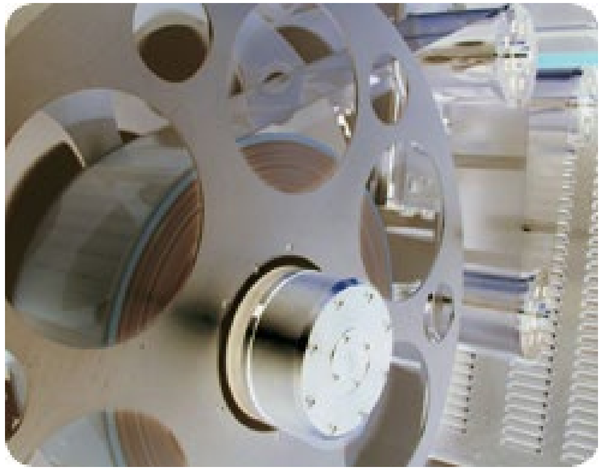


Assembly of RFID tags at 2M/hr (Alien Technology)

Fluidic Self-assembly (FSA)

Original assembly principle:

- Large-scale substrate with assembly sites, positioned at a sloped angle inside a water bath
- Parts delivered with flow of water
- Sink and slide over substrate (gravity driven), captured by assembly sites
- Additional parts are not captured because of good shape match between part and site
- Capillary forces during drying help alignment
- Evaporation and patterning of thin film metal (Al) for electrical connectivity

Fluidic Self-assembly (FSA)

Modified assembly principle:

- Replace fixed substrate by “endless” polymer film with embossed assembly sites
- Rolls of film with width from tens of cm to meters
- Continuous assembly process with parts feeding and recycling in water
- Lamination, laser patterning of vias, printing of metal patterns
- Assembly rate: 2M / hour

Fluidic Self-assembly (FSA)

- Alien Technology original business plan: self-assembly of high-resolution large-scale displays

ALIEN®

- Si amplifiers on molded plastic
- mating part shapes with gravity as driving force
- sub-micron alignment
- 99.9999% yield
  - 4-fold symmetry
  - double redundancy
  - excess supply of parts

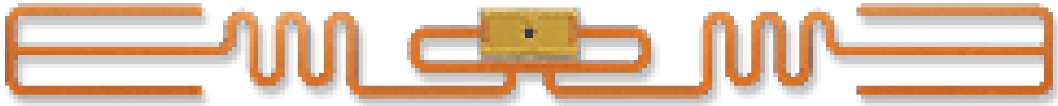
Fluidic Self-assembly (FSA)

- Alien Technology revised business plan: self-assembly of low-resolution low-cost displays on “smart” credit or cash cards for the European market.
- Substantial development contract with Philips in this area.

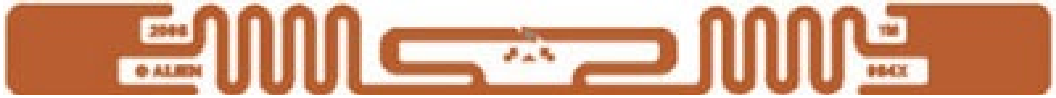
- Another pivot: RFID tags

Fluidic Self-assembly (FSA)

- Sample Products
  - Earlier: ALL-9238 tag "SquiggleT" antenna design, approximate size: 95mm x 10mm, small UHF form factor, very low-cost UHF tag, low-cost 4x6 label solution



  - Recent: ALN-9640 RFID tag is a high-performance, general purpose RFID inlay. For applications that demand more on-tag storage of up to 800 NVAM bits. This enables storage of data for the purpose of avoiding additional network access that would otherwise be required for data retrieval.



Part II:
Self-assembly by Shape Matching

Wafer-level and massively parallel assembly; assembly by energy minimization; using pallets and templates; how to deal with symmetric parts

Motivation

Background:

- Since the 1960's, integrated circuits (ICs) have been growing in complexity by about a factor of two every two years ("Moore's Law").
- Since the 1980's, IC technology has increasingly been adapted to build micro sensors and actuators.

Question:

- How does design methodology and manufacturing technology adapt to this increasing complexity and diversity?

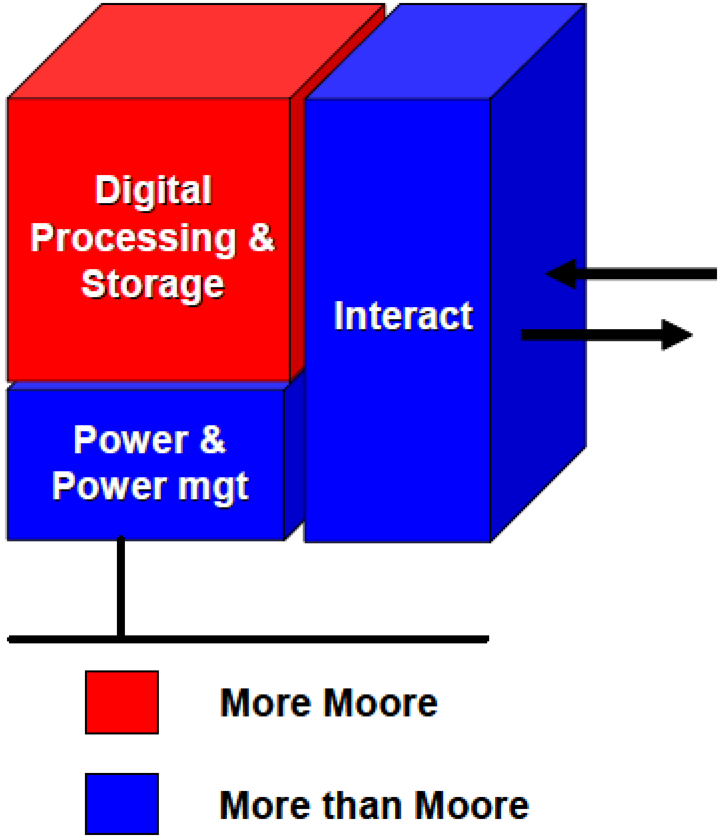
Motivation

“More-Moore”: Scaling

Continued shrinking of physical feature sizes of the digital functionalities (logic and memory storage) in order to improve density (cost per function reduction) and performance (speed, power).

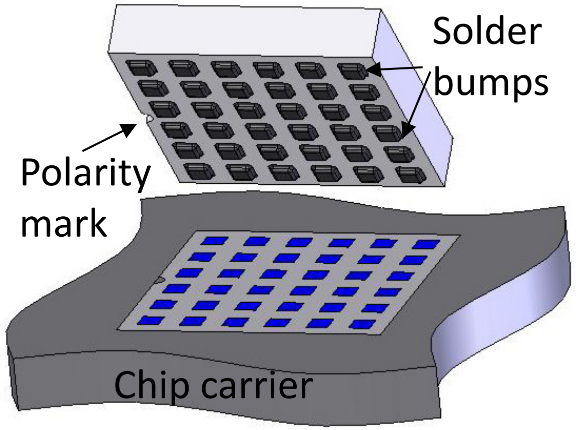
“More-than-Moore”: Functional Diversification

Incorporation into devices of functionalities that do not necessarily scale according to "Moore's Law“, but provide additional value in different ways. The "More-than-Moore" approach allows for the non-digital functionalities to migrate from the system board-level into the package (SiP) or onto the chip (SoC).



Wolfgang Arden et al. “More-than-Moore” white paper 2010

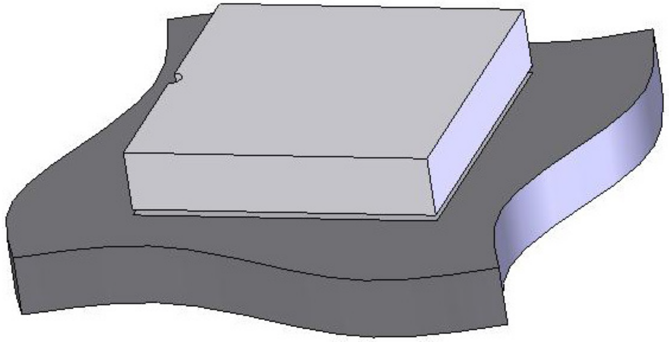
MEMS Packaging: Flip-chip Bonding



I. Placement

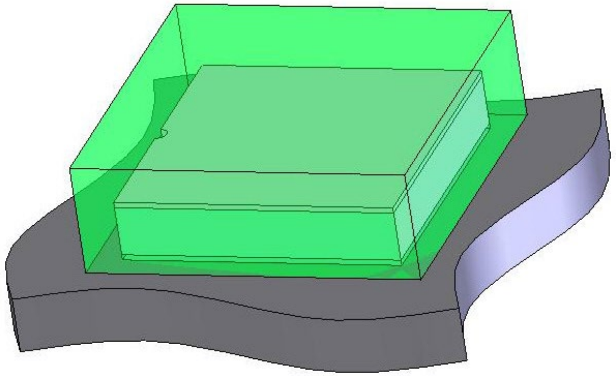
- Unique orientation
- Accurate alignment

- Coplanarity of solder bumps
- Controlled pressure
- Maximum bump density



II. Die attachment
(*solder reflow*)

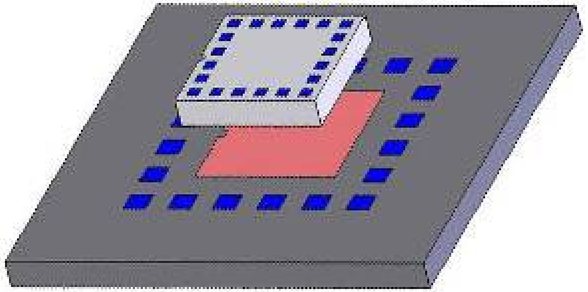
- Protective body
- Heat dissipation
- Vacuum sealing
- Possible optical path



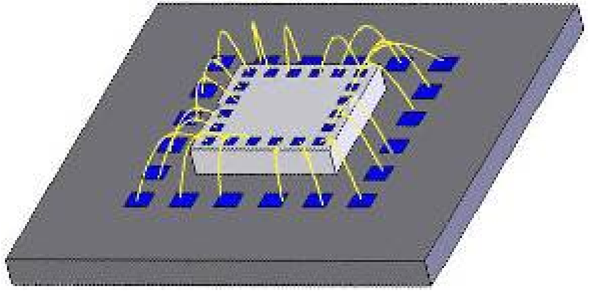
III. Encapsulation

MEMS Packaging: Wire Bonding

Up to 80% of a MEMS device cost may be determined by its packaging process.

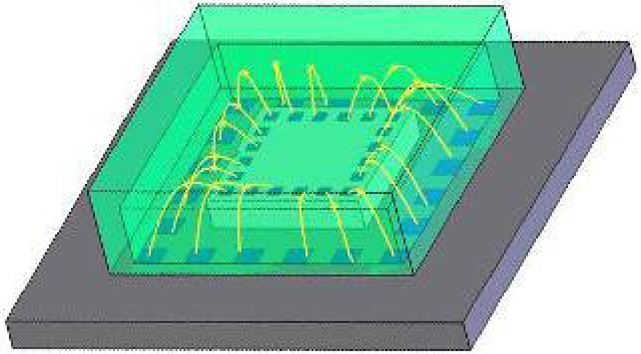


I. Placement



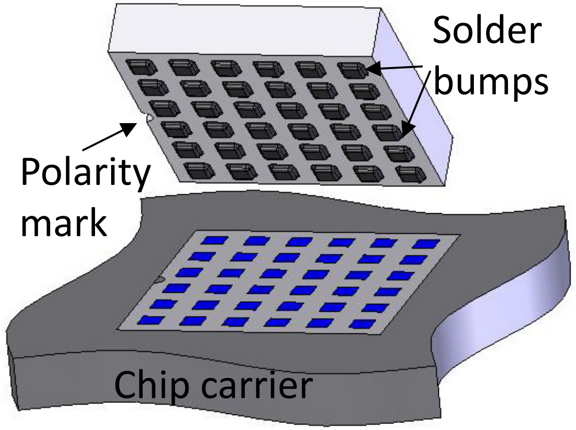
II. Die attachment

Greater misalignment tolerance than flip-chip bonding.

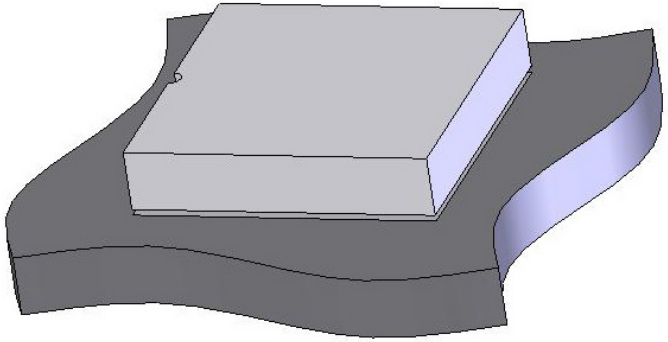


III. Encapsulation

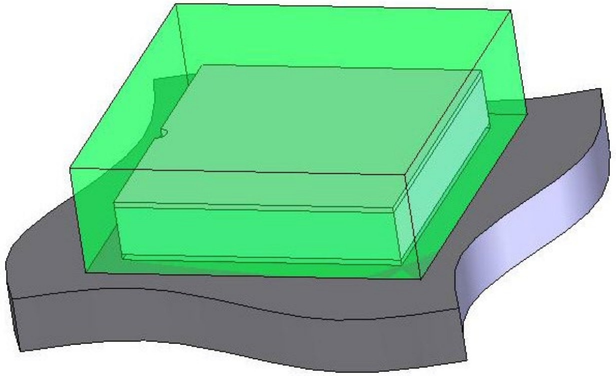
Chip Placement by Self-assembly



I. Placement



II. Die attachment
(*solder reflow*)



III. Encapsulation

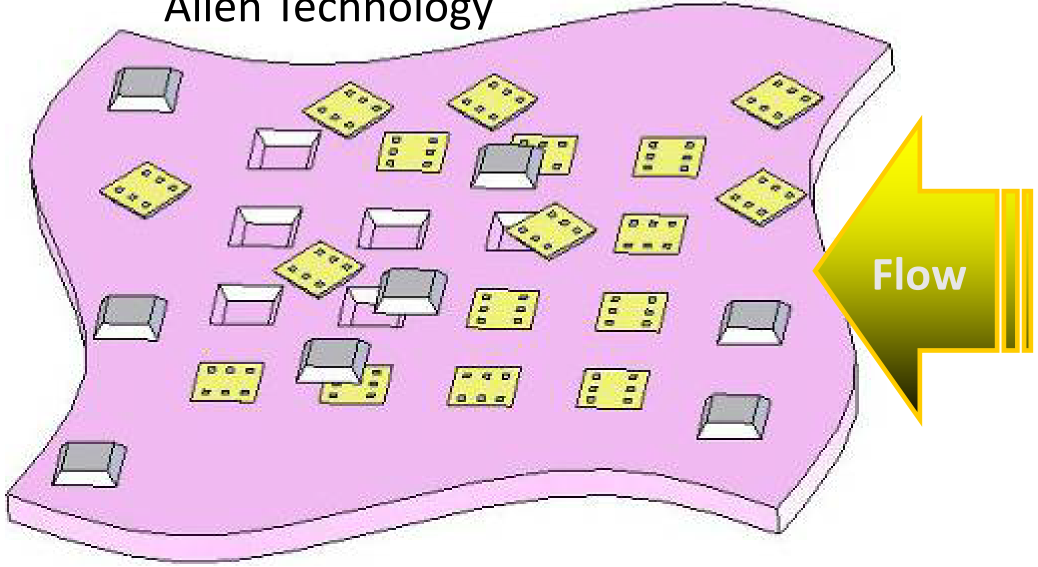
“Palletizing” of Assembly Components

- Self-assembly (or conventional assembly) may deliver the components into their final position.
  - Example: RFID chips in Alien Technology’s FSA.

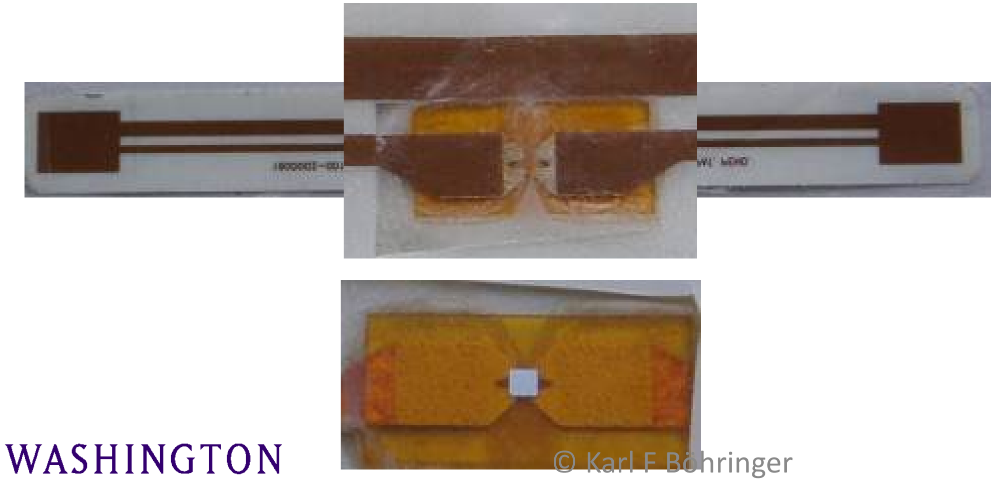
- Alternatively, they may provide an ordered arrangement from which the final assembly can be achieved efficiently.
  - Example: wafer-level transfer and bonding.

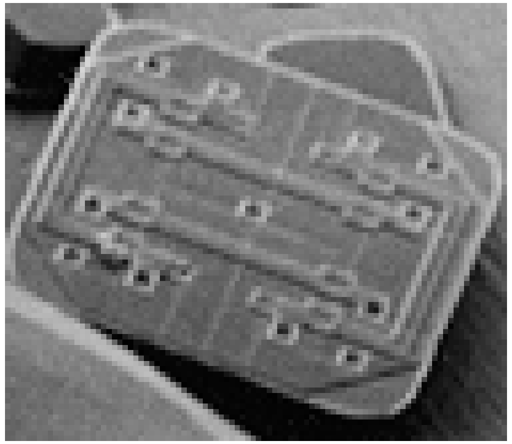
Fluidic Self-assembly with Shape-matching

Alien Technology

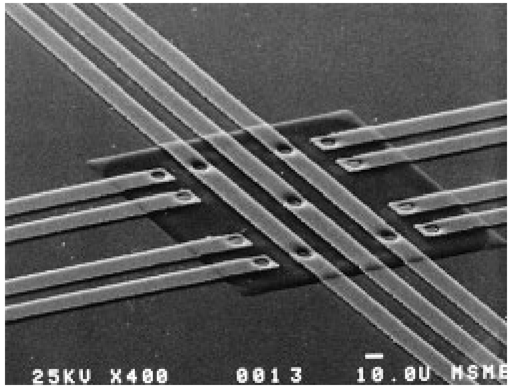


Application: RFID tag fabrication



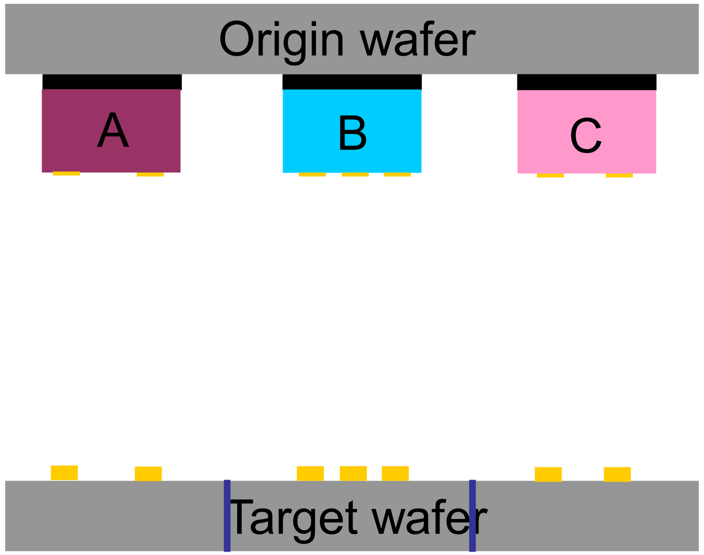


Nano block



Electrical wiring

Wafer-to-wafer Transfer



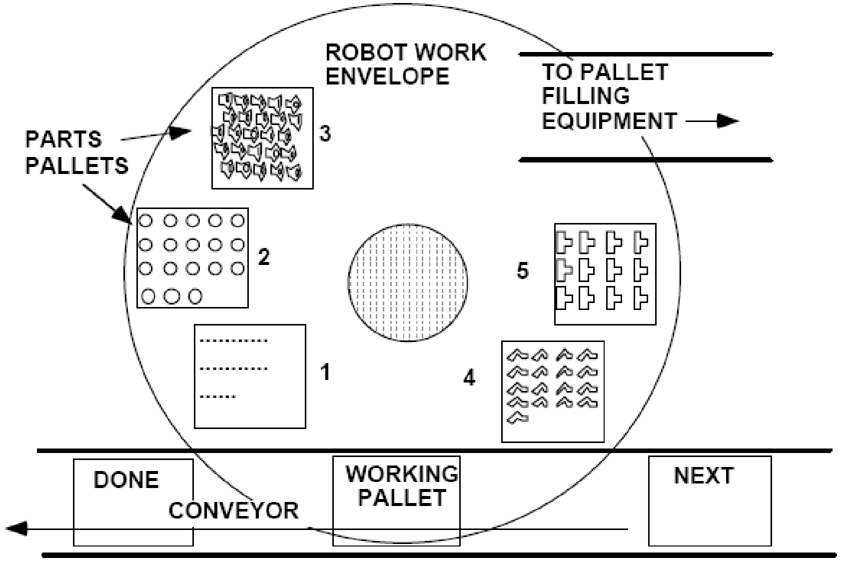
- 🟨 Au bump
- ■ Sacrificial layer

Dicing

Compare: Robotic Parts Feeding

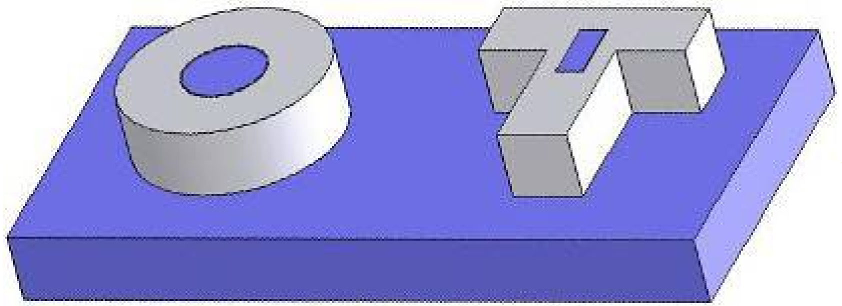
- Palletizing is very common in robotic assembly.
- Parts are delivered in bulk, typically into a vibratory parts feeder.
- The vibratory parts feeder is designed such that parts separate and move along tracks with obstacles that let correctly oriented parts through but reject wrongly oriented parts.
  - Each part requires a new track design.
- SONY's APOS became famous for using shape-matching in parts feeding.
  - The design of their trays was considered a "black art".

Robotic Parts Feeding and Assembly

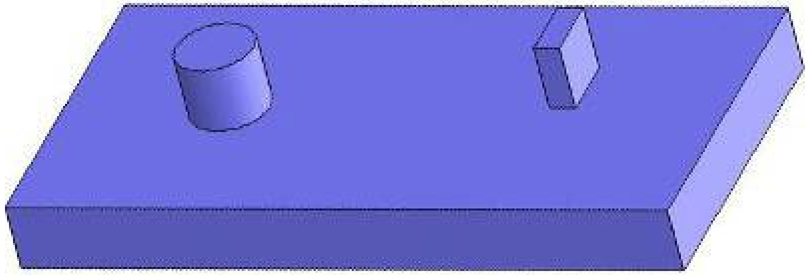


Part feeding

Pick and place



Assembled parts



Fixtures on substrate

Shape Matching Self-assembly

Self-assembly by shape matching can occur in a liquid environment (e.g., fluidic self-assembly by Alien) or in air

1. Structured particles: the components have complementary shapes that fit into each other in a unique way
2. Binding force: gravity or surface forces (capillarity, van der Waals, electrostatics)
3. Environment: a fluid helps with the delivery of components
4. Driving force: agitation provides transport while the system minimizes potential energy during assembly

Example 1: Palletizing Parts in a Shape-matching Template

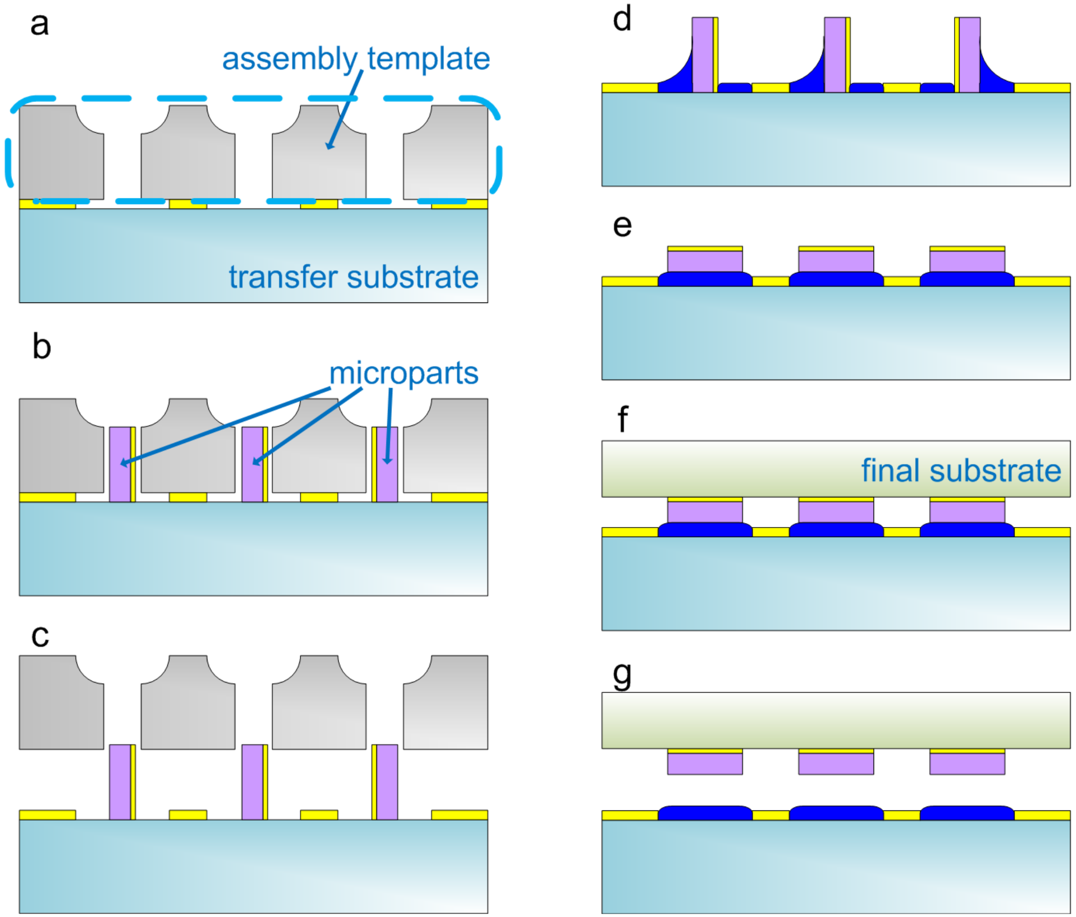
Applications: flip-chip, SMT assembly

Templated Self-assembly

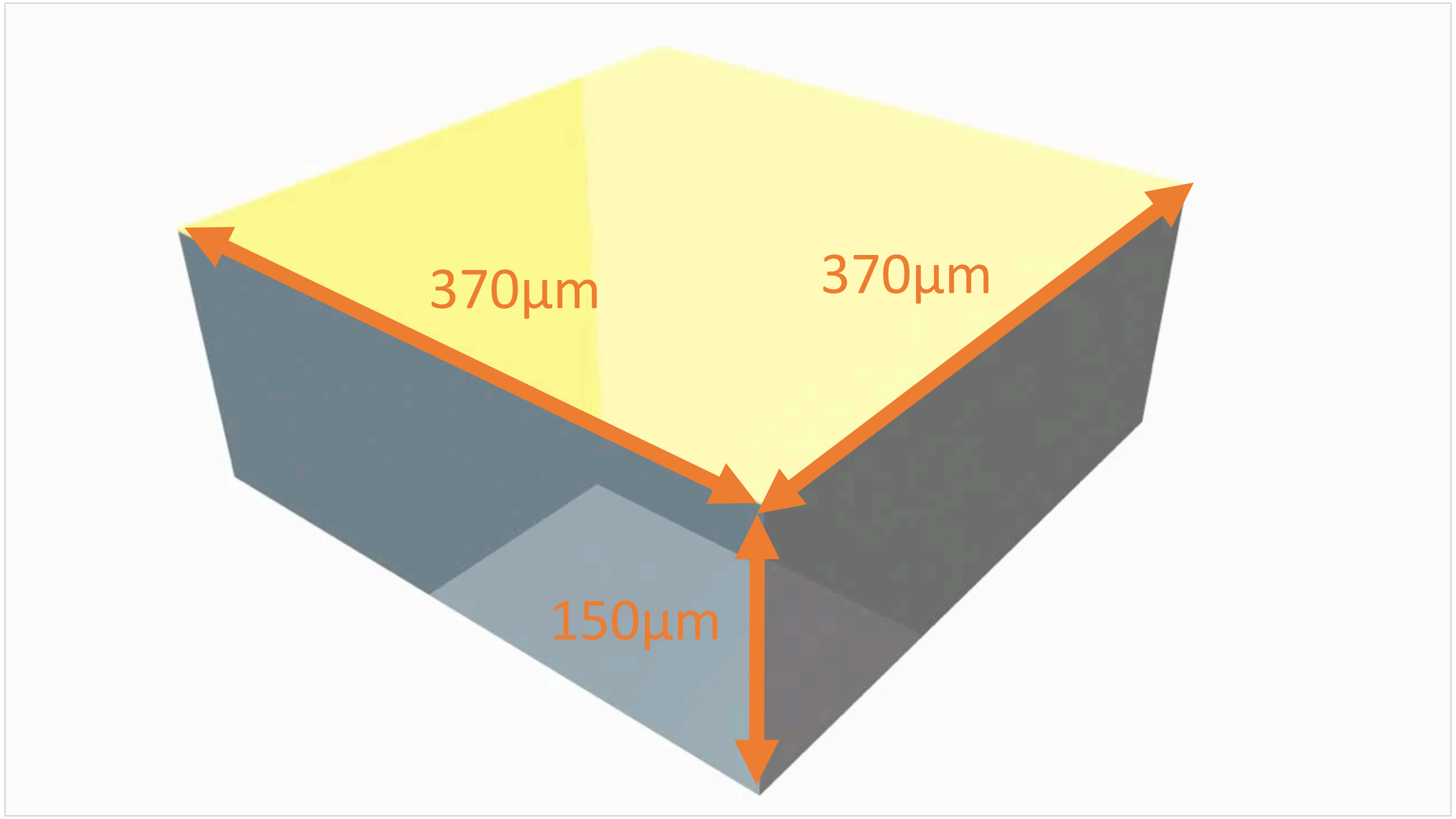
- Parts are delivered in a random walk driven by vibration
- Parts fall into vertical slots
  - This provides highest density in assembly template
- Template is removed, parts remain on assembly substrate
  - Capillary forces help with accurate alignment and attachment

Work by Hoo, Baskaran, Böhringer 2010-2014

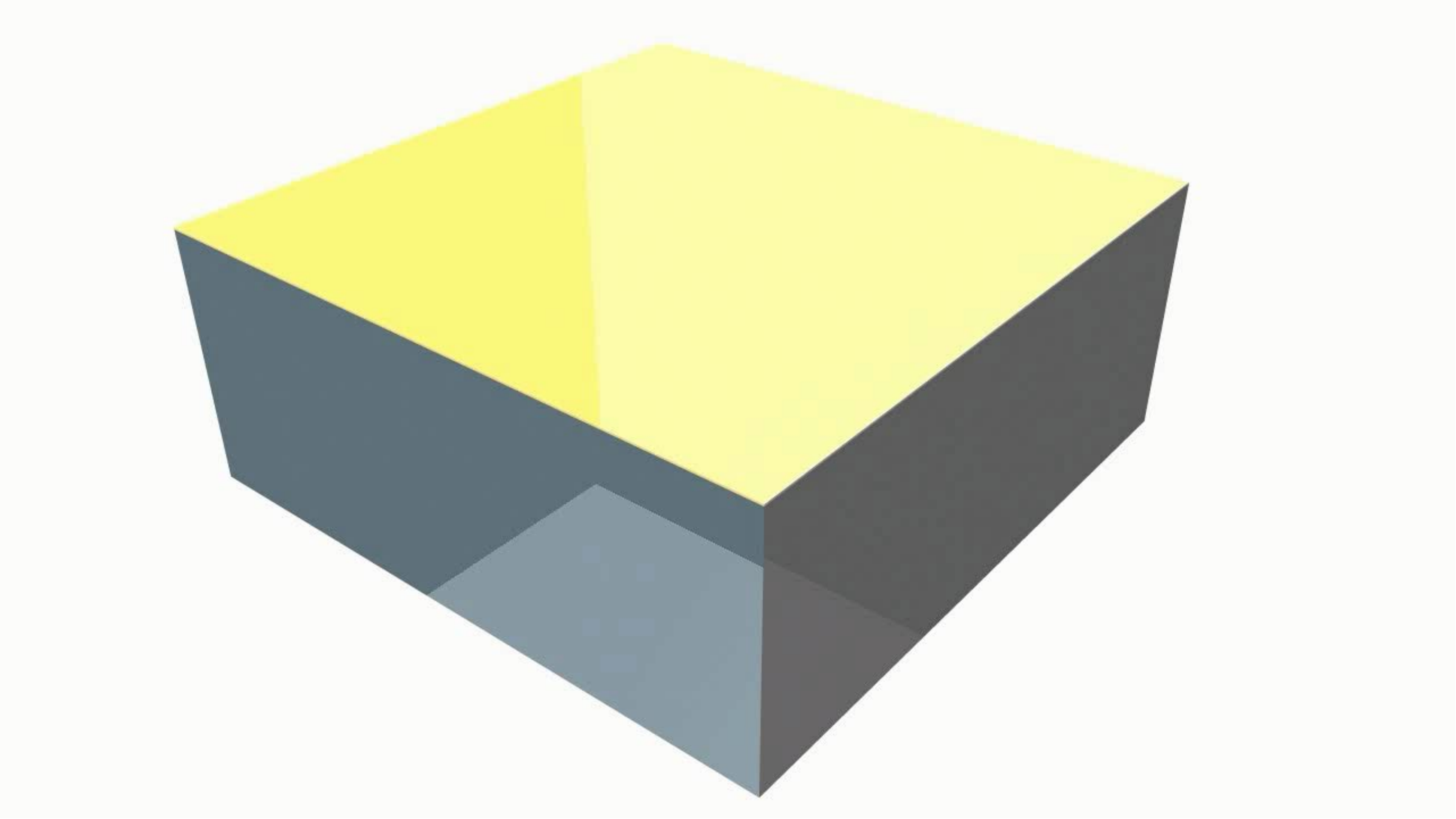
Assembly Process Flow



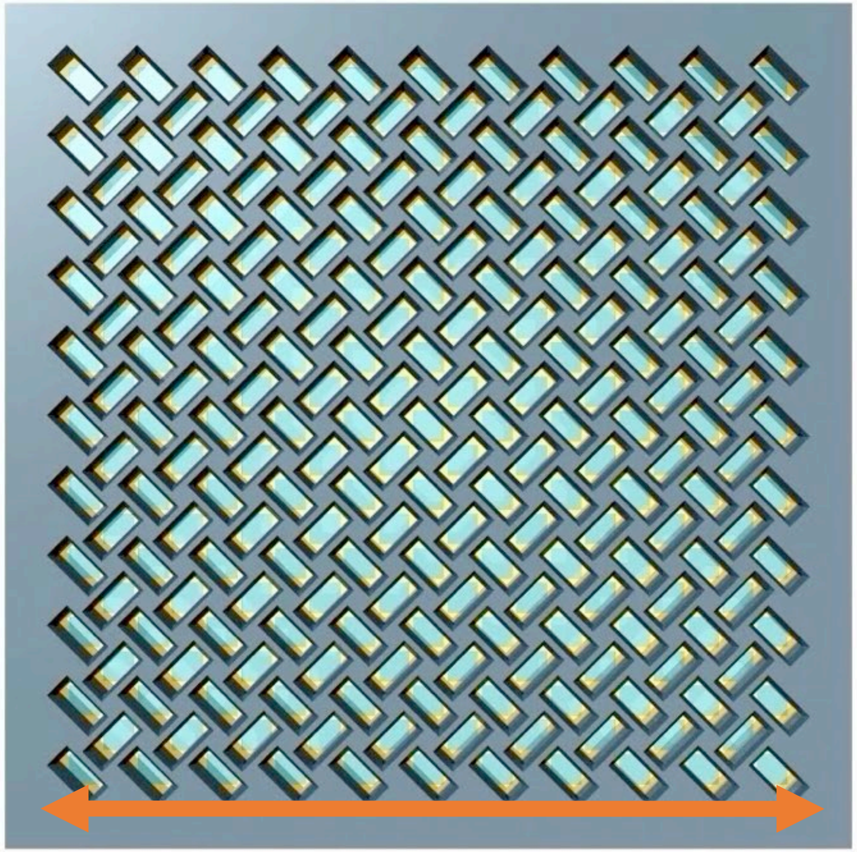
Components: Microparts



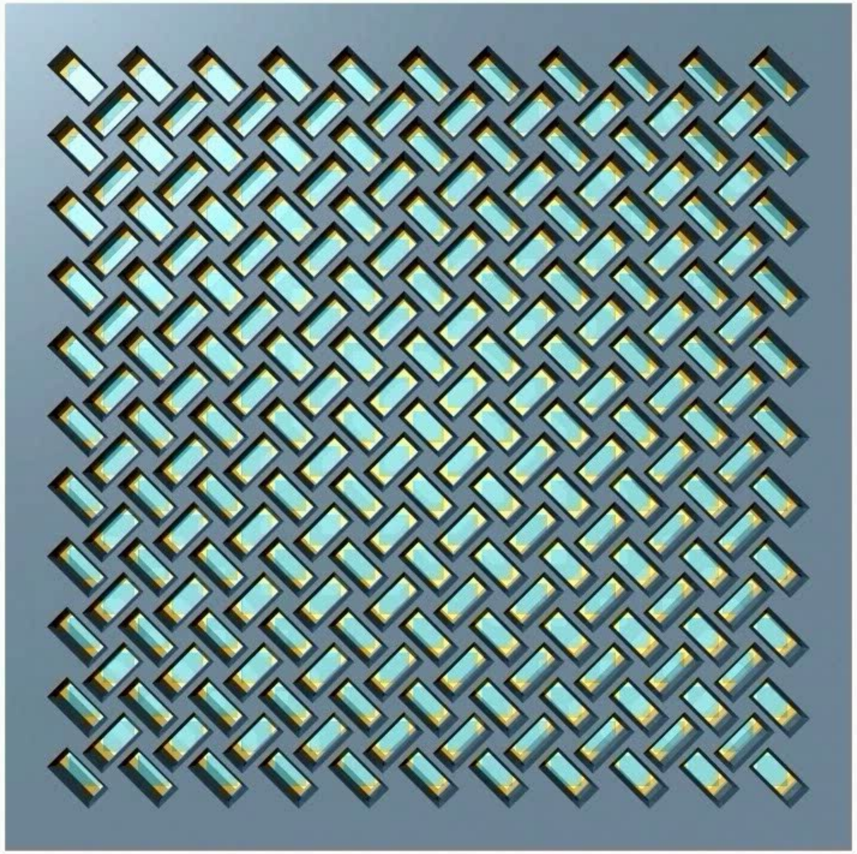
Components: Microparts



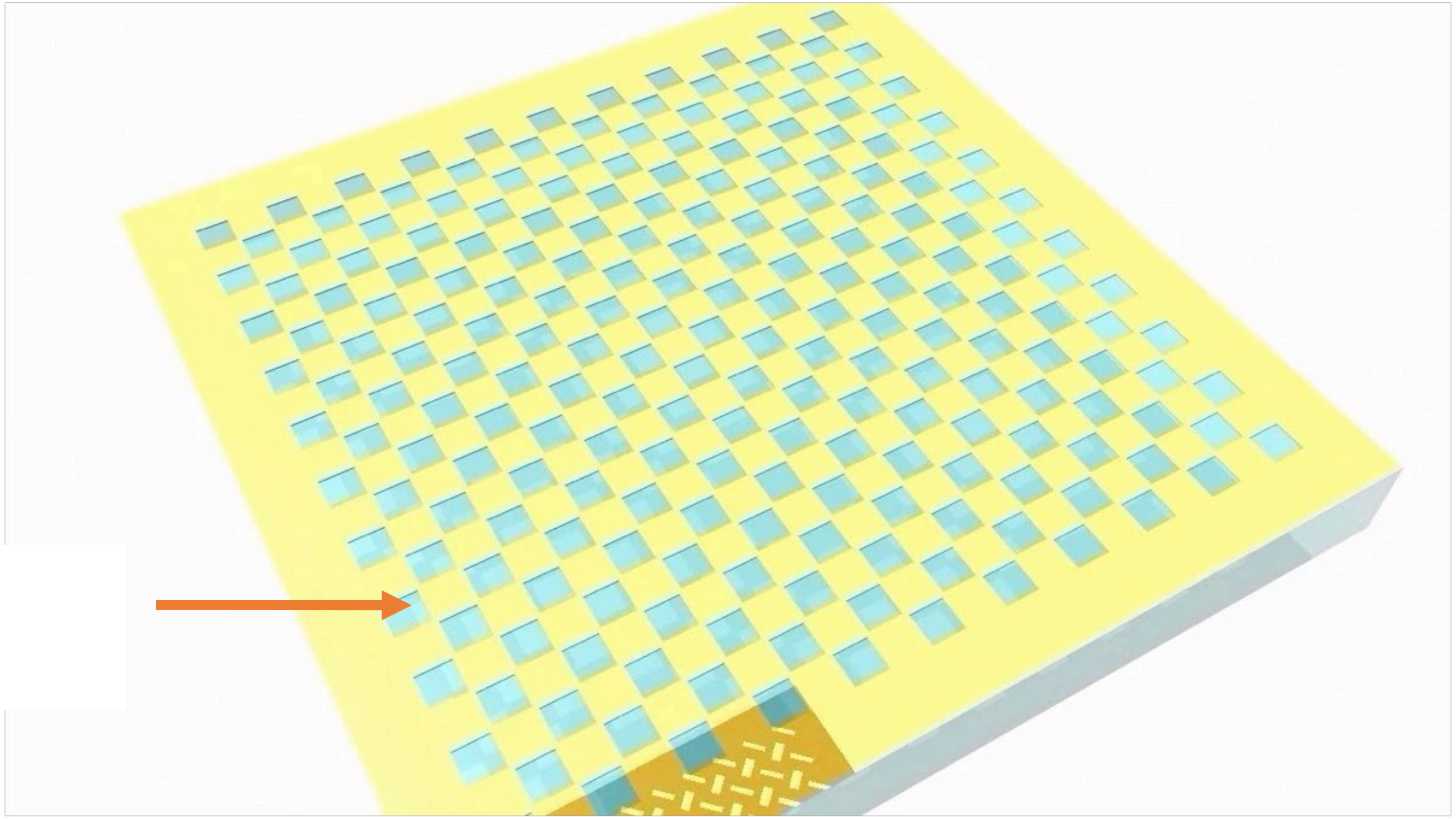
Assembly Template



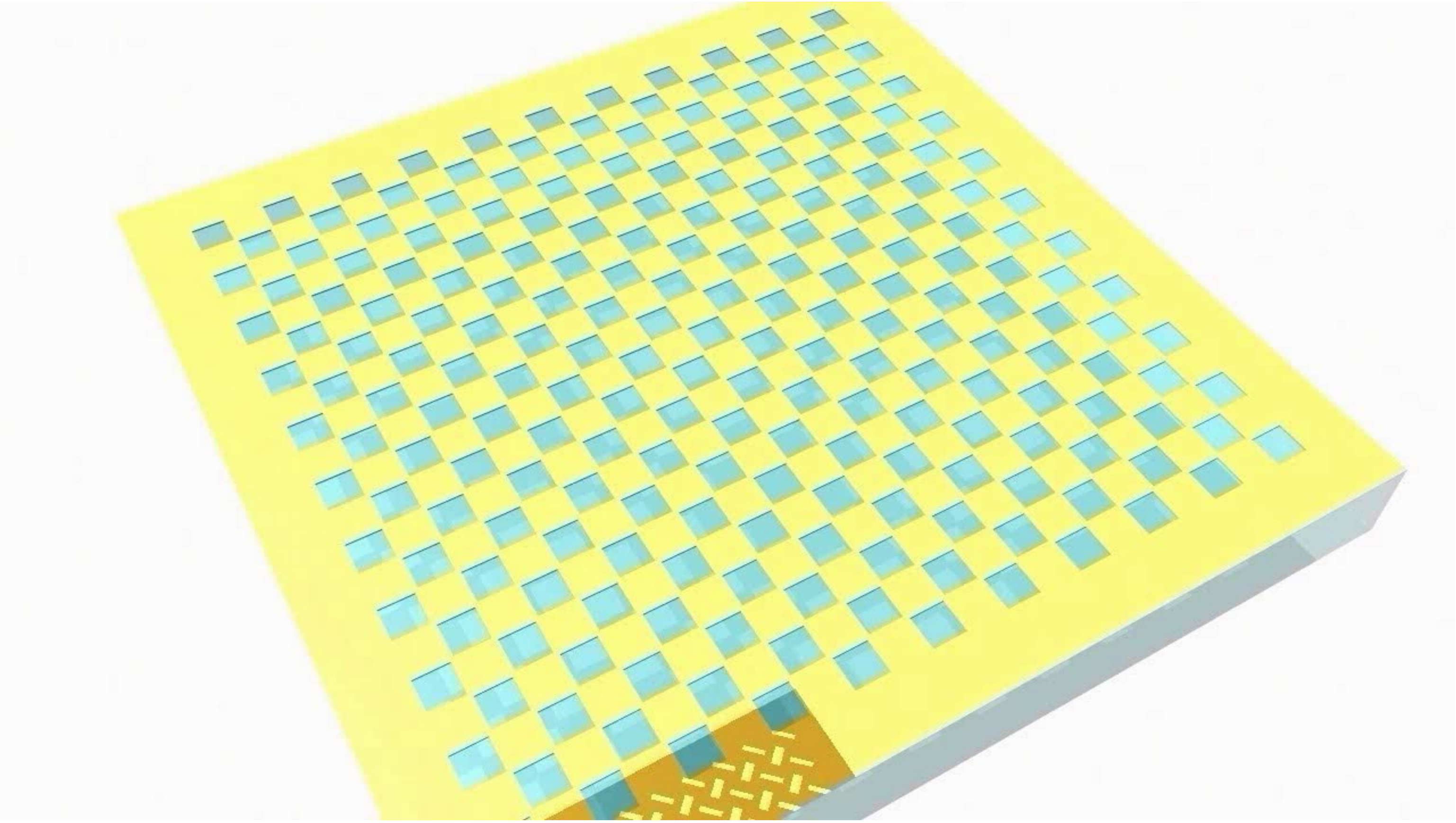
Assembly Template



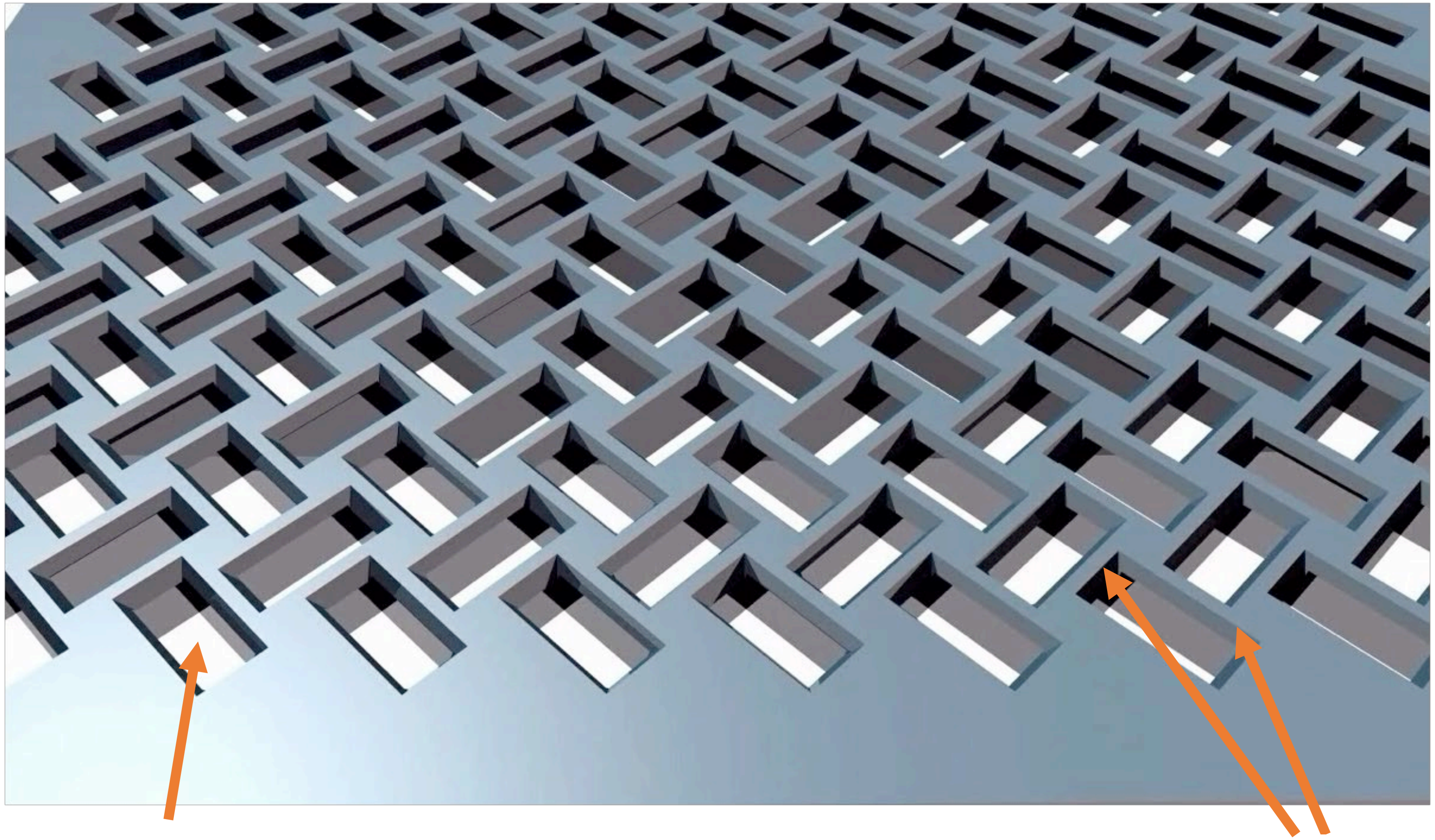
Transfer Substrate



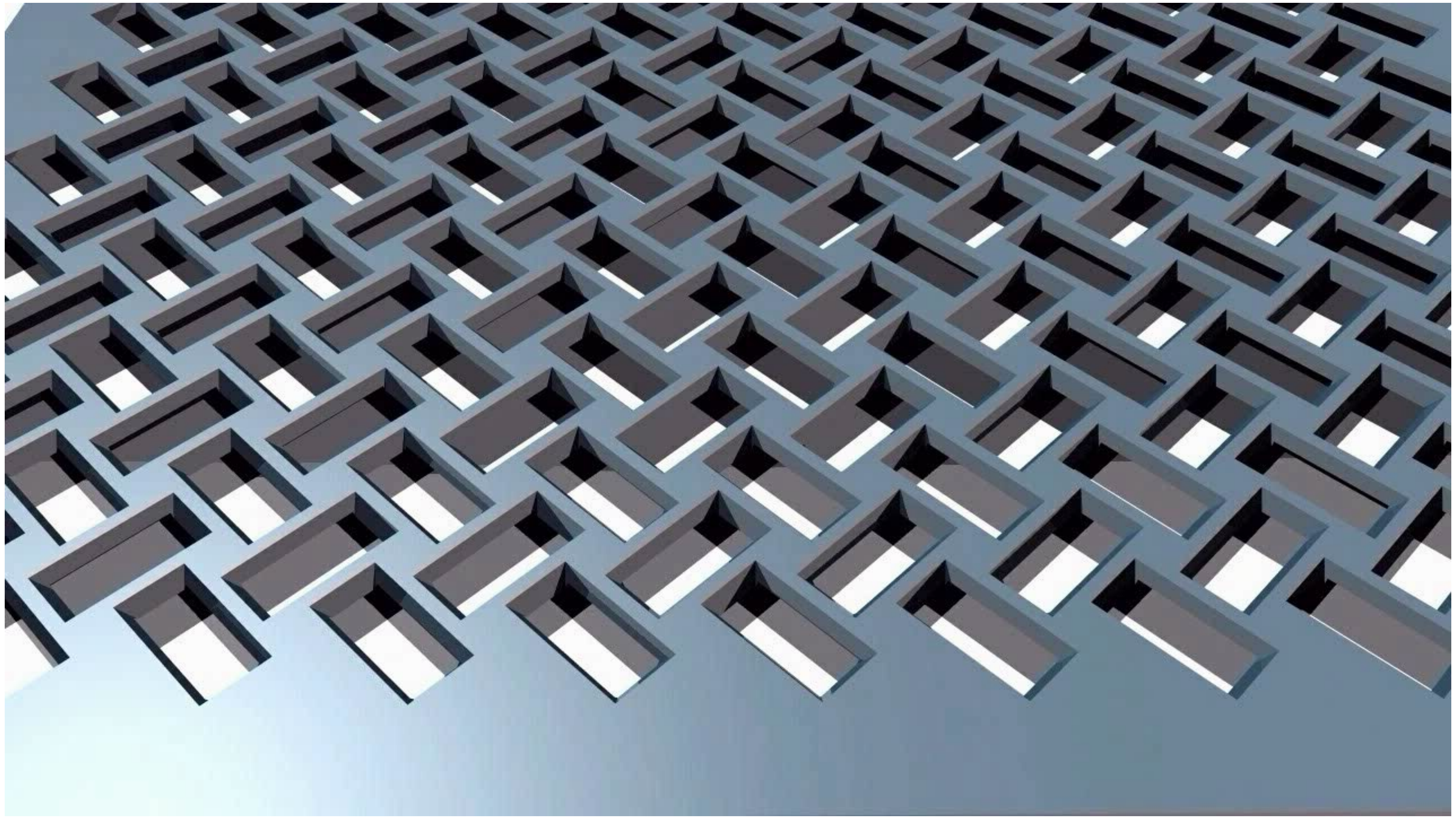
Transfer Substrate



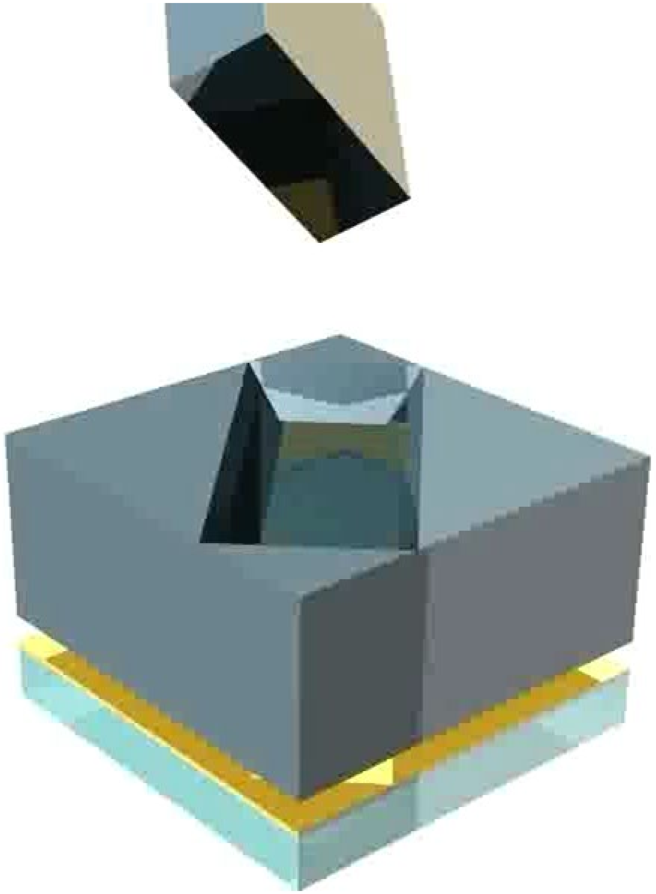
Assembly Template



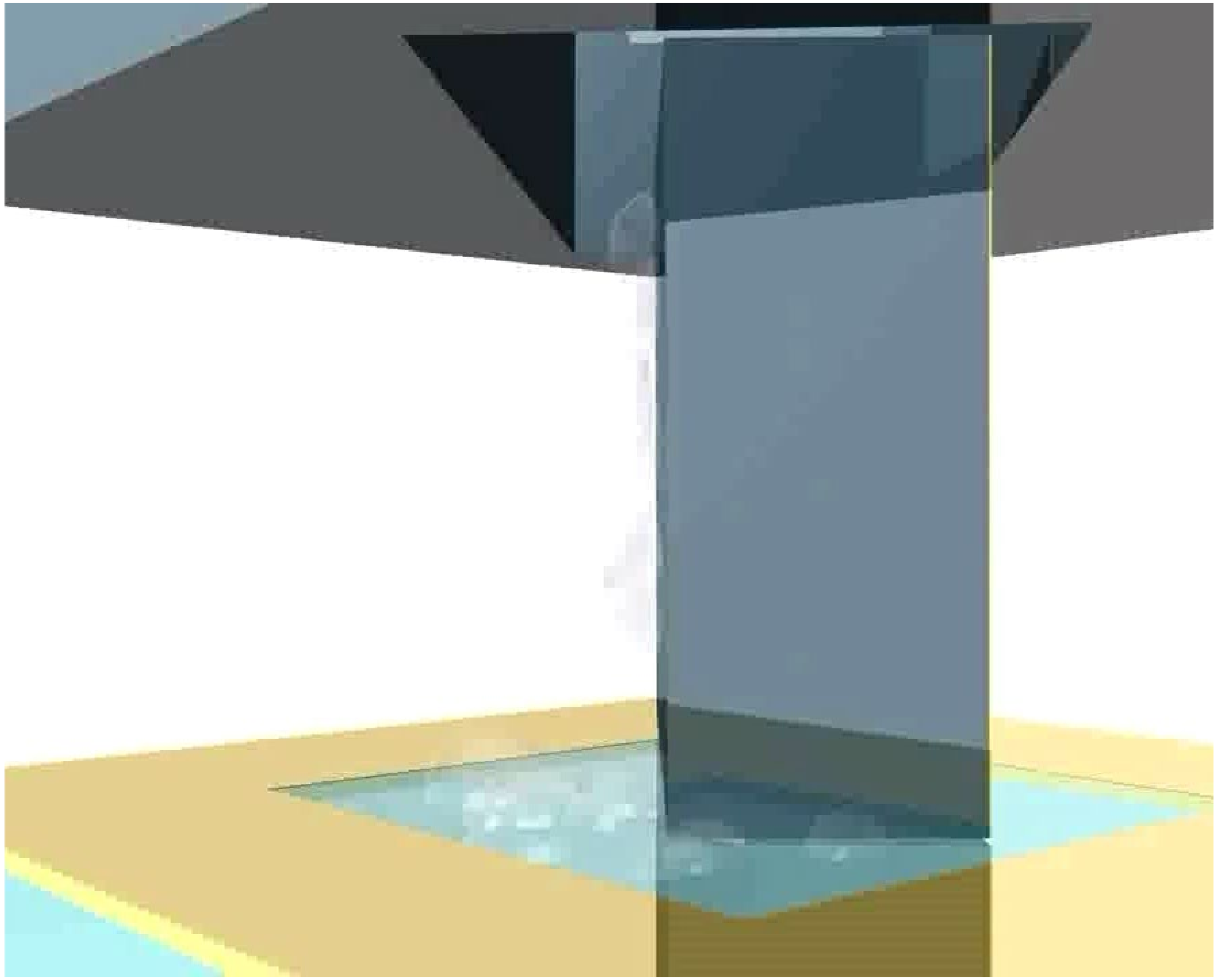
Assembly Template



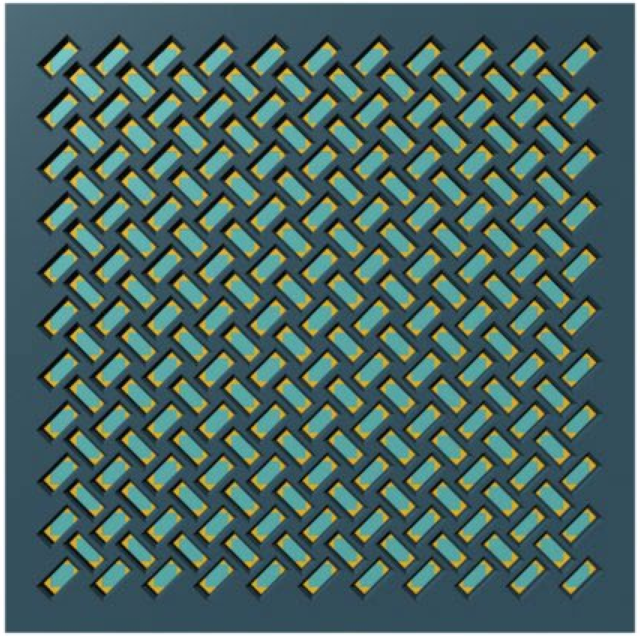
Templated Self-assembly Process



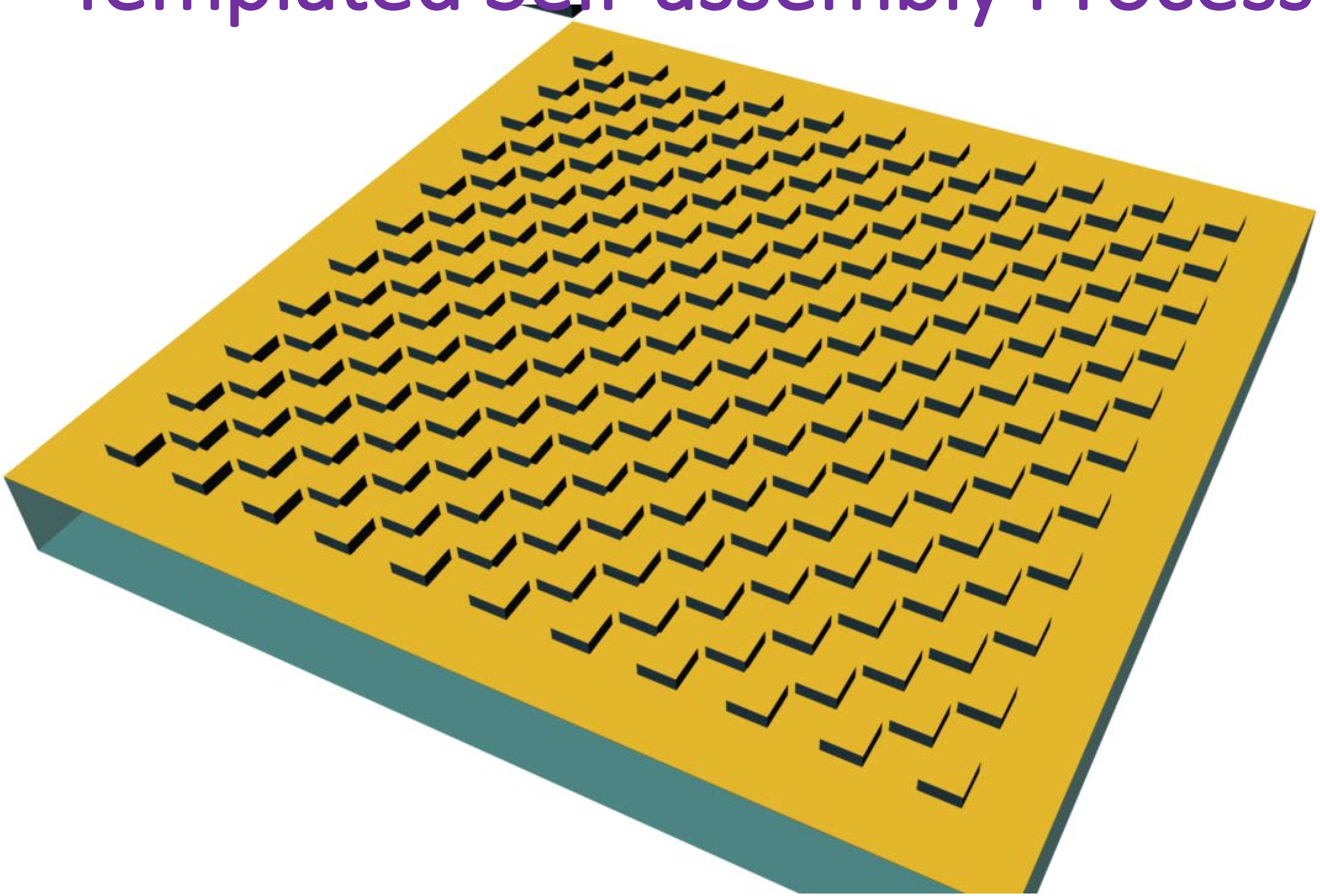
Templated Self-assembly Process



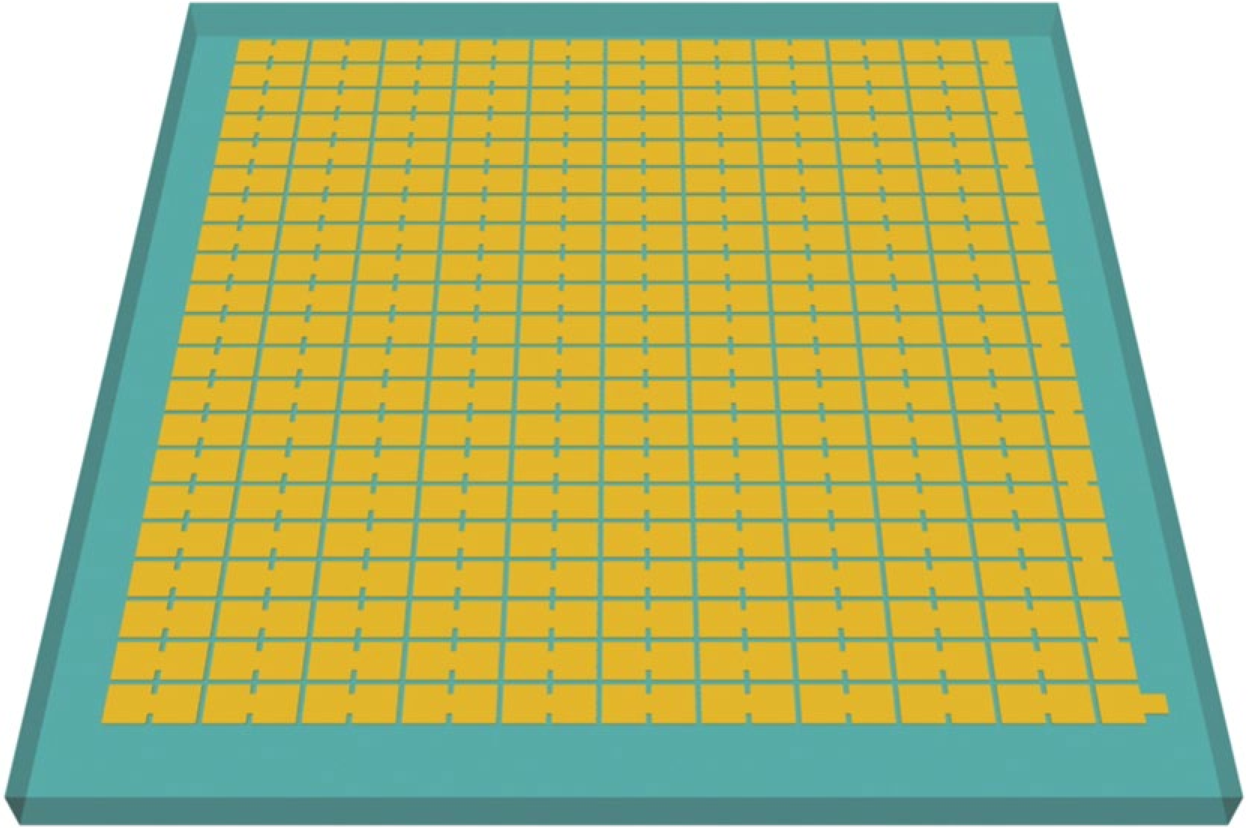
Templated Self-assembly Process



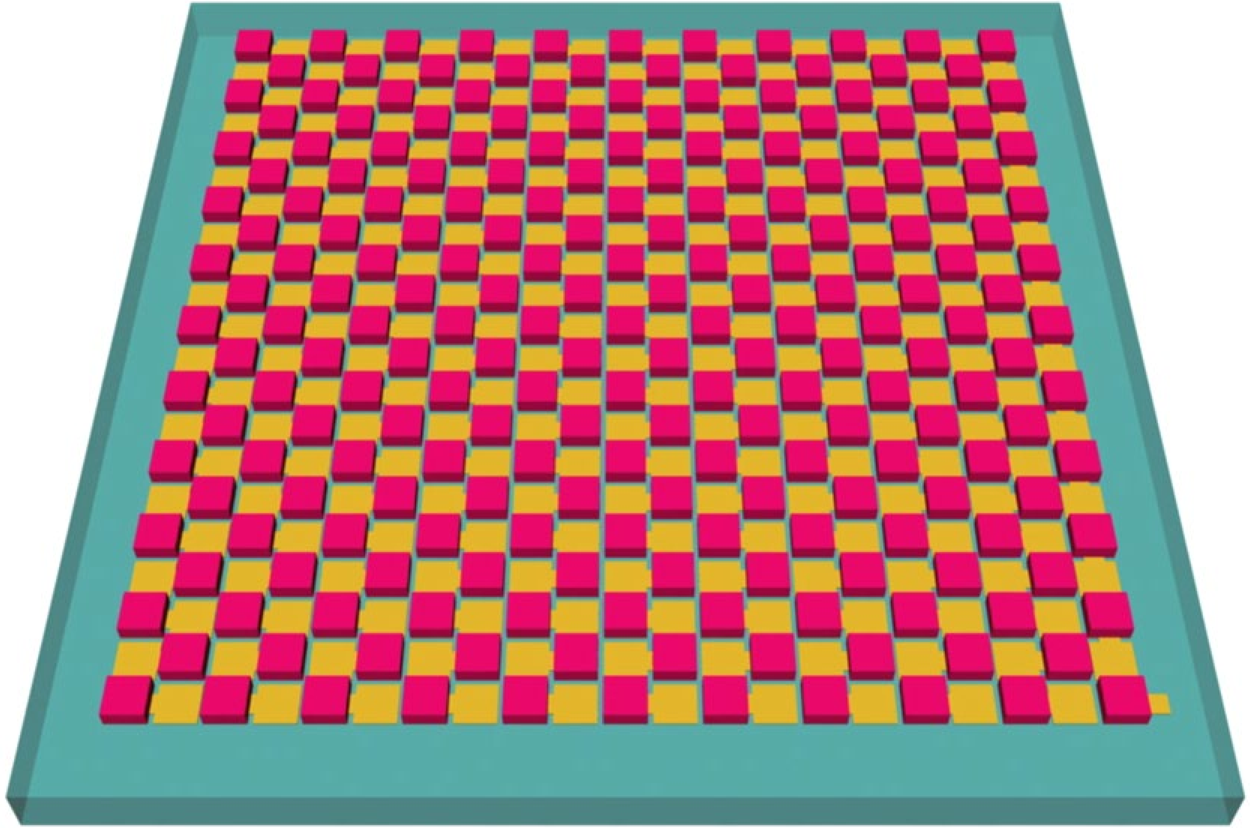
Templated Self-assembly Process



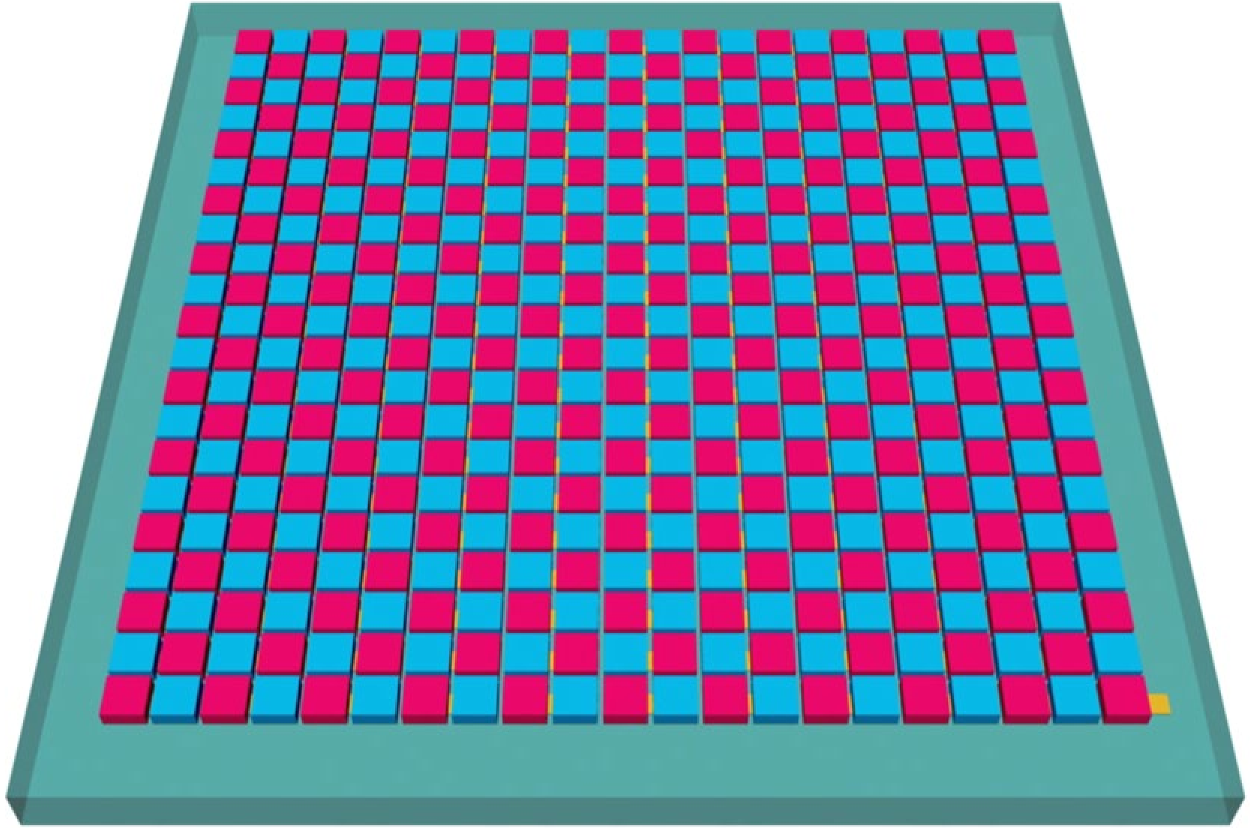
Templated Self-assembly Process



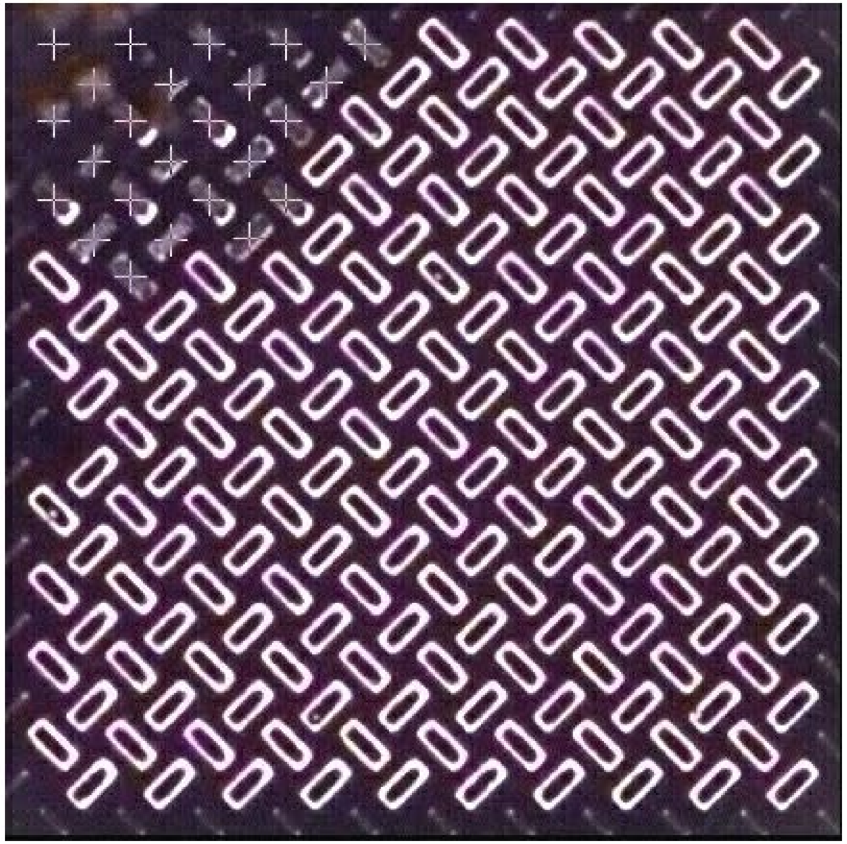
Templated Self-assembly Process

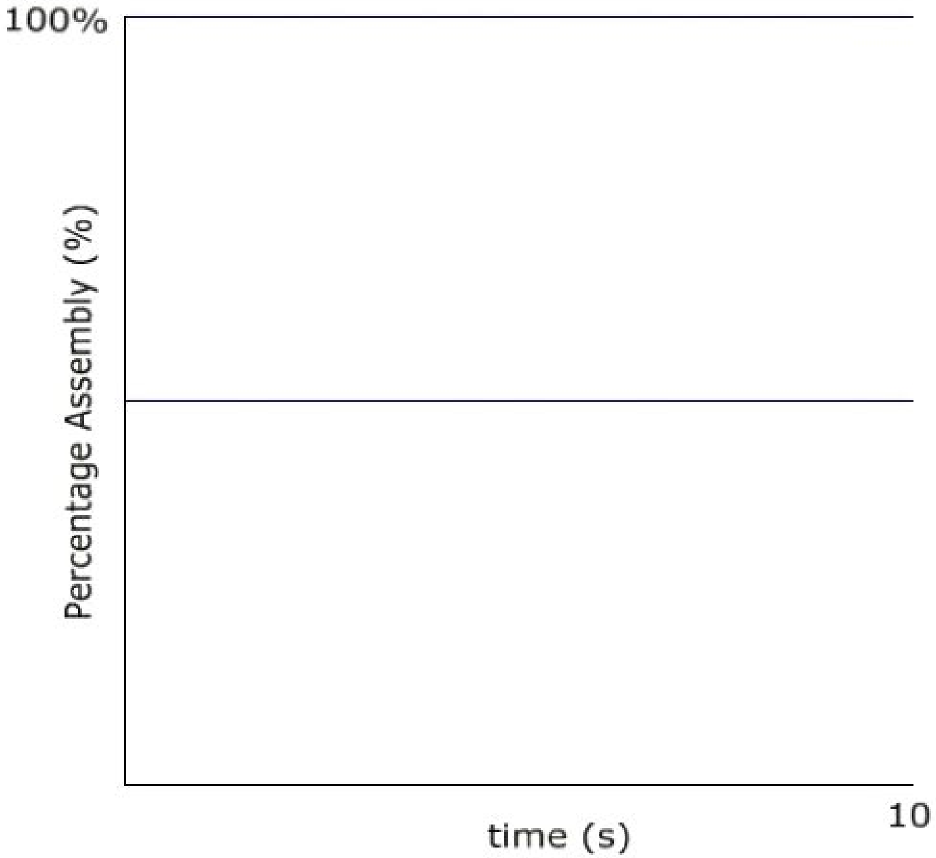


Templated Self-assembly Process



Vibratory Delivery for Self-assembly

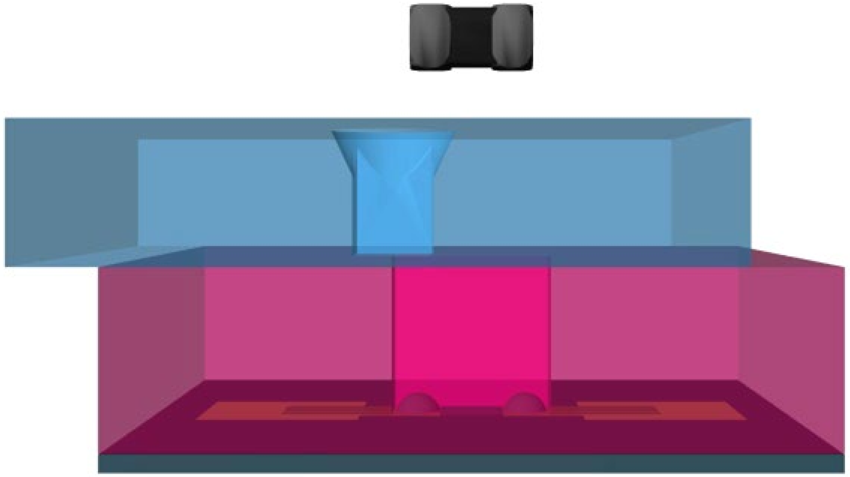




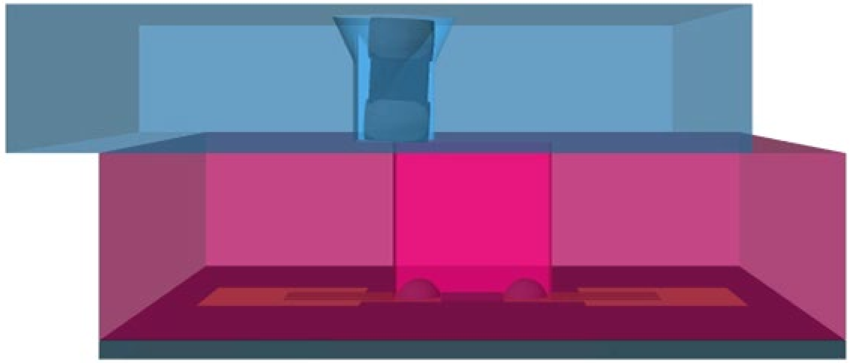
Self-assembly of Surface Mount Technology Components

- Shape-matching assembly with vertical template
- Enforce exactly one component per site
- Symmetry of simple SMT components does not pose difficulties (except for diodes)

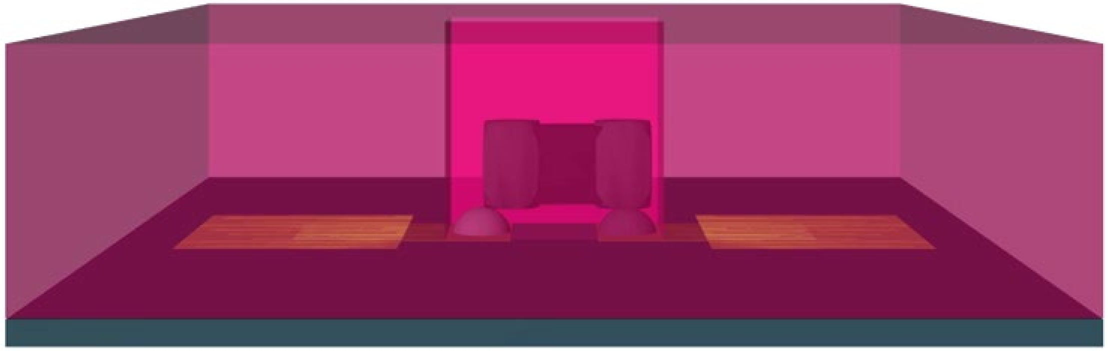
01005 SMT Self-assembly



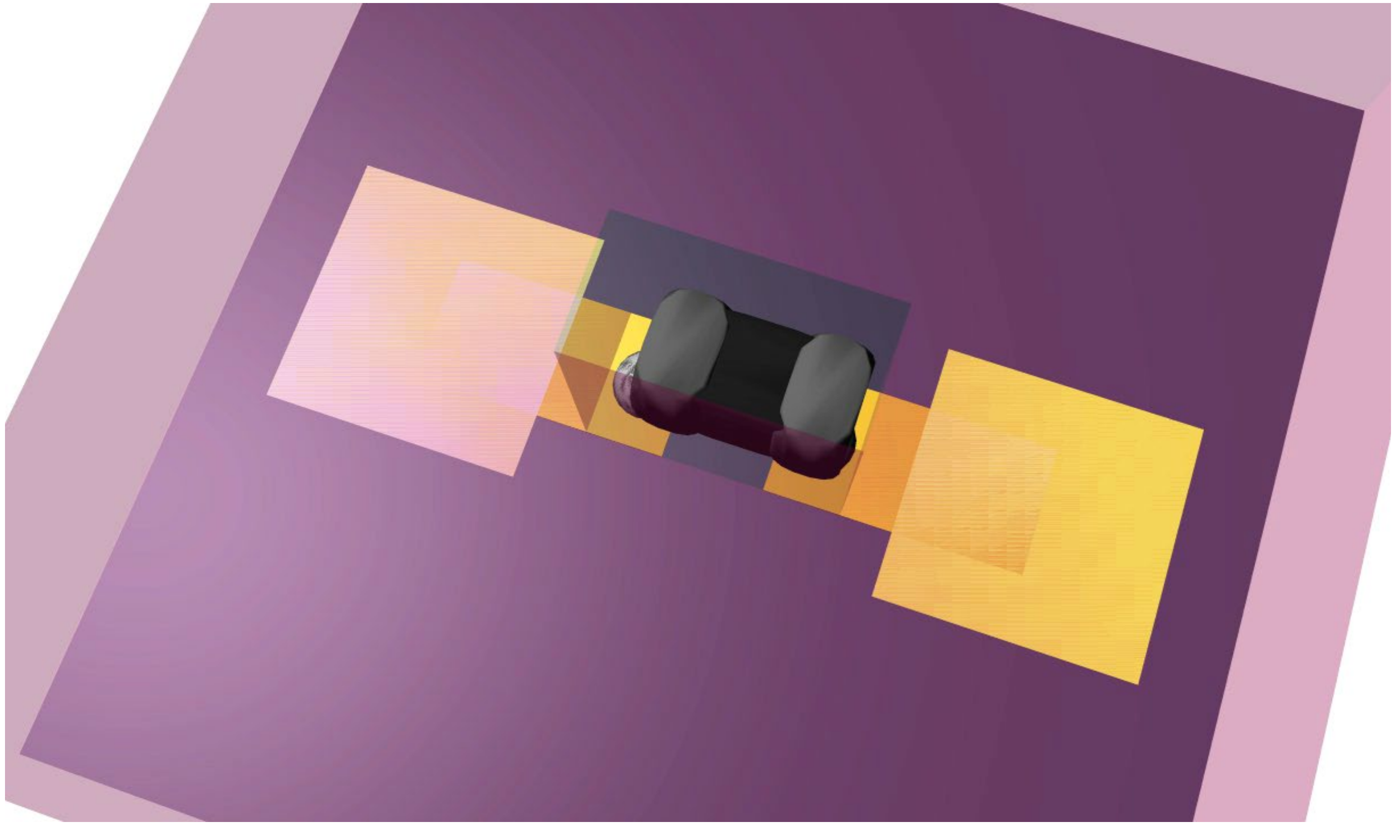
01005 SMT Self-assembly



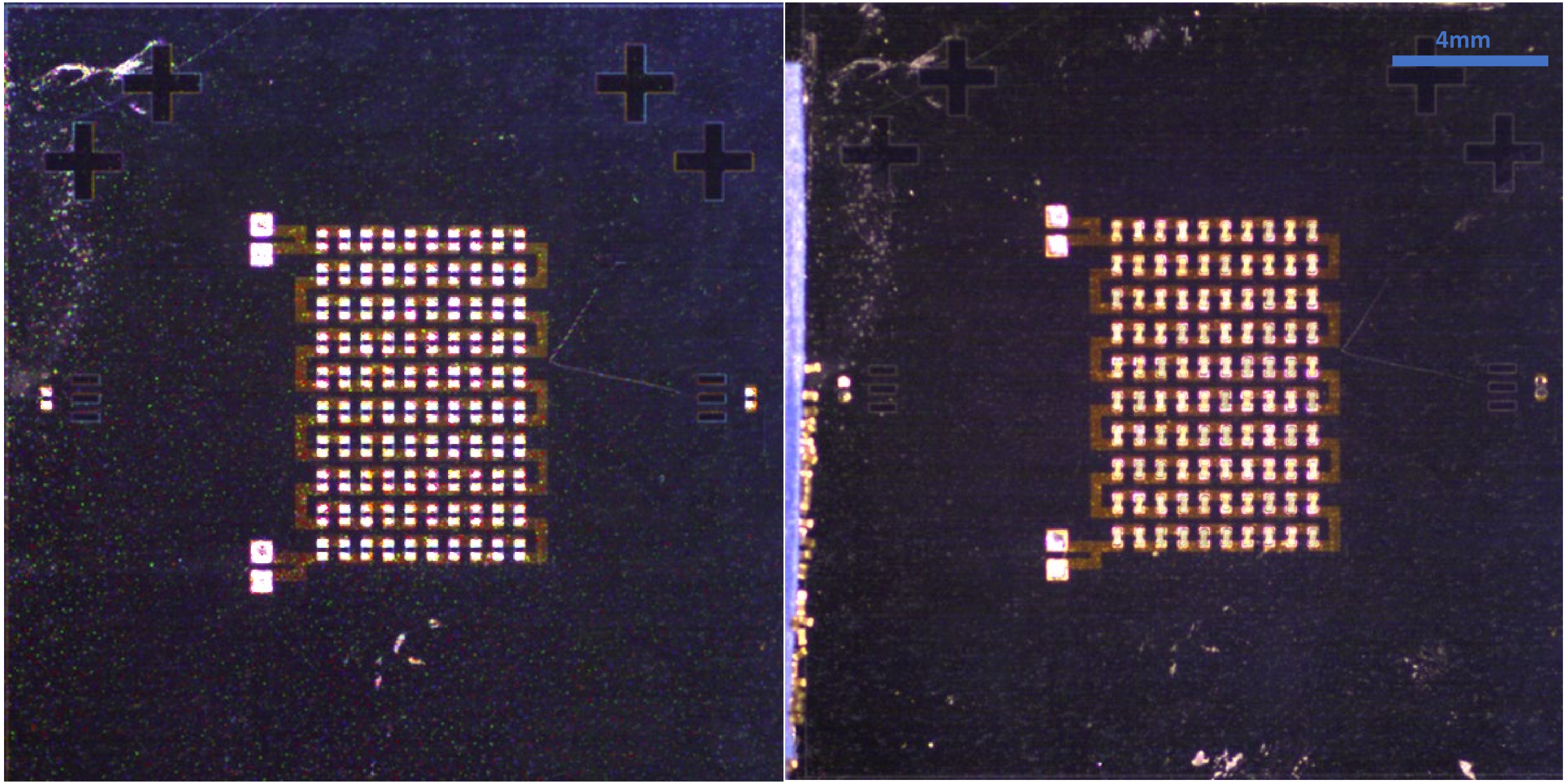
01005 SMT Self-assembly



01005 SMT Self-assembly

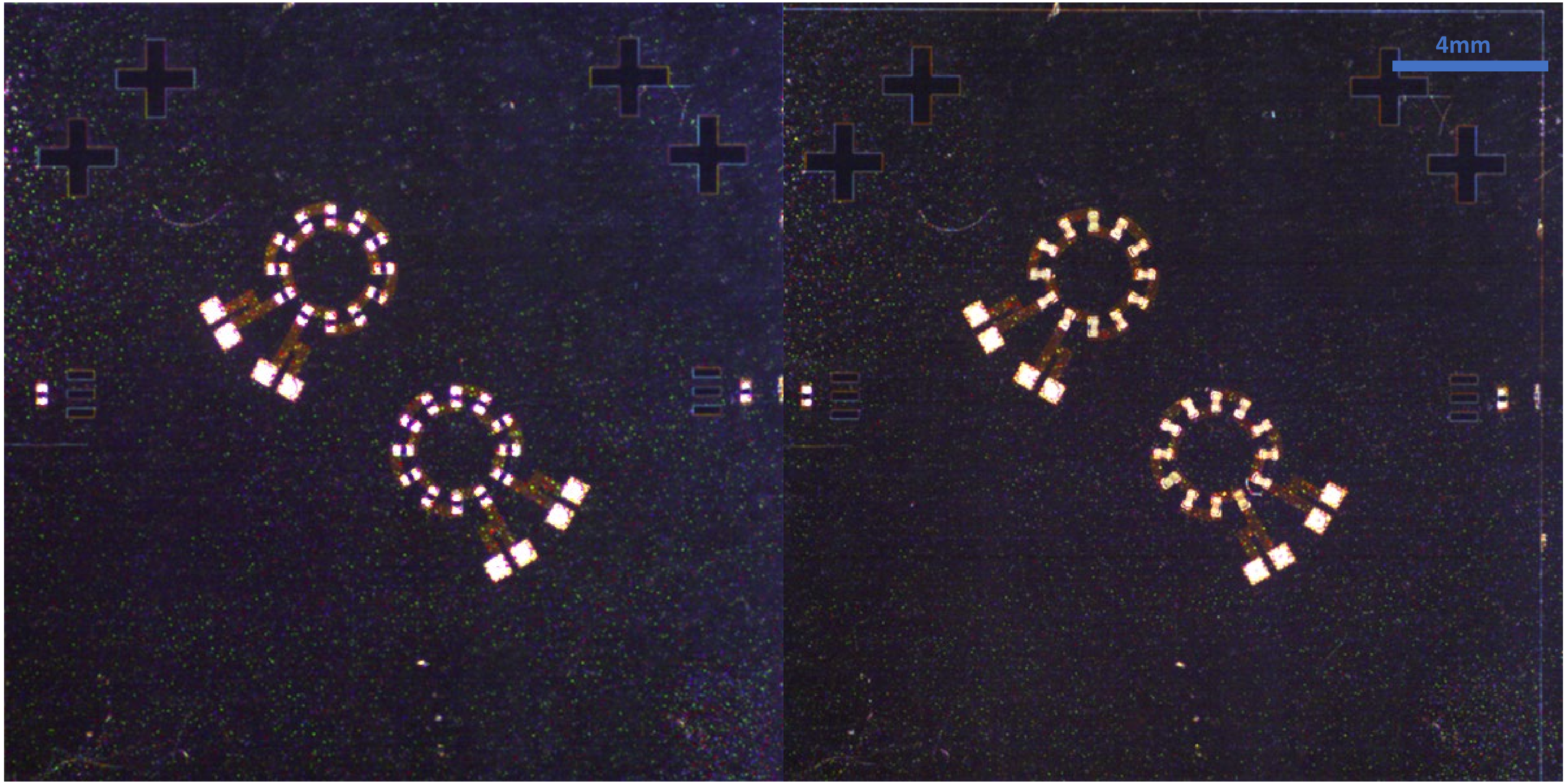


SMT Self-assembly Results



100 component series circuit assembly

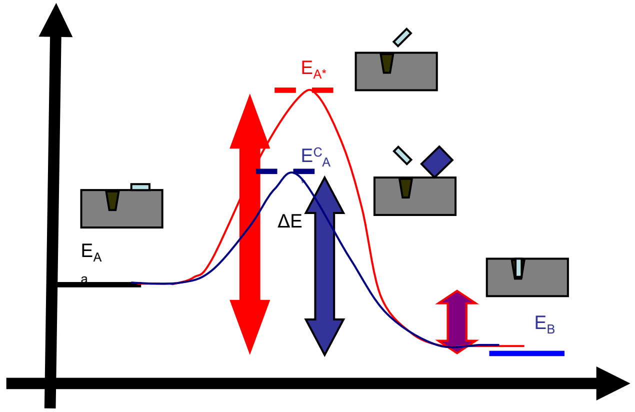
SMT Self-assembly Results

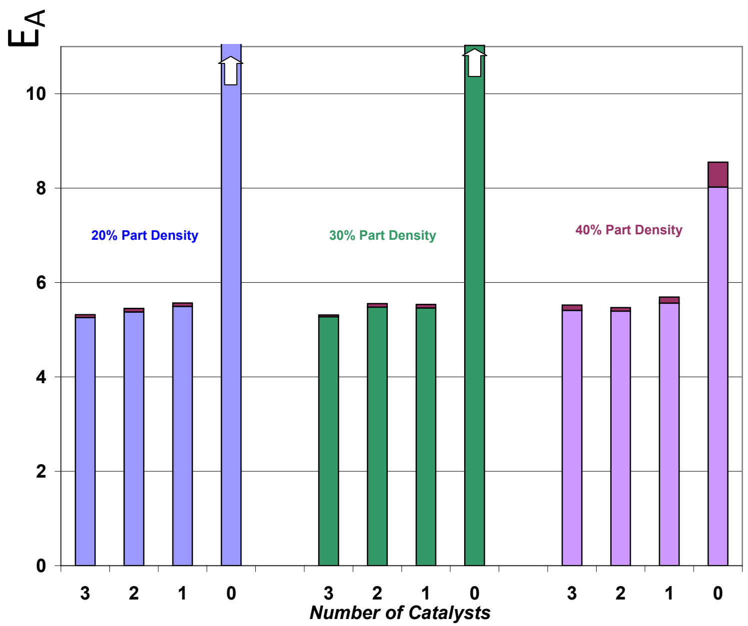


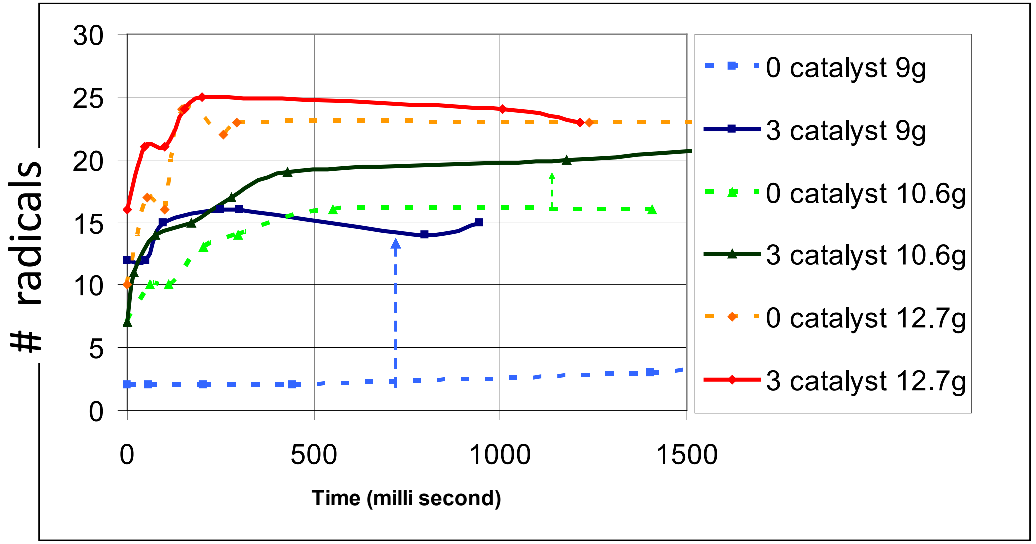
Circular 12 component series circuit assembly

Micro-self-assembly Catalysts

Introduce components that increase number of ‘free radicals’ but do not interfere with assembly sites
[*IEEE MEMS* ‘08]







Example II: Shape-matching with Unique Orientation

Challenge in self-assembly: symmetric component geometries

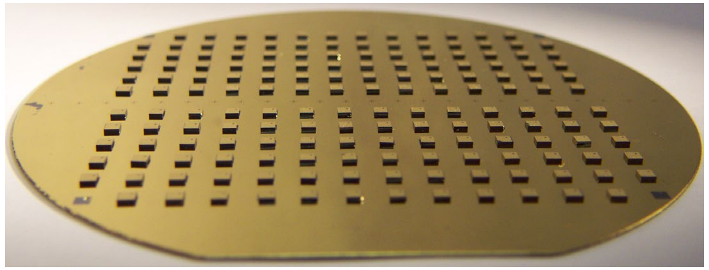
Self-assembly with Symmetric Components

- If the components are symmetric with regards to the assembly forces then the component cannot be assembled into a unique orientation.

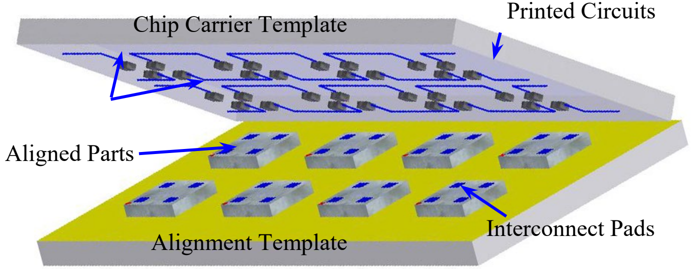
- Solutions:
  1. Components have to be designed with symmetry (e.g., redundant bond pads).
  2. Features have to be added that break the symmetry.

Batch Packaging of Micro Devices with Uniquely Orienting Self-Assembly in Air

- To assemble microchips with multiple interconnect pads, the alignment orientation must be unique to achieve correct electrical connections to the chip carrier template.
- The major two steps: (1) face orienting and palletizing parts onto an alignment template; (2) trapping and uniquely aligning parts to binding sites.
- [J. Fang et al. *IEEE MEMS* ‘05]



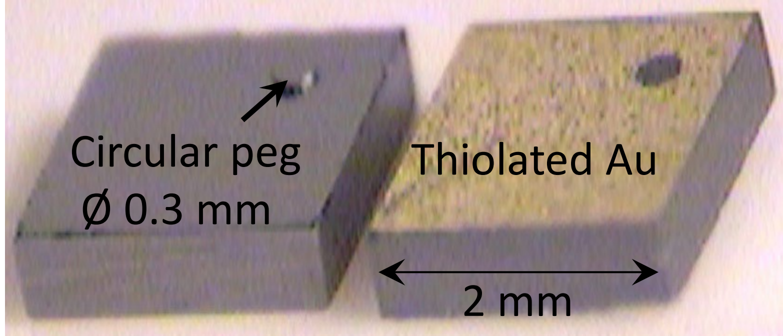
164 silicon parts self-aligned on a 4-inch alignment template.



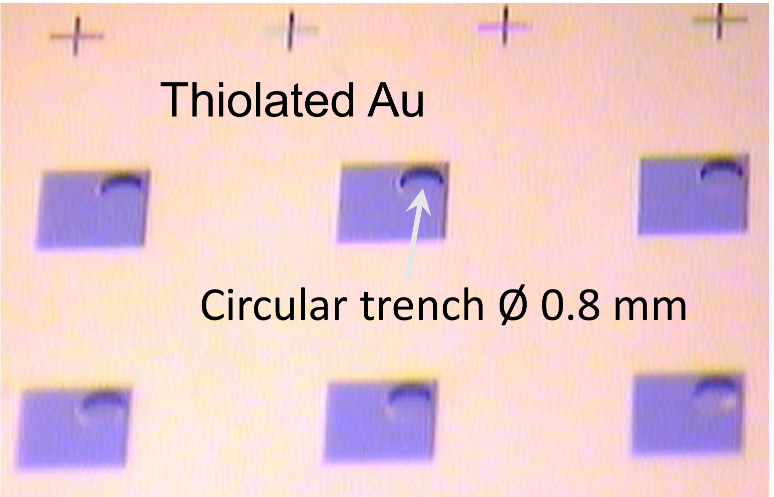
Wafer level flip-chip bonding scheme for the mounting of uniquely aligned microchips onto a chip carrier template with electrical circuits.

Parts & Receptor Sites

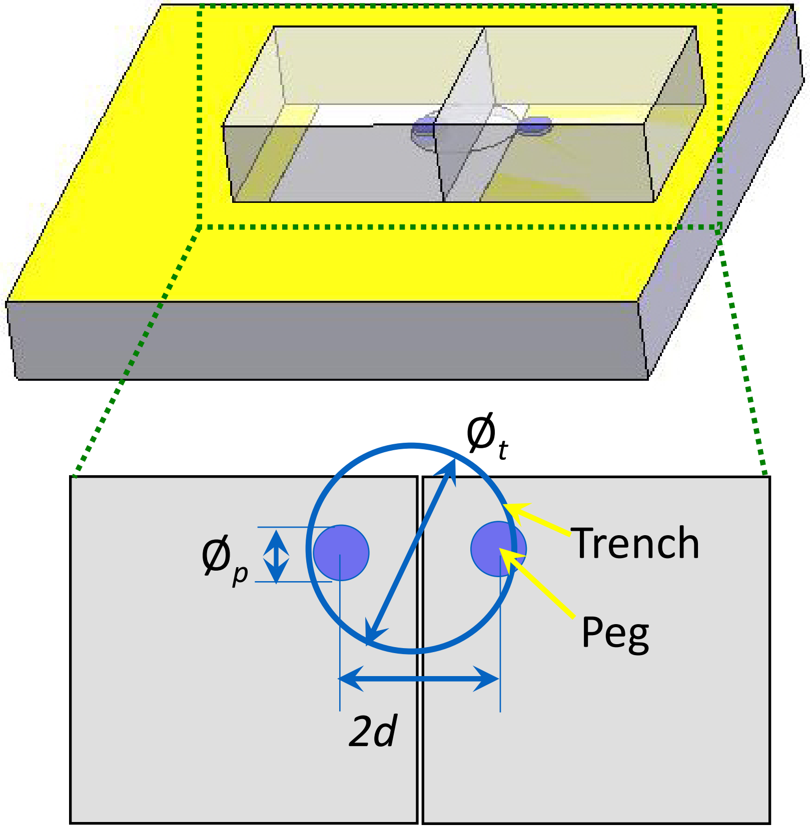
Top and bottom views of part



Array of receptor sites



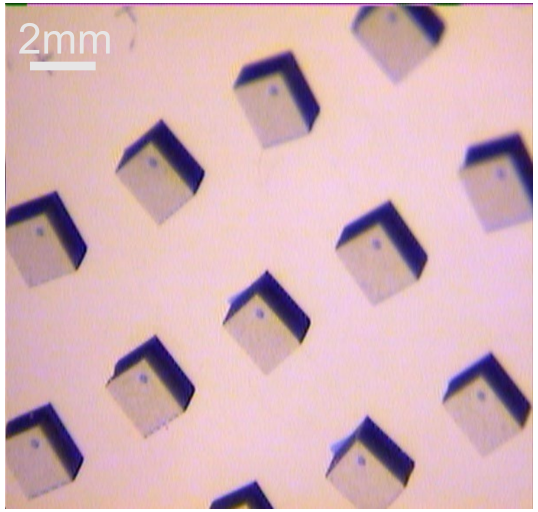
Design rule for one-to-one registration



$$Ø_t < Ø_p + 2d$$

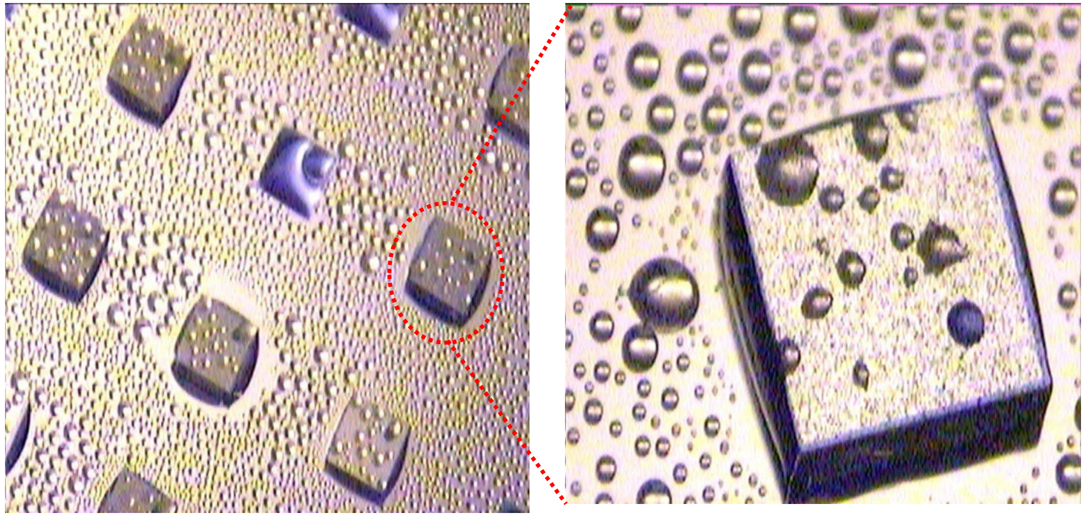
Two-Step Alignment

Step I

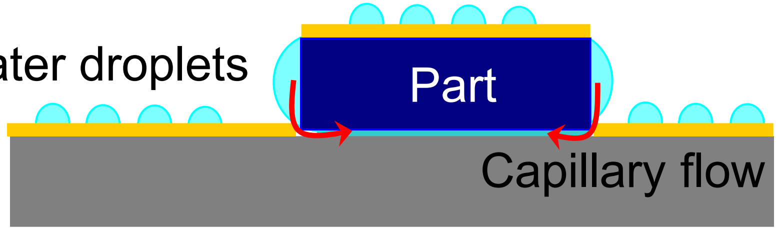


Gravity driven alignment

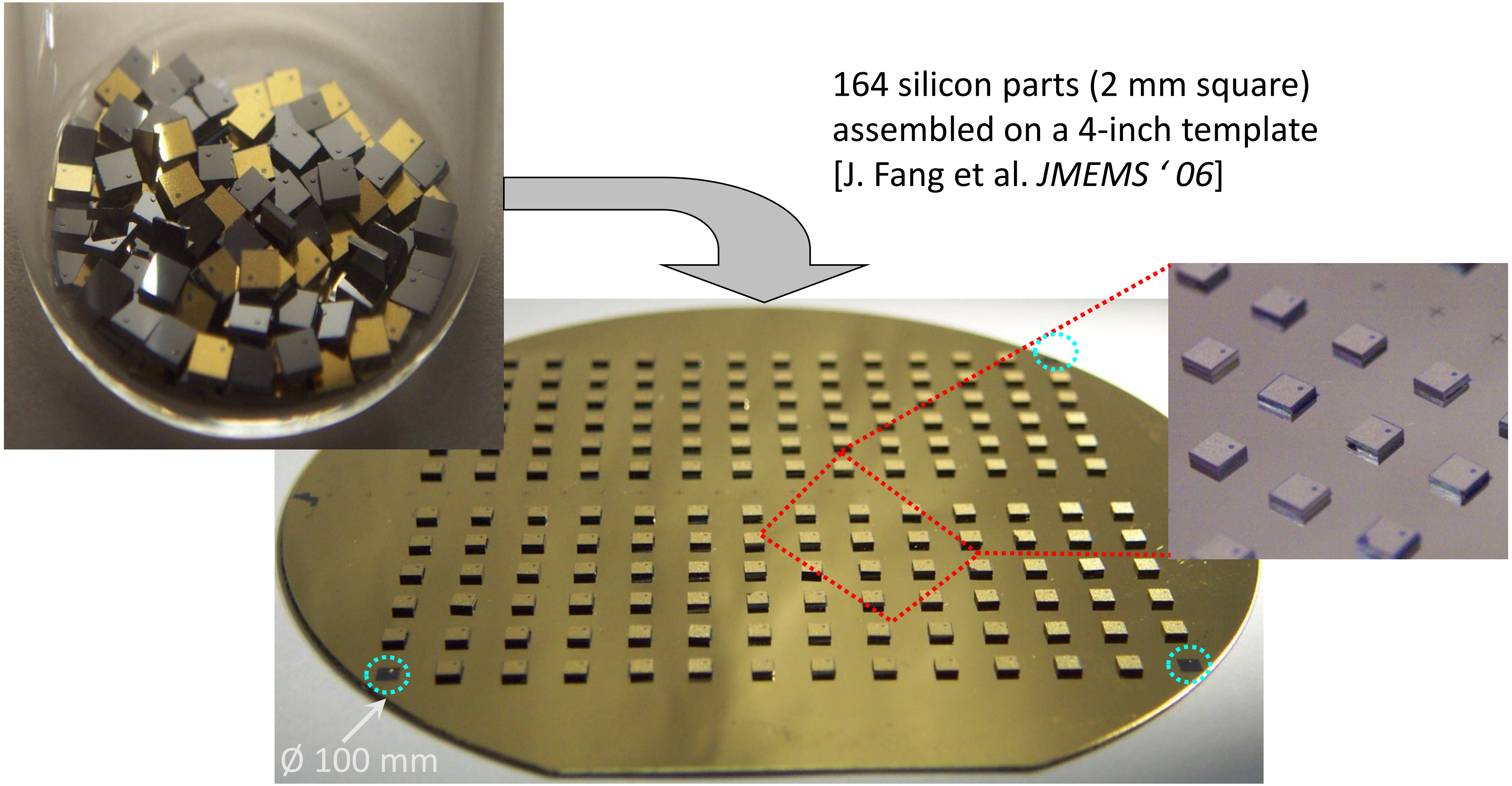
Step II



Capillary force driven alignment with water steam

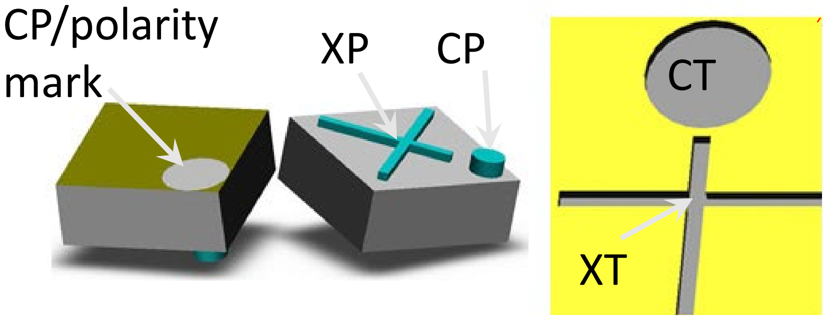


Uniquely Orienting Self-assembly



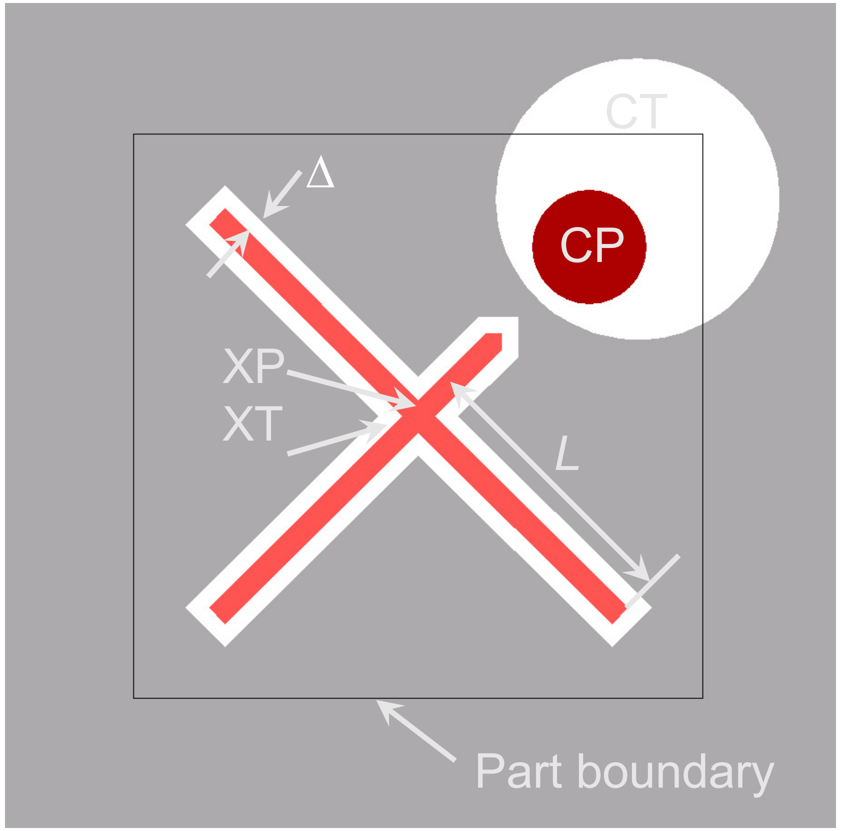
164 silicon parts (2 mm square)
assembled on a 4-inch template
[J. Fang et al. *JMEMS ‘ 06*]

Dry Self-Assembly with Unique Orientation



Design Rules for Alignment Features

Exact alignment top-view layout

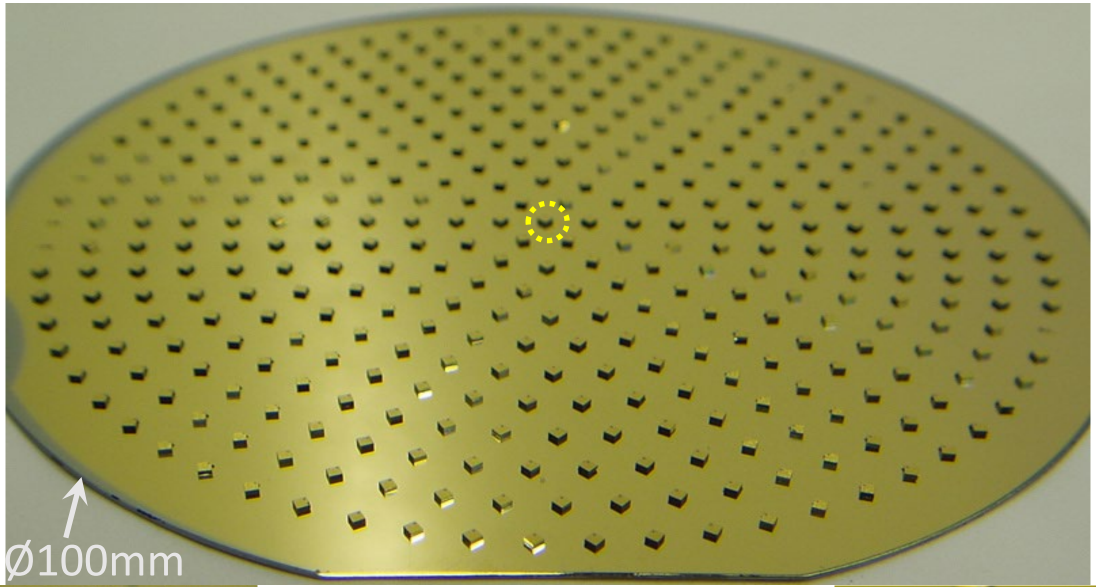


1. CT / XT exclusively adopts CP / XP
2. One CT adopts only one CP for one-to-one registration
3. Clearance Δ ~ 10-20 µm
4. Beam length *L* as long as possible to minimize rotational misalignment
5. Spacing between receptor sites large enough for neighboring parts to rotate about their CPs

Maximum misalignments:

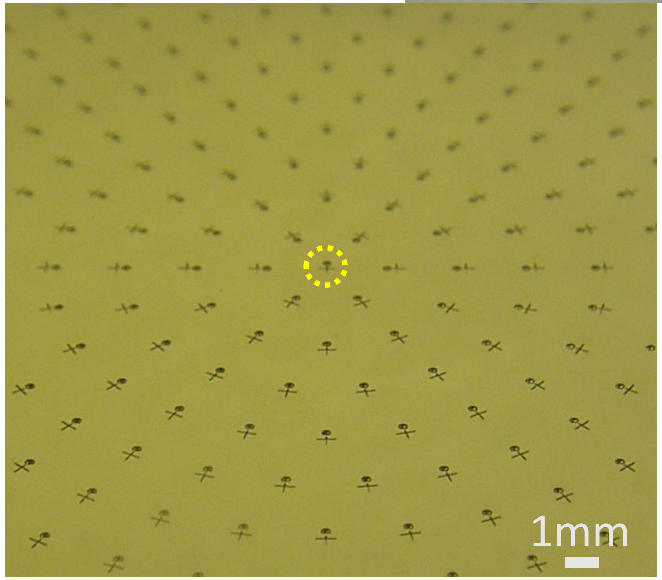
Translational = ±Δ, Rotational = $\tan^{-1}(\Delta/L)$

Assembly Result I



Polar array of
receptor sites

▽



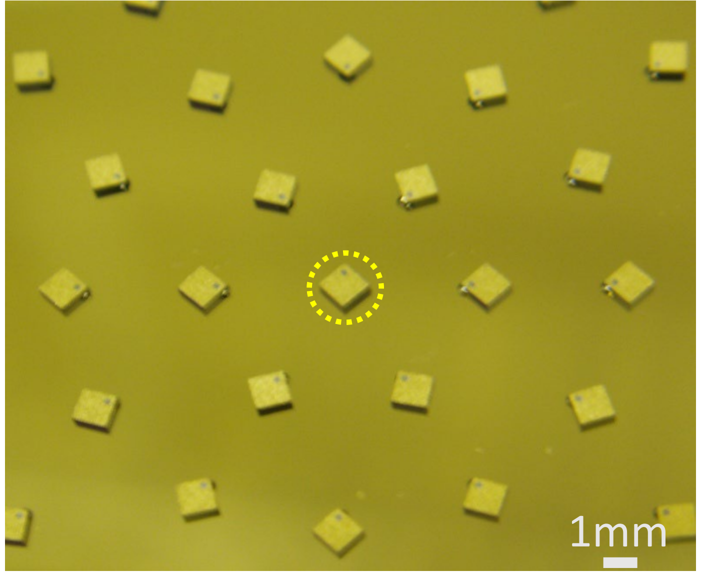
△

388 parts assembled on a 4-inch ALT with 397 receptor sites after 10 minutes agitation
(Yield = 97.7%)

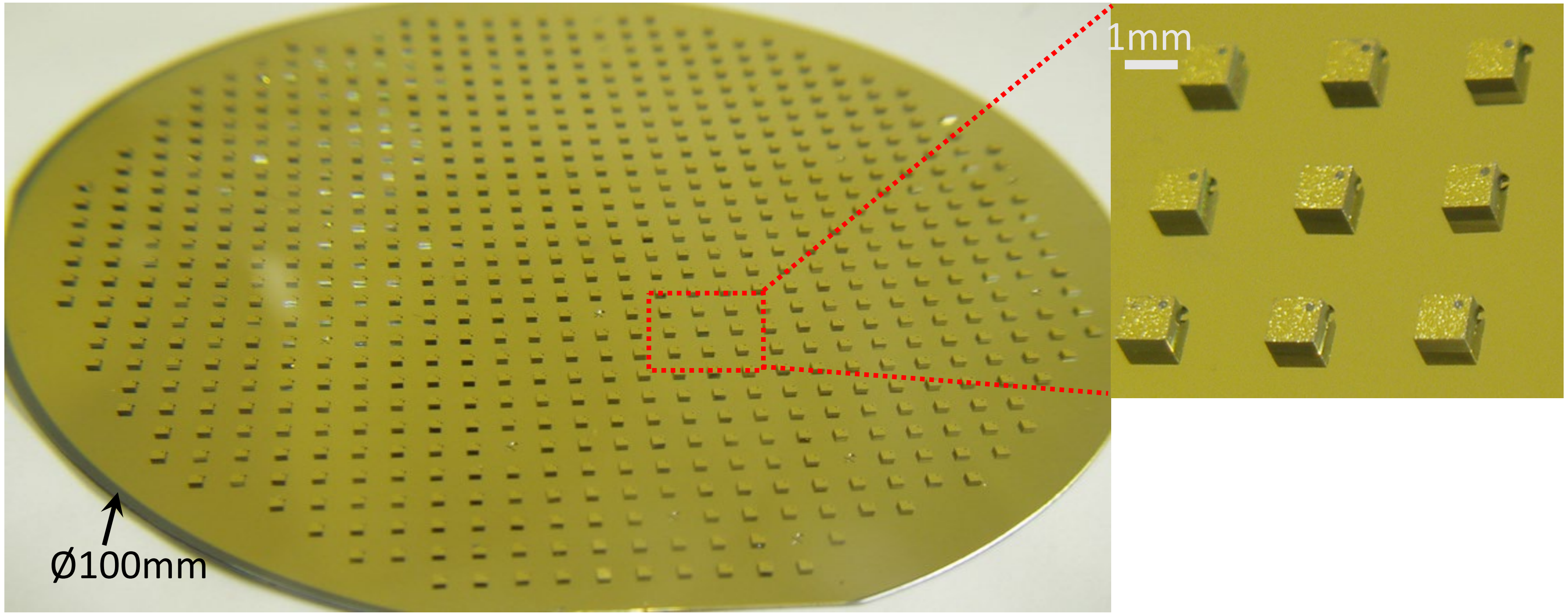
(Part redundancy = 50%)

ALT center parts

▽



Assembly Result II

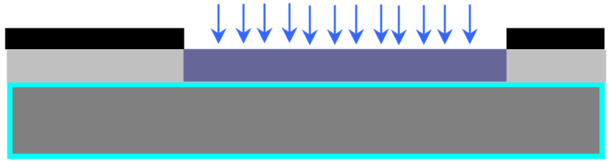


710 parts assembled on a 4-inch ALT with 720 receptor sites after 10 minutes agitation (Part redundancy = 50%) (Yield = 98.6%)

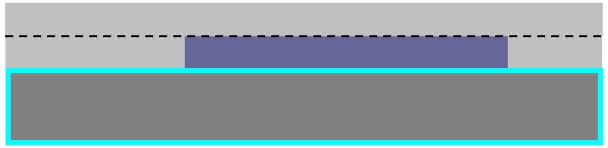
Application to Non-Silicon Parts

I. Spincoat 1st layer SU8

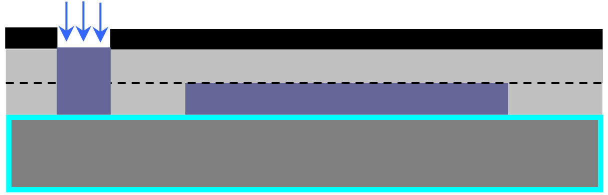
II. UV expose XP



III. Spincoat 2nd layer SU8

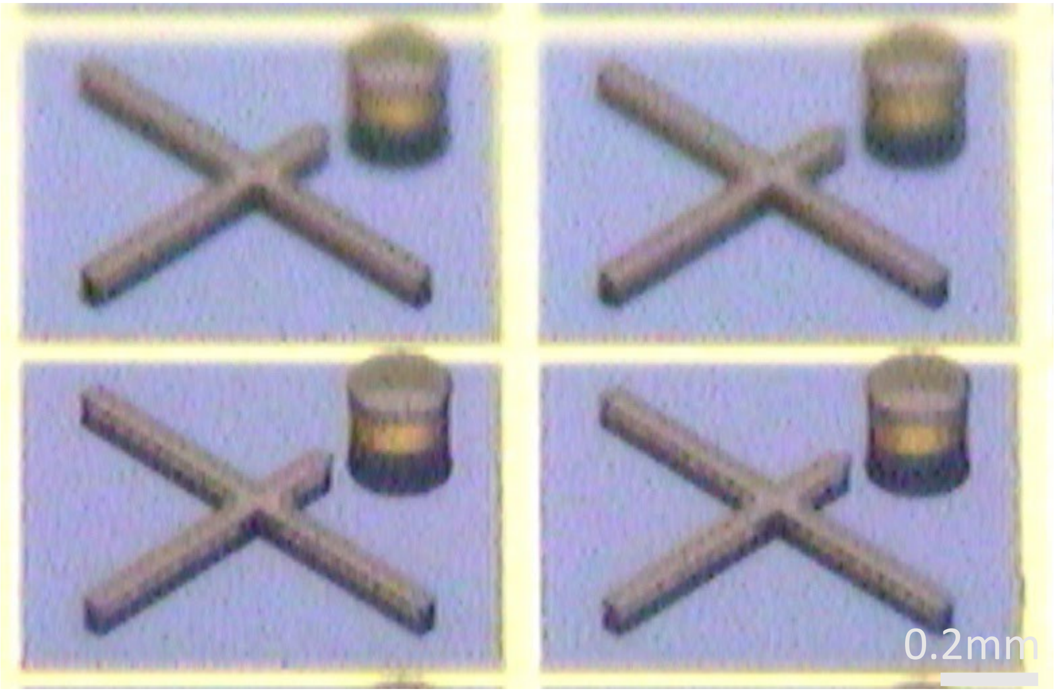


IV. UV expose CP

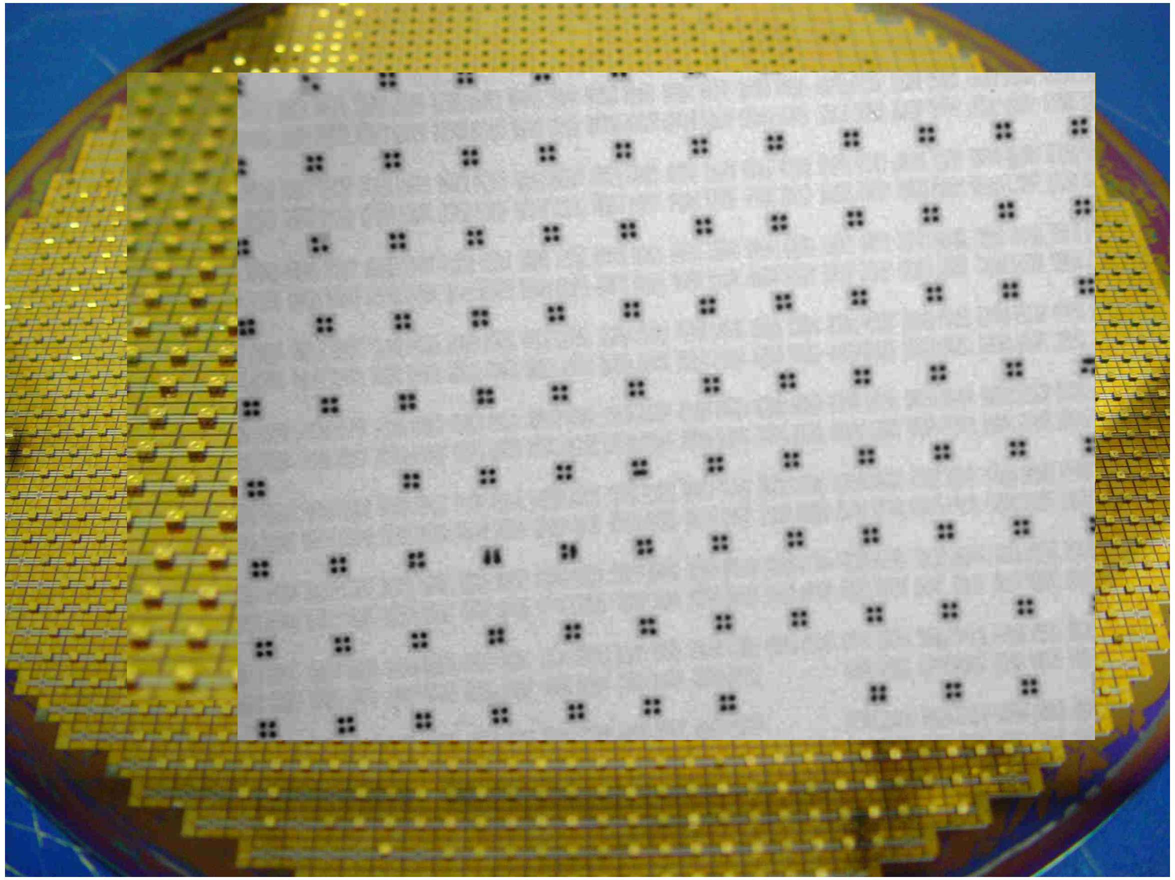


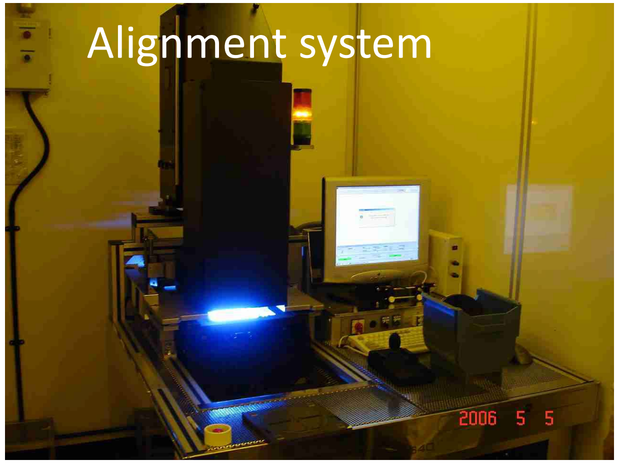
V. SU8 developed

Alignment features fabricated with SU8-2025



Industrial-scale Self-assembly





Self-assembly and bonding of chips on 8” wafer
(collaboration with ASTAR IME, Singapore)

Part III: Self-assembly Using Surface Tension

Capillary force driven assembly; programmable self-assembly by surface modulation; scalable assemblies at the air-water-solid interface

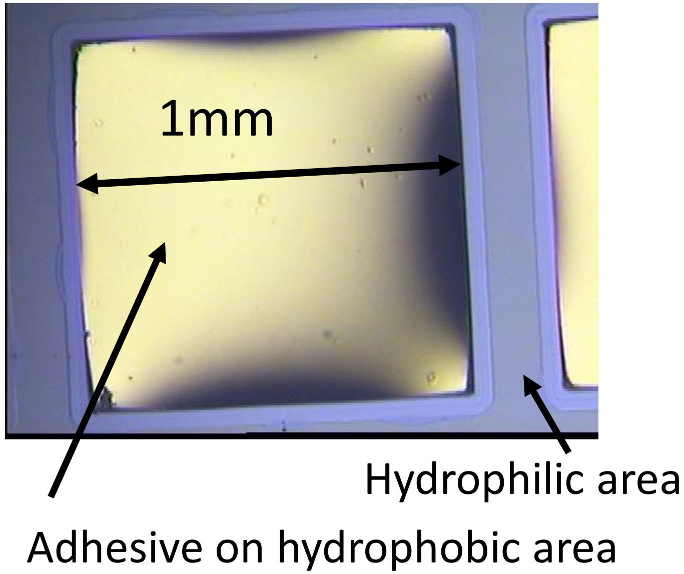
Surface Tension Driven Self-assembly

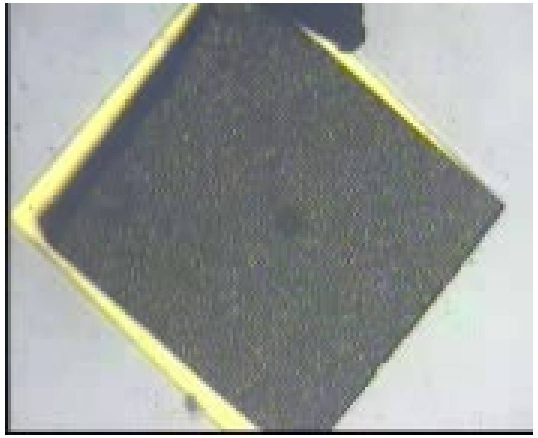
- Surface forces tend to dominate as components shrink below one mm
- Capillary forces have been widely used for assembly because of their favorable strength, range, predictability and controllability
- Disadvantage: components are exposed to liquids (water, oil, etc.) and may need special (hydrophobic, hydrophilic) surface treatments

Surface Tension Driven Self-assembly

Dip coating forms adhesive droplet on hydrophobic areas:

- reduce friction
- provide longer range capillary forces (>>1µm)
- act as photo- or heat-polymerizable glue





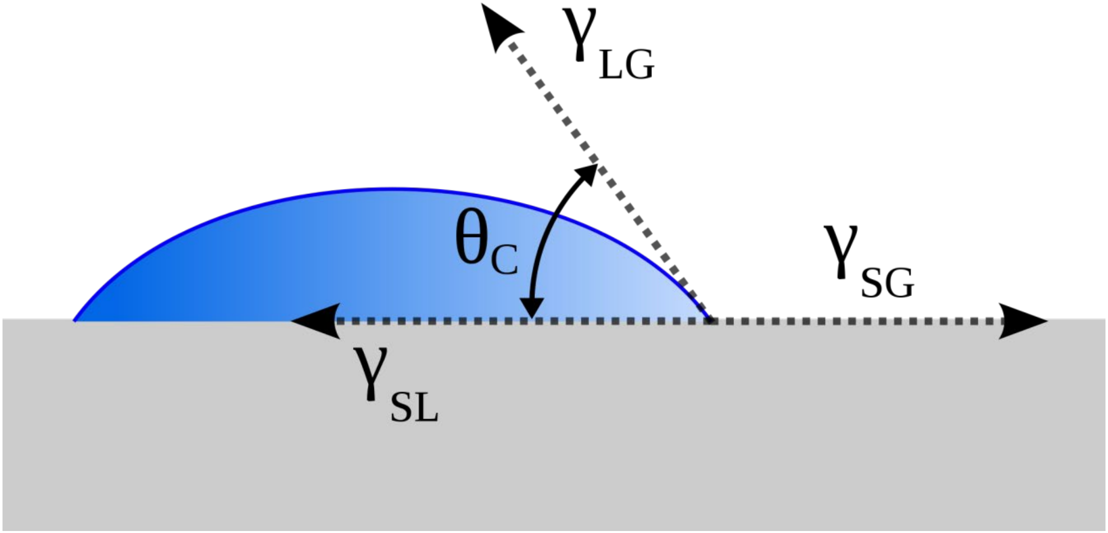
Video: X. Xiong ‘00

Young’s Equation

Thermodynamic equilibrium of a sessile drop:

$$\gamma_{SG} = \gamma_{SL} + \gamma_{LG} \cos(\theta_C)$$

- Surface energy γ
- Interfaces:
  Solid, Liquid, Gas
- Contact angle θ_C



Surface Tension Driven Self-assembly

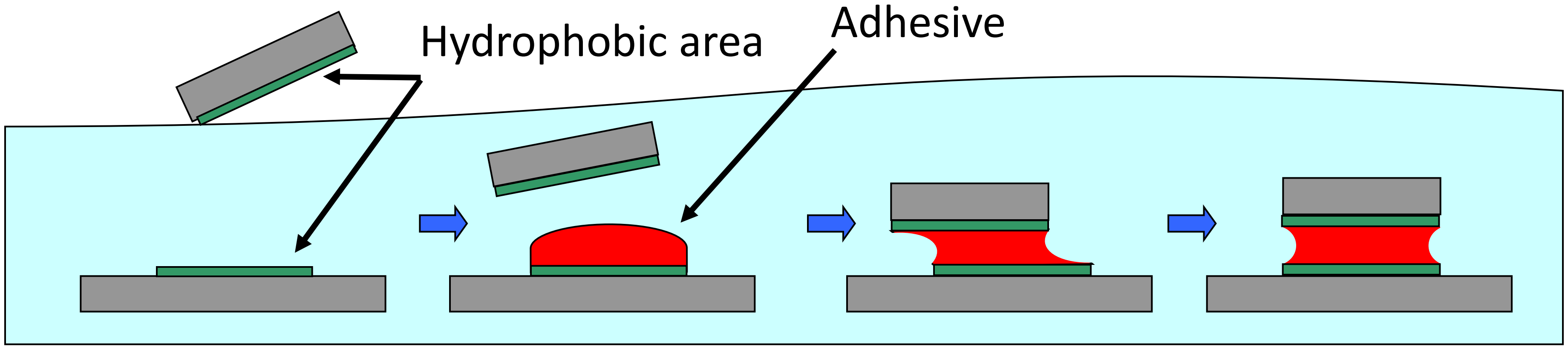
Self-assembly with surface tension can occur in a liquid environment or in air; it relies on an interface between two fluid phases.

1. <u>Structured particles:</u> the components have complementary patterns of hydrophobic and hydrophilic regions, which shape the liquid meniscus between components and binding sites
2. <u>Binding force:</u> capillary force, minimization of surface energy
3. <u>Environment:</u> a fluid helps with the delivery of components
4. <u>Driving force:</u> agitation provides transport until the system minimizes surface energy during assembly

Surface Tension Driven Self-assembly

Driving force for assembly: minimization of surface energy with hydrophobic-hydrophilic interfaces

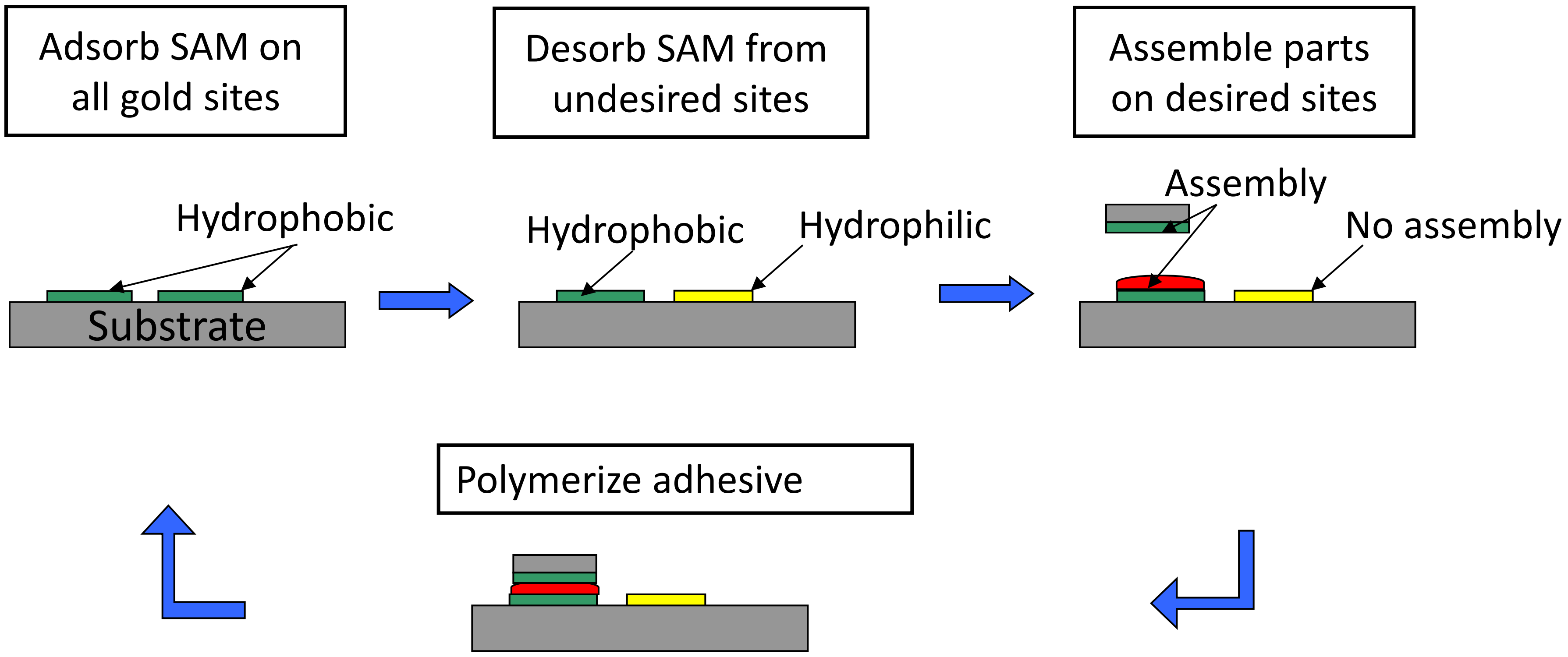
- Alkanethiol self-assembled monolayer (SAM) on Au forms hydrophobic surface
- Organic lubricant adhesive



[Srinivasan et al.'99, Whitesides et al.'90s]

Programmable Self-assembly

Organization of **different** parts onto desired locations



Adsorb SAM on all gold sites

Desorb SAM from undesired sites

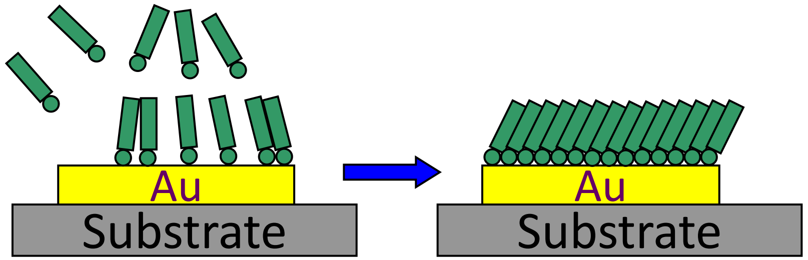
Assemble parts on desired sites

Polymerize adhesive

Modulation of Surface Energies

Hydrophilic → Hydrophobic

Adsorption of alkanethiol SAM

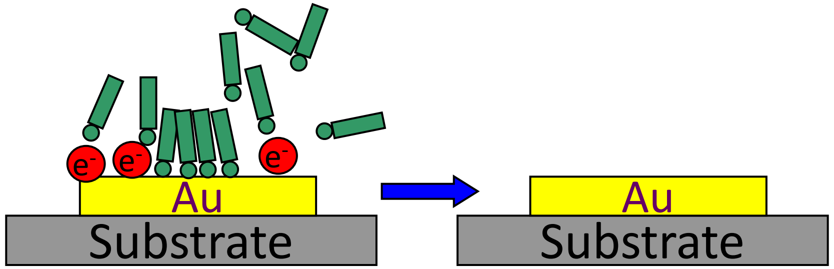


Adsorption is accomplished by soaking surfaces in ethanolic alkanethiol solution.

Hydrophobic → Hydrophilic

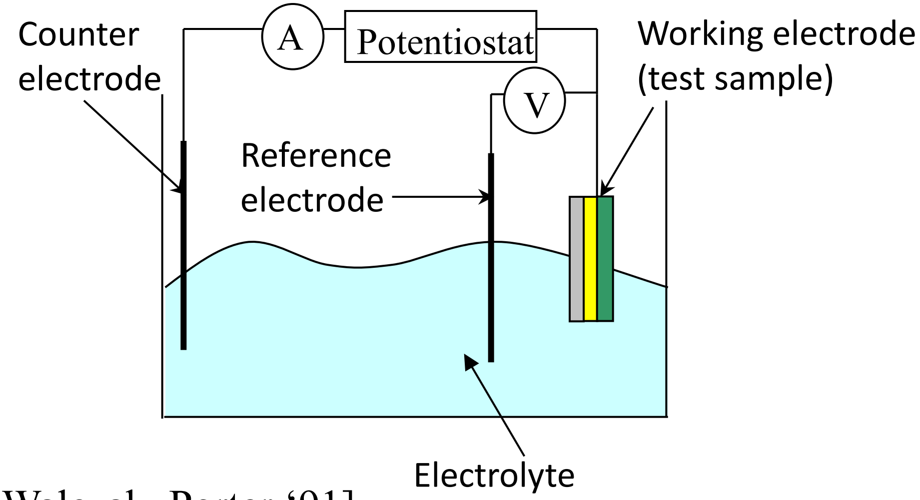
Reductive desorption of SAM

$CH_3(CH_2)_nS–Au + e^- \rightarrow CH_3(CH_2)_nS^- + Au$

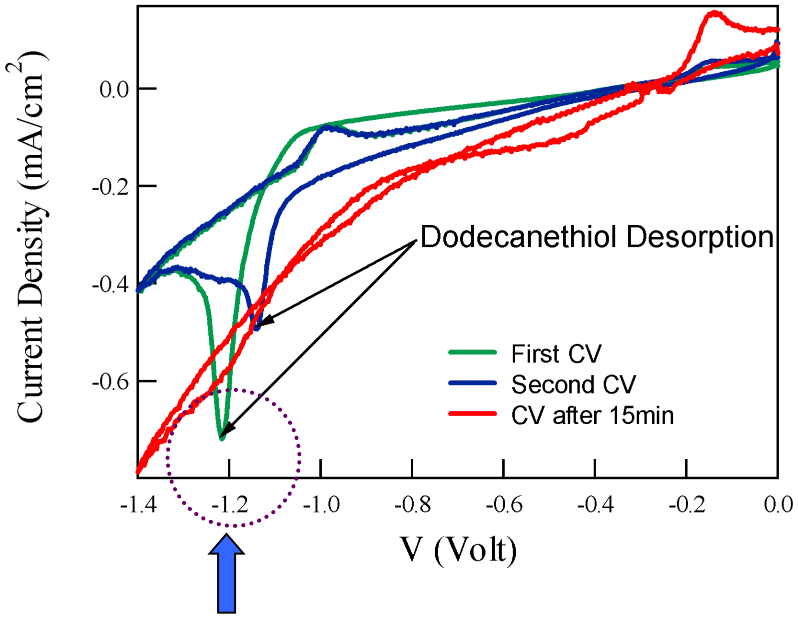


Desorption is accomplished by applying a negative voltage to the Au electrode.

SAM Reductive Desorption Characterization on Gold (111)



[Walczak, Porter '91]
[Weisshaar, Porter'92]

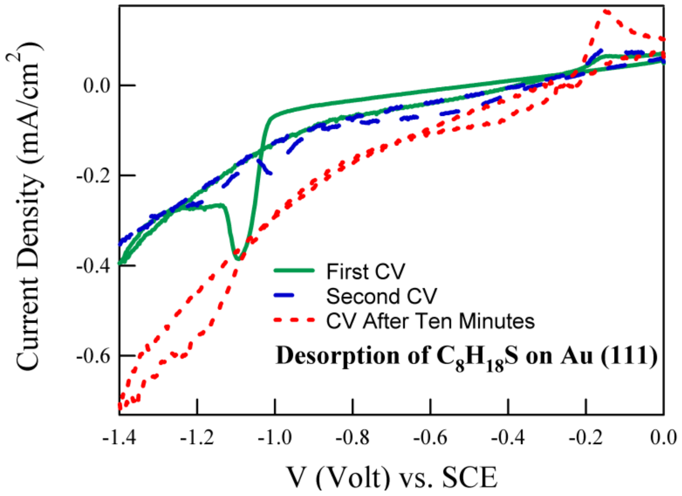


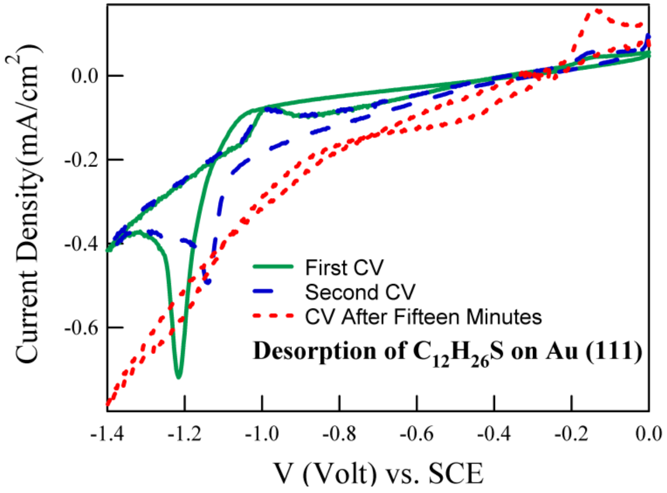
Peaks of SAM desorption

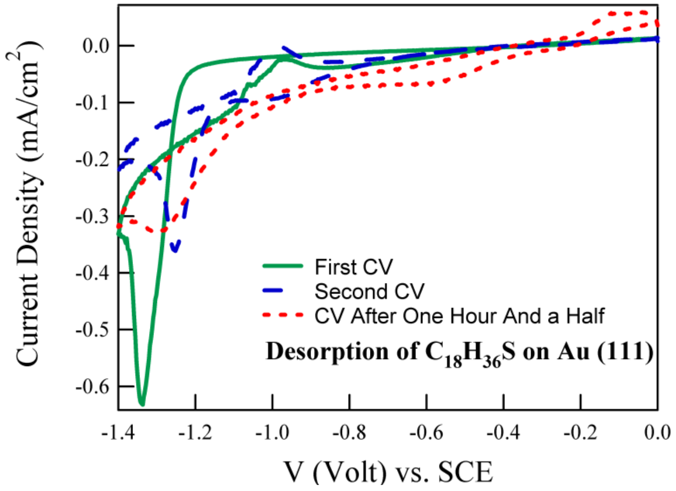
Experiment setup:

- Au (111) surfaces with SAM
- Reference electrode: SCE
- Electrolyte: 0.5M KOH

Optimization of SAM Desorption





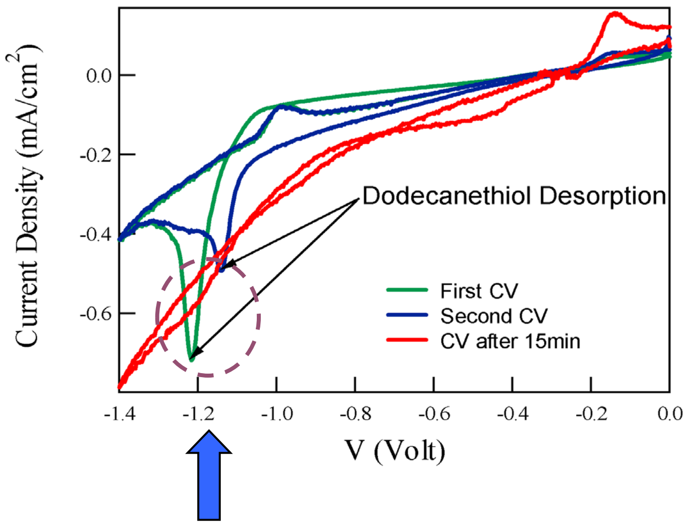


Desorption of different alkanethiol SAMs on Au(111) (C_3H_8S, $C_8H_{18}S$,$C_{12}H_{26}S$, $C_{18}H_{38}S$)

C_3H_8S	$C_8H_{18}S$	$C_{12}H_{26}S$	$C_{18}H_{38}S$
Unstable	10min	15min	4hours

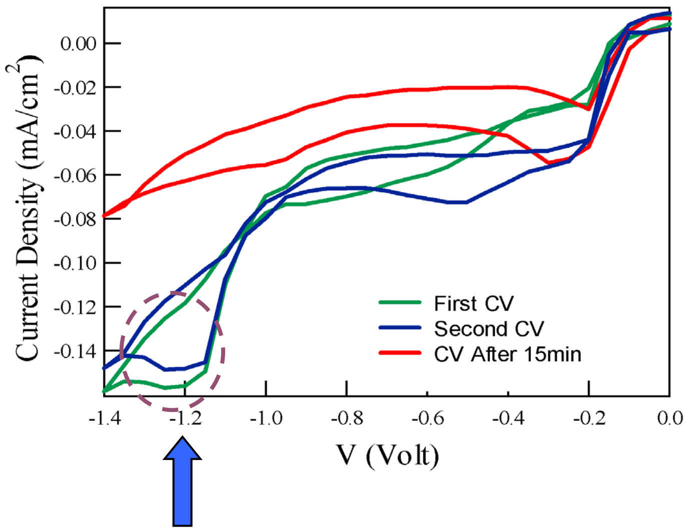
Substrate Dependence of SAM Reductive Desorption

SAM desorption from Au(111) on mica



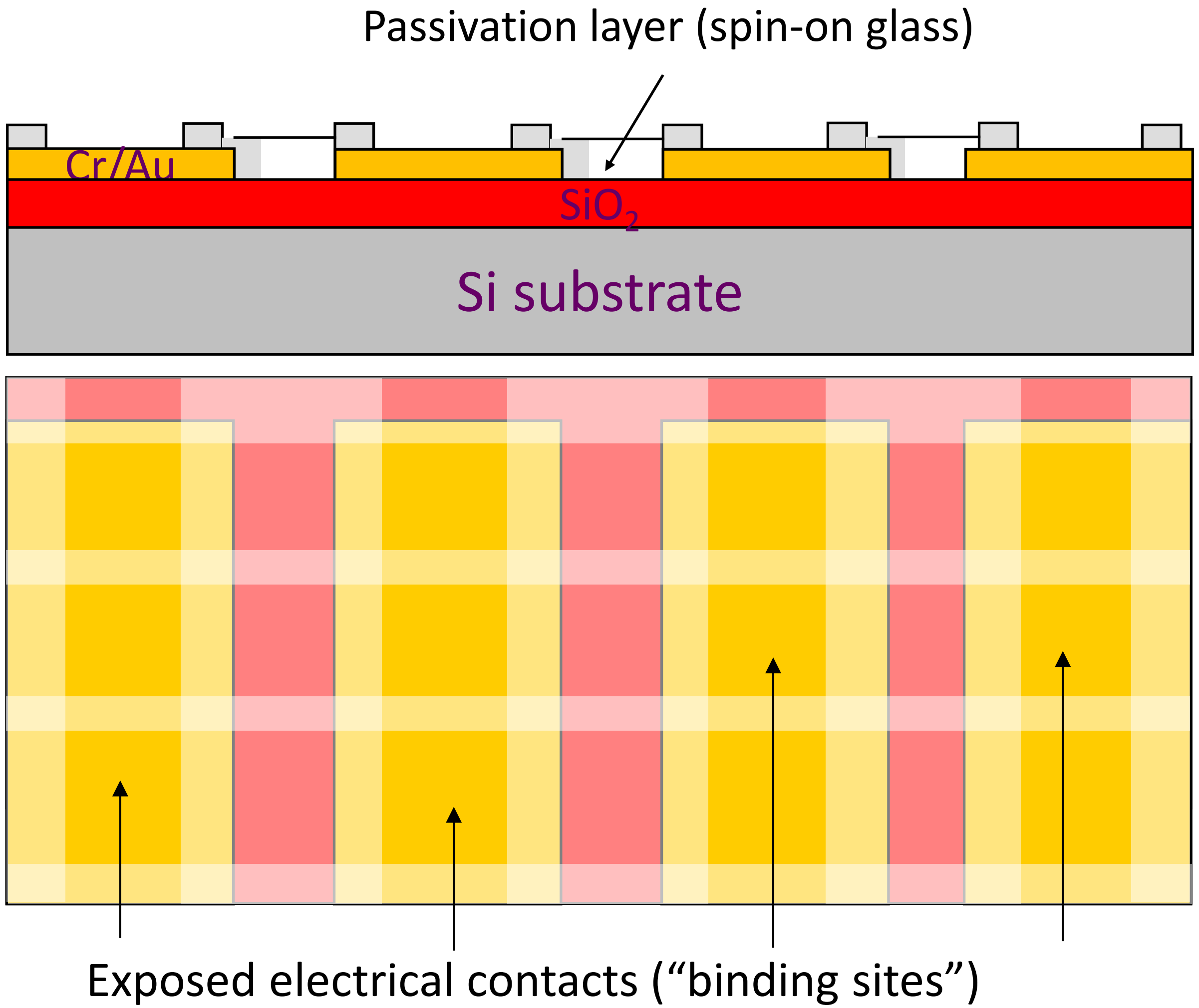
Peaks of SAM desorption

SAM desorption from polycrystalline Au on Si



Broadened peaks of SAM desorption

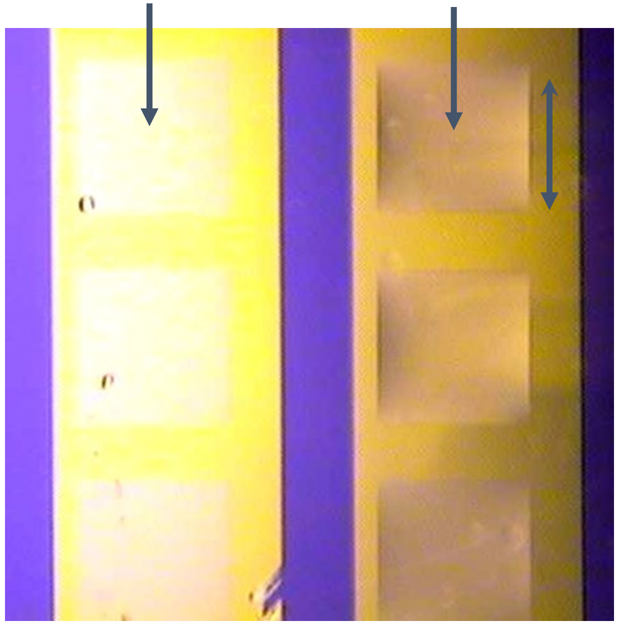
Fabrication of Substrate



SAM Desorption and First Assembly Batch

No adhesive on hydrophilic surfaces

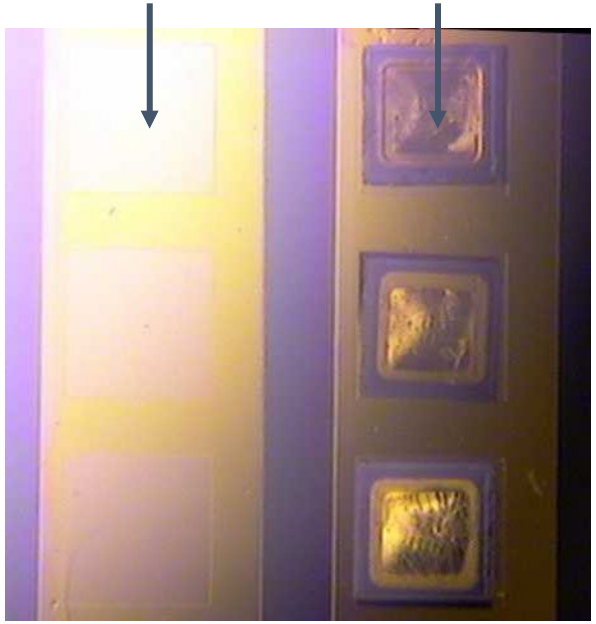
Adhesive on hydrophobic surfaces



1mm

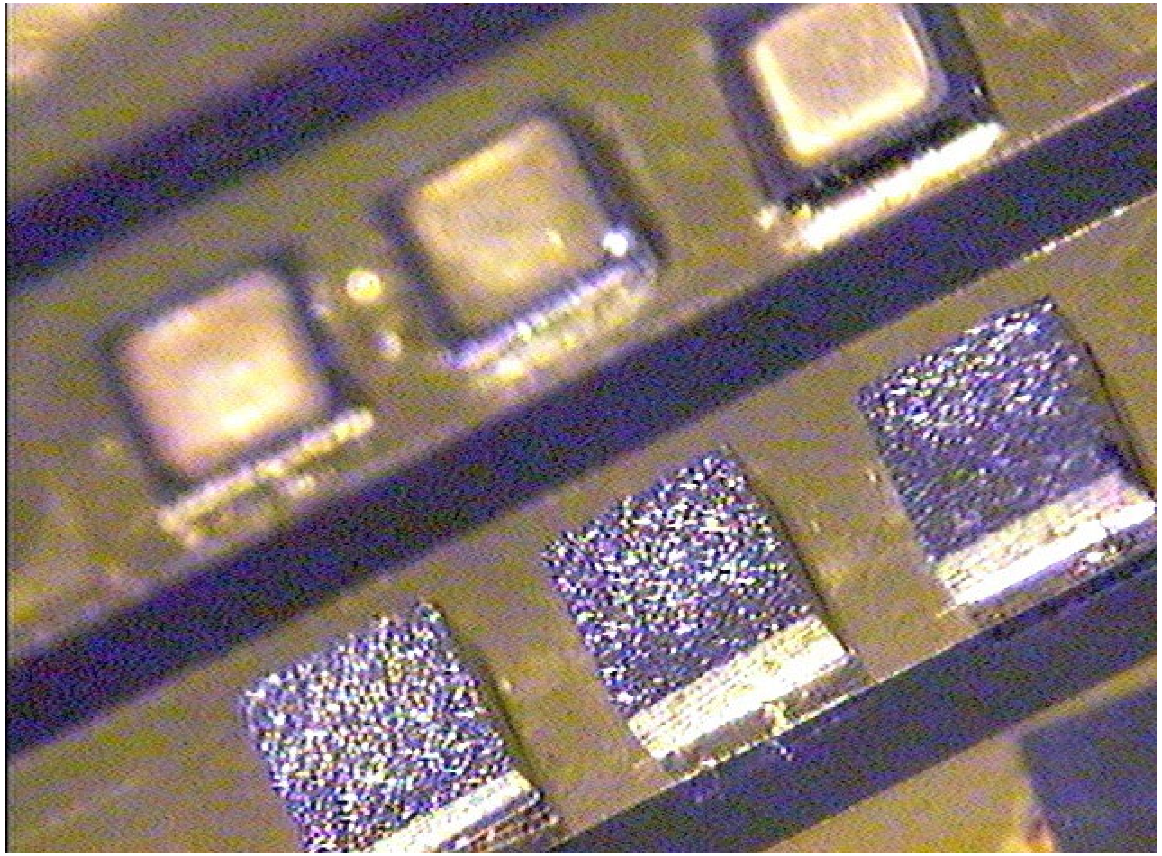
Free spot

Assembled part



SAM desorption from left column of sites only

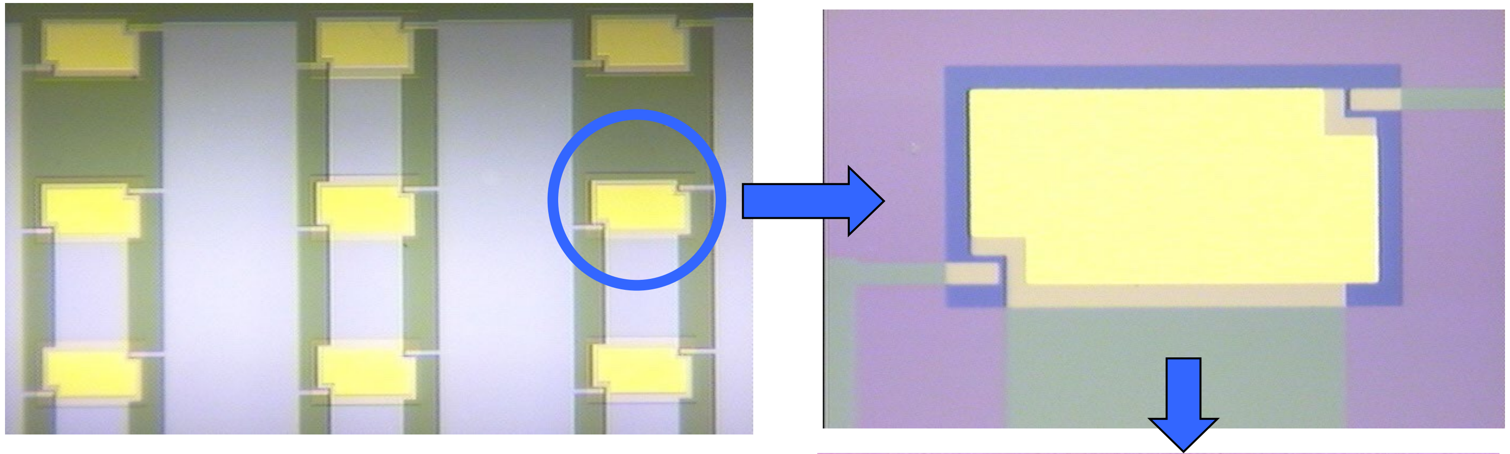
Second Assembly Batch



[X. Xiong et al. *Transducers* '01, *JMEMS* '03]

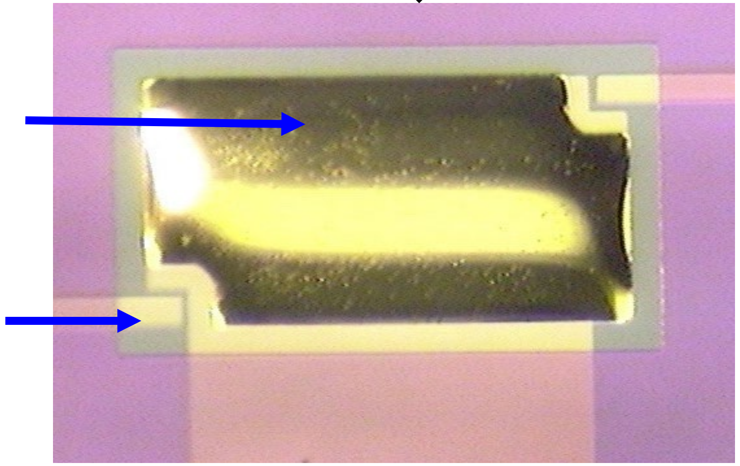
Adding Electrical Connectivity

Top view of a fabricated substrate for LED assembly

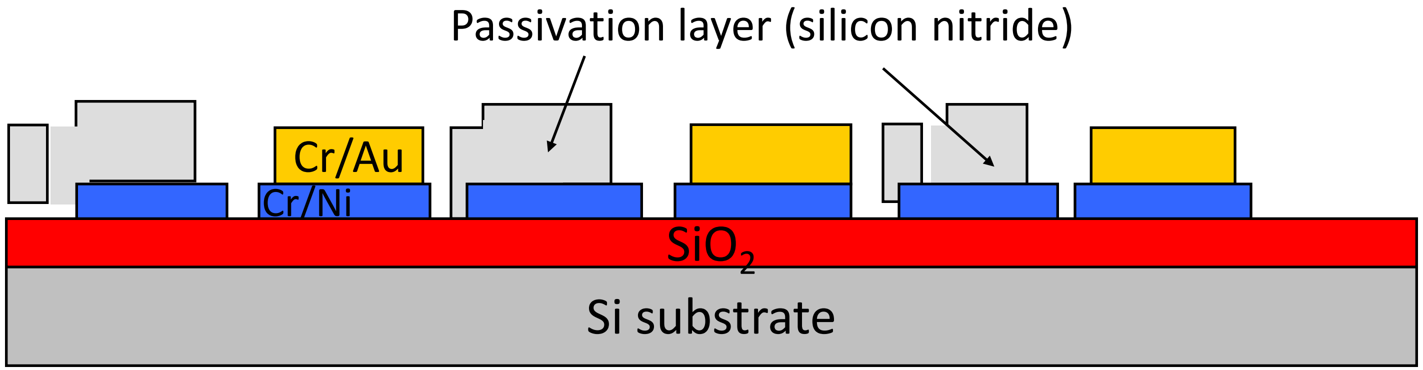


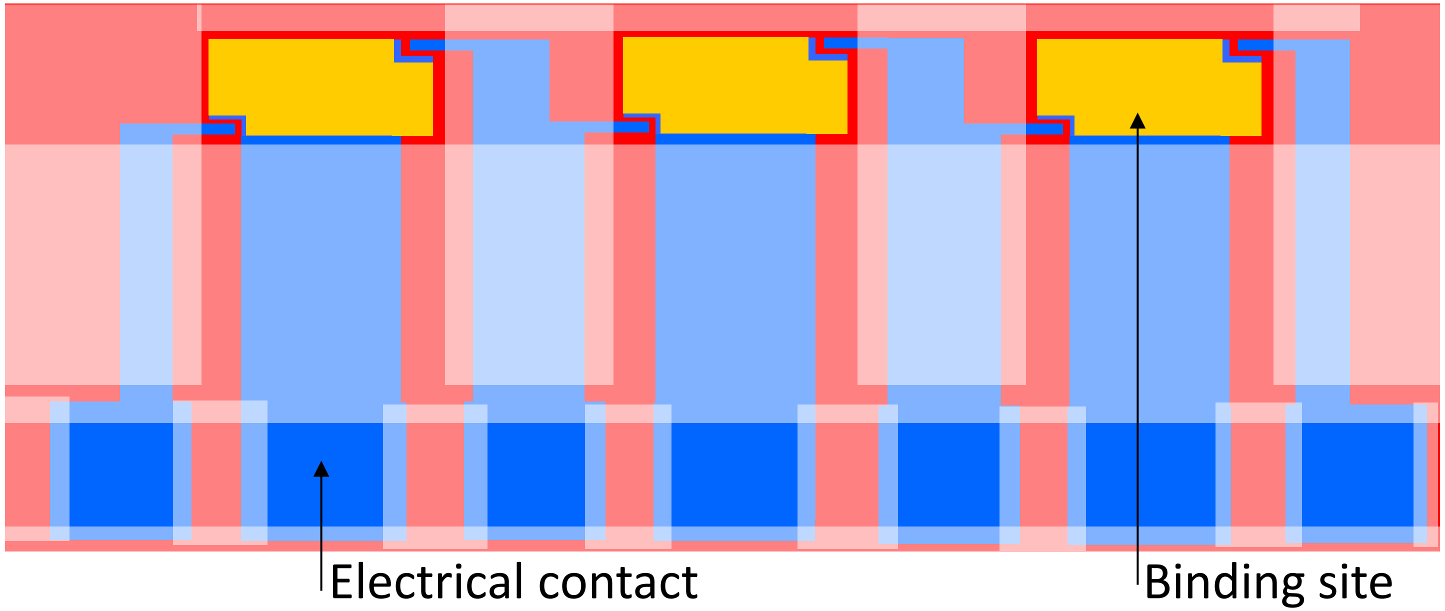
Adhesive wets Au binding site

Ni electroplating seed is free from adhesive



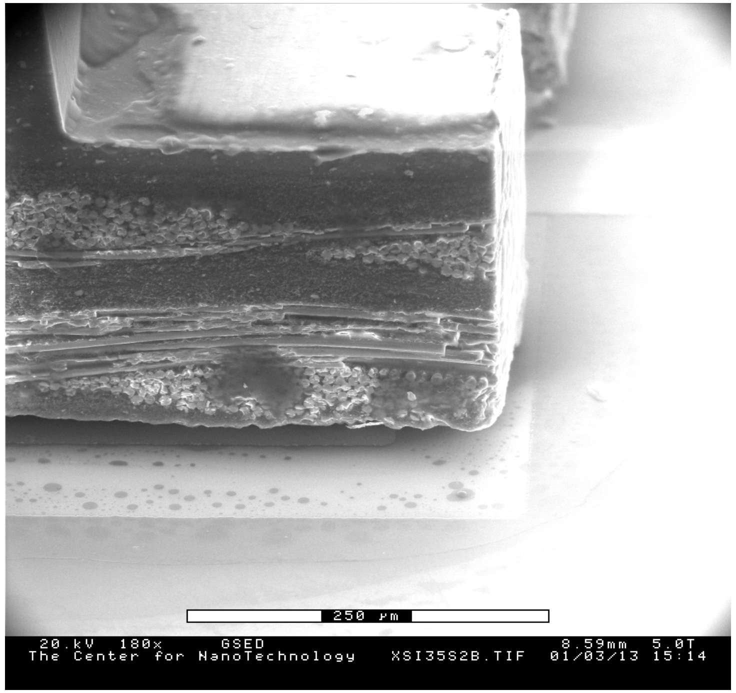
Fabrication of the Substrate for LED Assembly



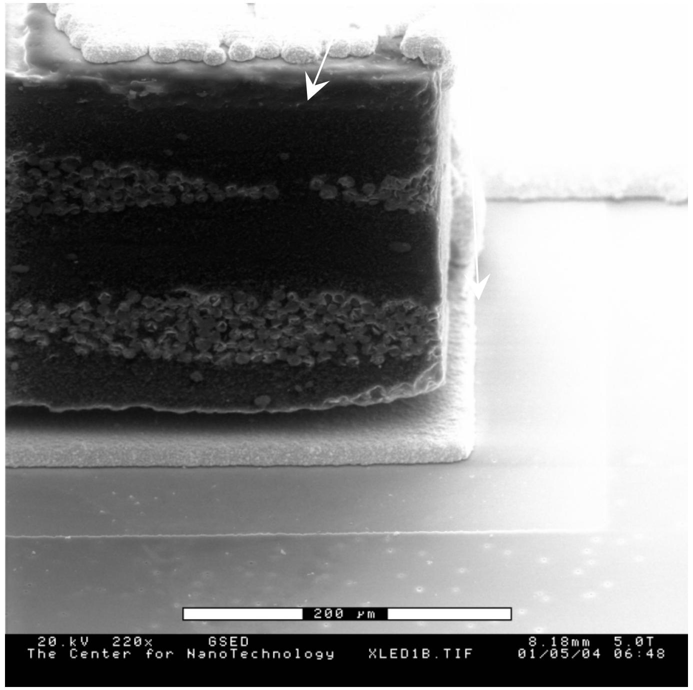


Electrical Connection by Electroplating

Gap between an assembled LED and substrate is ~ 20µm



Electrical connection established by plated solder

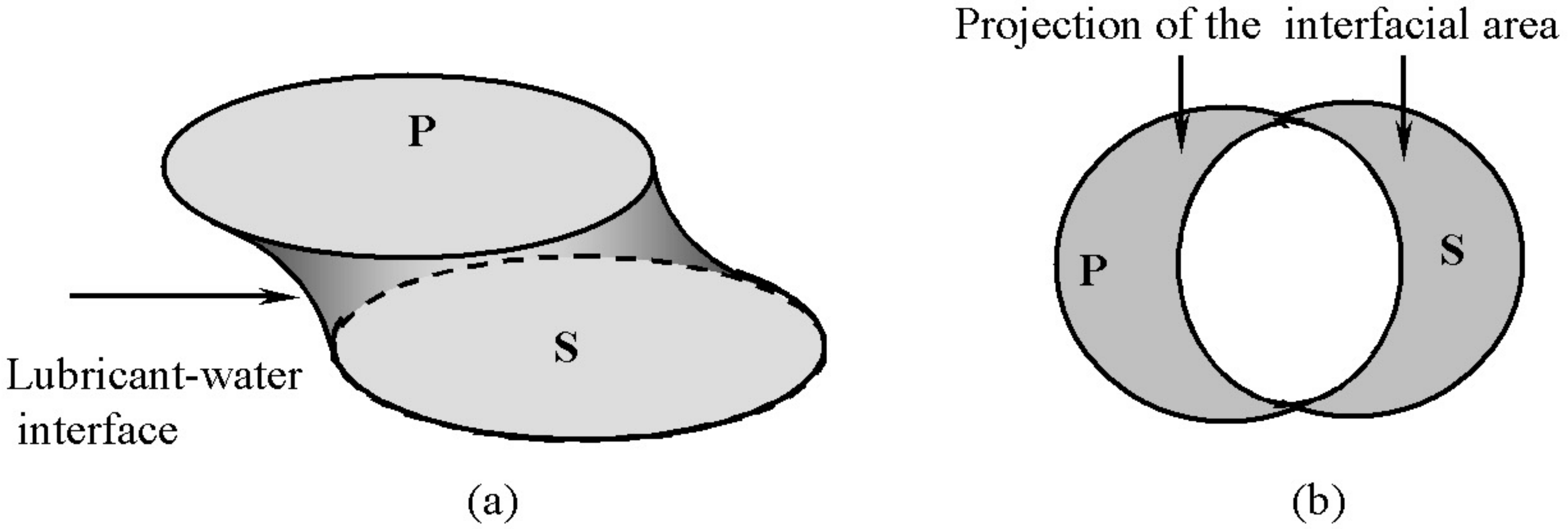


Self-assembled LED with Electrical Connections

[X. Xiong et al., *JMEMS* '03]

Modeling the Binding Energy

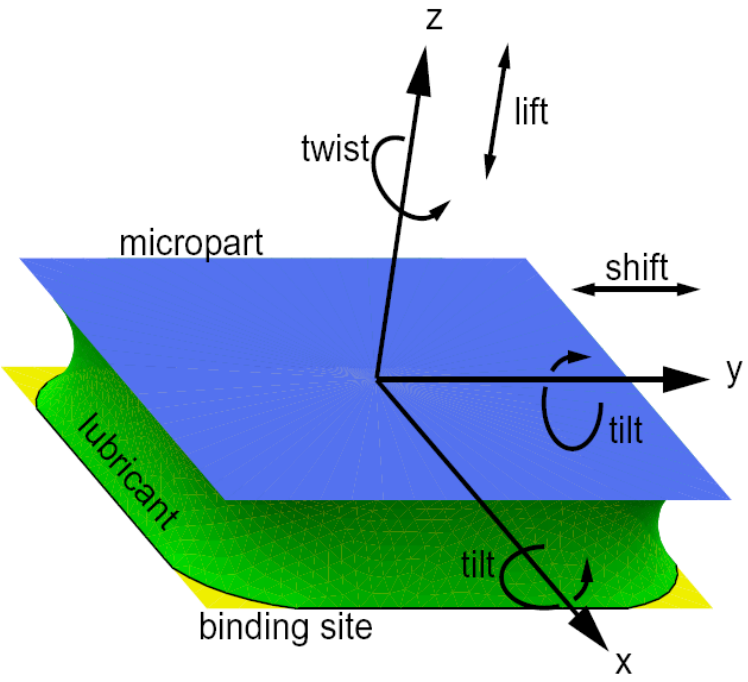
- Calculate the adhesive-water-interface between part *P* and binding site *S*

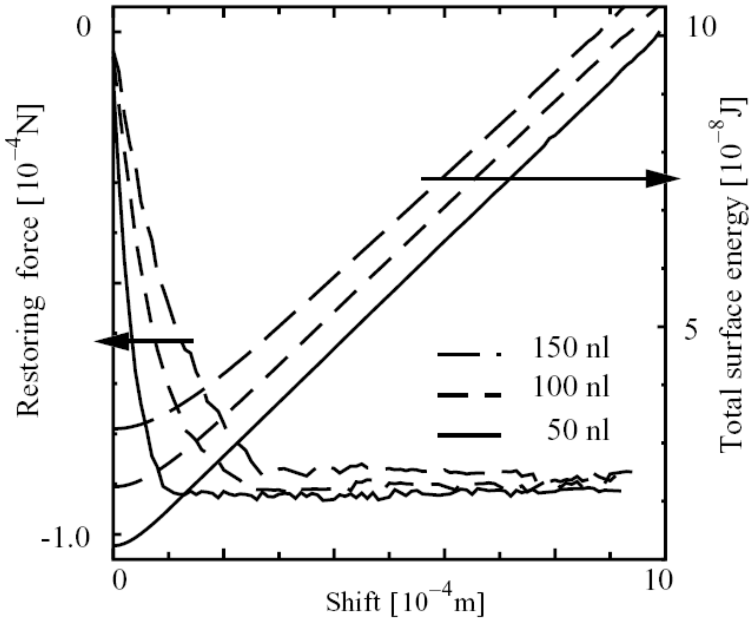


  - For small aspect ratios, interface can be approximated by partial shape overlap of *P* and *S*
  - Shape overlap easy to calculate analytically

Modeling the Binding Energy

FEM analysis [Lienemann et al., *Sensors Update* '03] shows linear relationship between displacement and surface energy when displacement > adhesive thickness





Shape Overlap Model

Use geometric shape overlap model to evaluate energy profile of binding sites

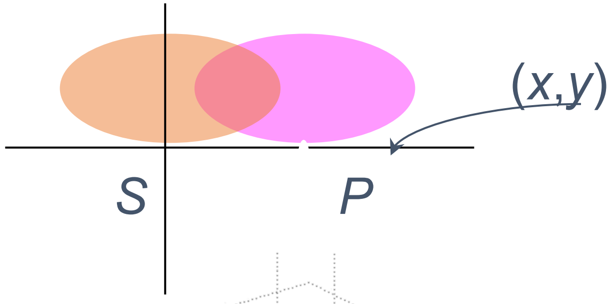
Efficient implementation:

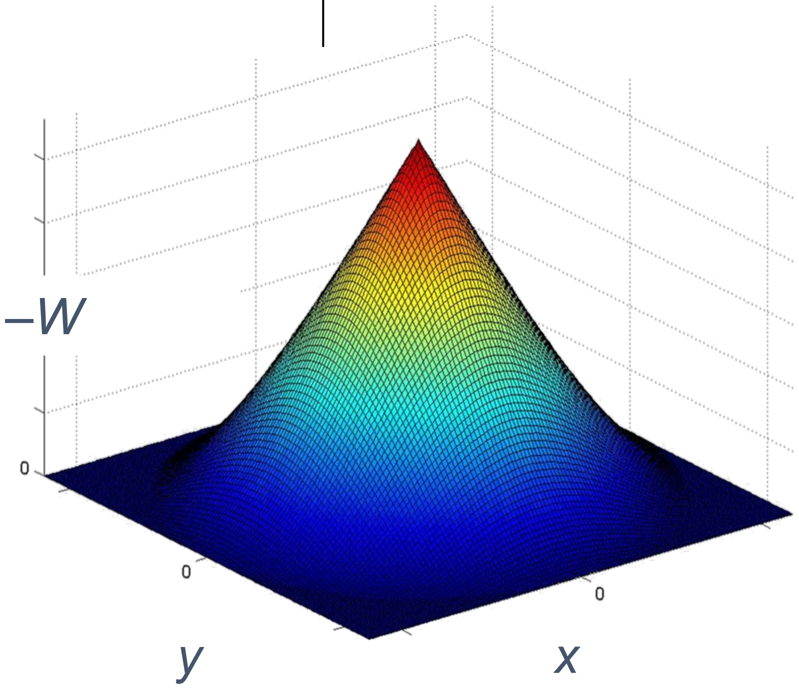
(1) digitize arbitrary binding site designs

(2) convolute areas

Physical motivation:

- adhesive forms bridge between sites
- projection of liquid: $S \cup P$
- projection of meniscus (if $S \cap P \neq \varnothing$):
  $A = |S-(S \cap P)| + |P-(S \cap P)|$
  $= |S| + |P| - 2|S \cap P|$
  $= \text{const} - 2|S \cap P|$
- surface energy: $\partial W \sim -\partial A \sim \partial|S \cap P|$

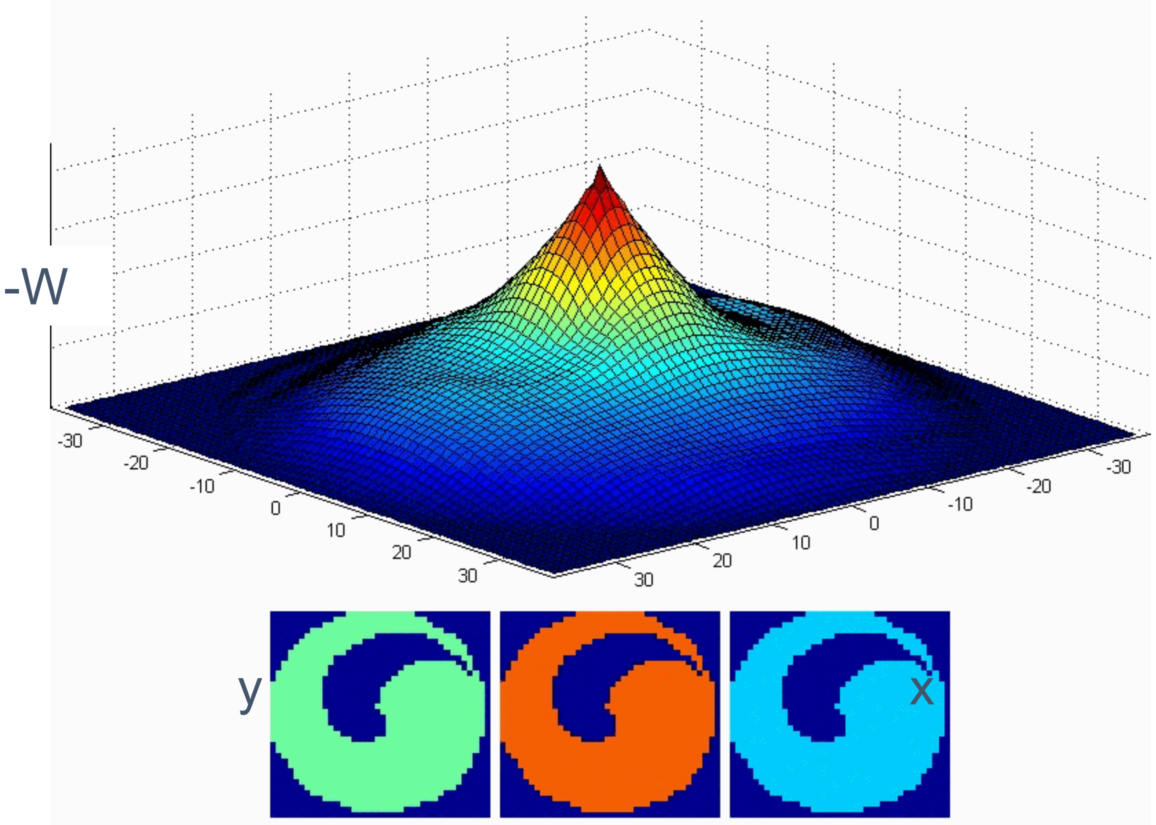




overlap area in C-space

Binding Site Design

- <u>Binding site shape optimization:</u>
  (a) de-convolution?
  (b) Monte Carlo search, genetic algorithms for optimal binding site design?
- <u>Uniqueness Problem:</u>
  For a given part (e.g., a diode) does there exist a binding site design with unique energy minimum?

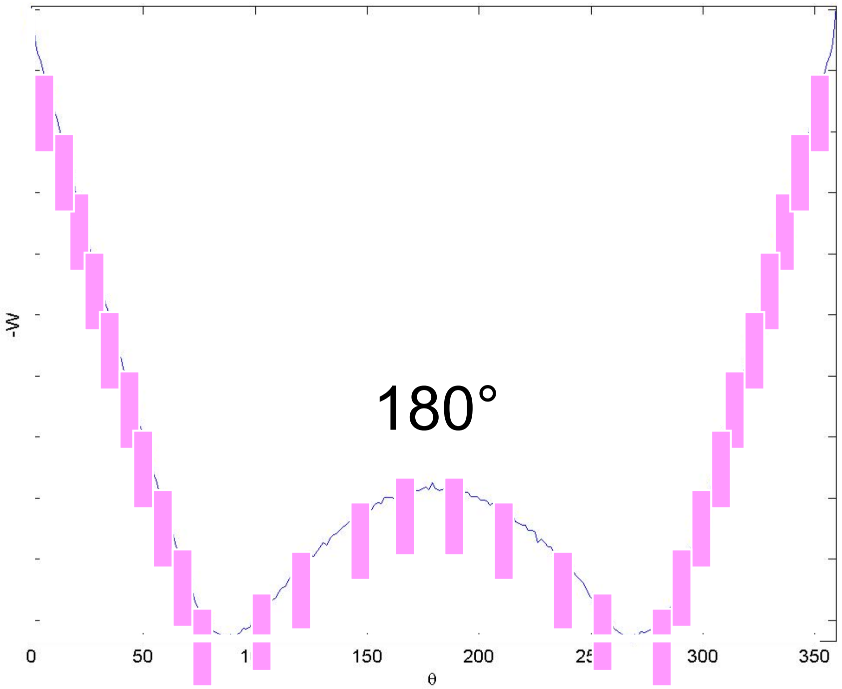


Böhringer KF, Srinivasan U, Howe RT. Modeling of capillary forces and binding sites for fluidic self-assembly. *MEMS 2001. 14th IEEE International Conference on Micro Electro Mechanical Systems* 2001 Jan 25 (pp. 369-374).

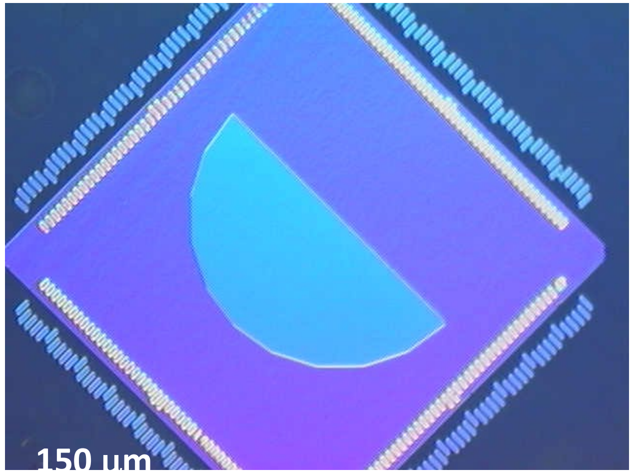
Semicircles

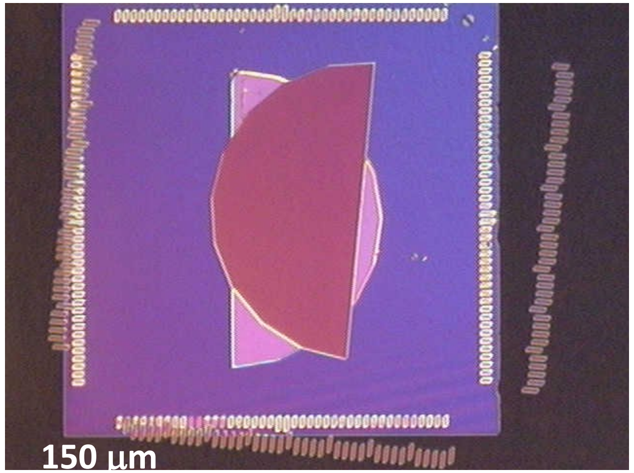
Unique orientation?

- ~40% alignment yield observed
- local energy minimum at 180°



overlap area vs. θ

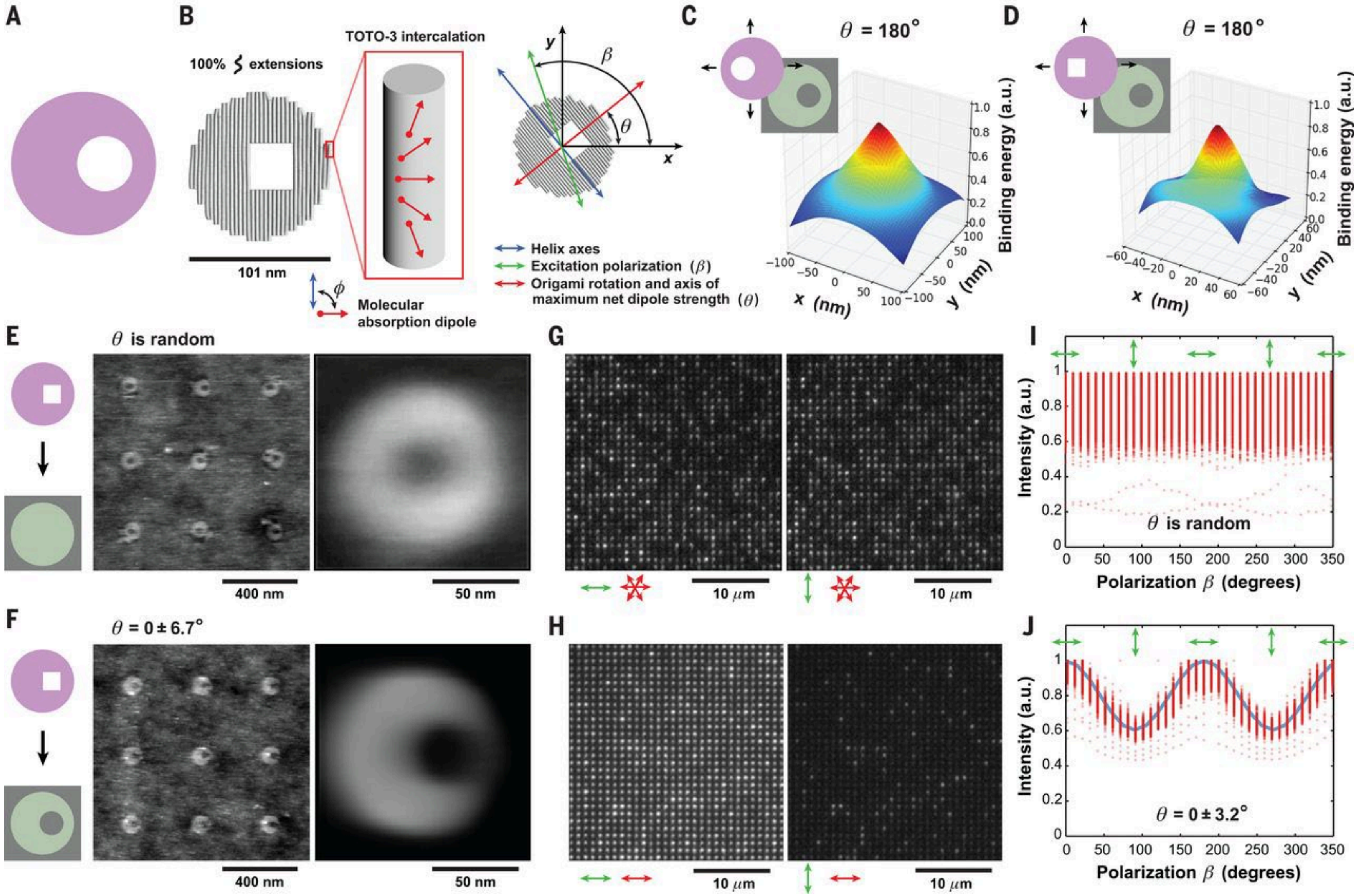




Non-unique energy minimum

(Microscope pictures: U. Srinivasan)

Positioning and Orienting of DNA Origami

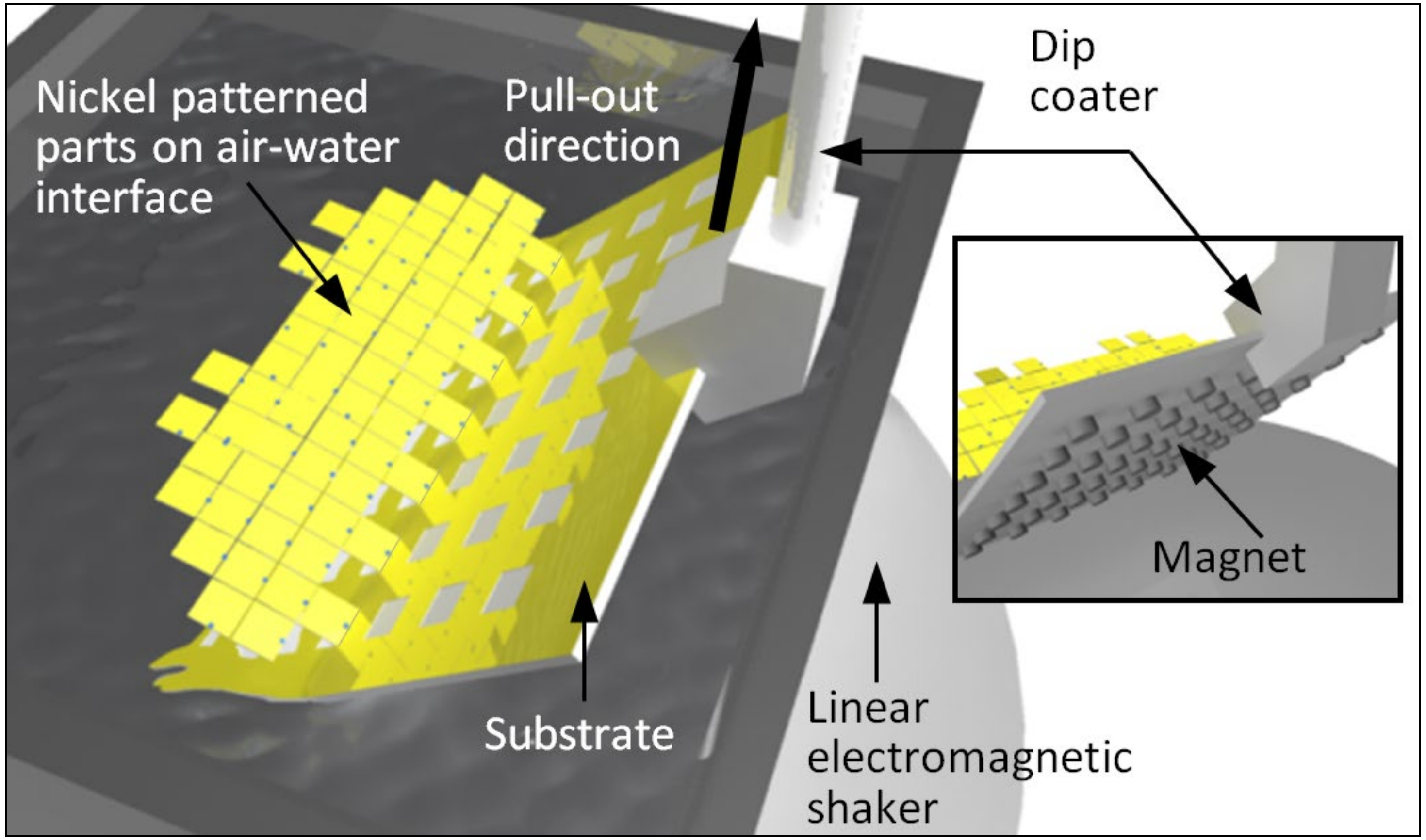


Ashwin Gopinath *et al.*, Absolute and arbitrary orientation of single-molecule shapes. *Science* **371**,eabd6179 (2021). DOI:10.1126/science.abd6179

Self-assembly at the Air-Liquid-Water Interface

Continuous assembly on hydrophobic-hydrophilic substrates; unique orientation by magnetic force; applications: thin and fragile chips, large scale roll-to-roll assemblies.

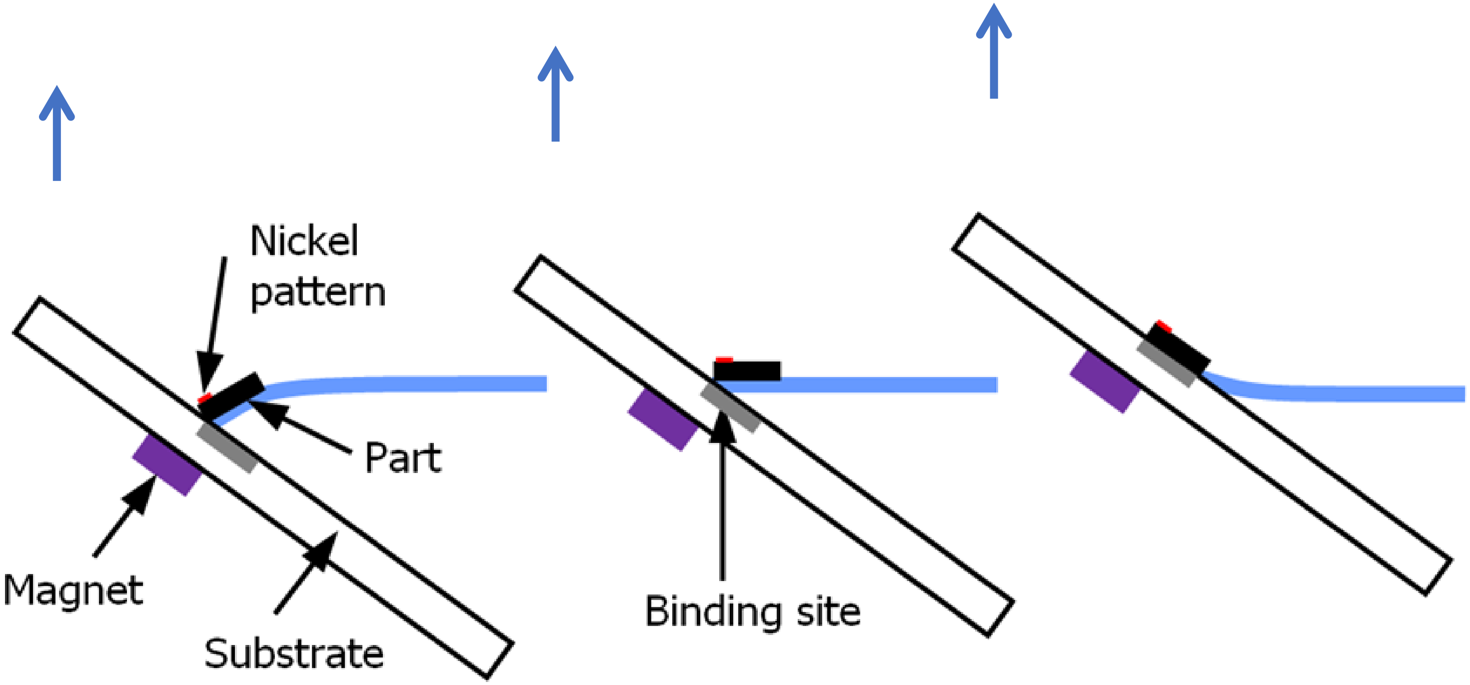
Fluidic Self-assembly at Air-water-solid Interface



Currently: Si substrate. Extendable to roll-to-roll processing. [Park et al. *Transducers*'11]

Fluidic Self-assembly at Air-water-solid Interface

Steps to successful assembly:

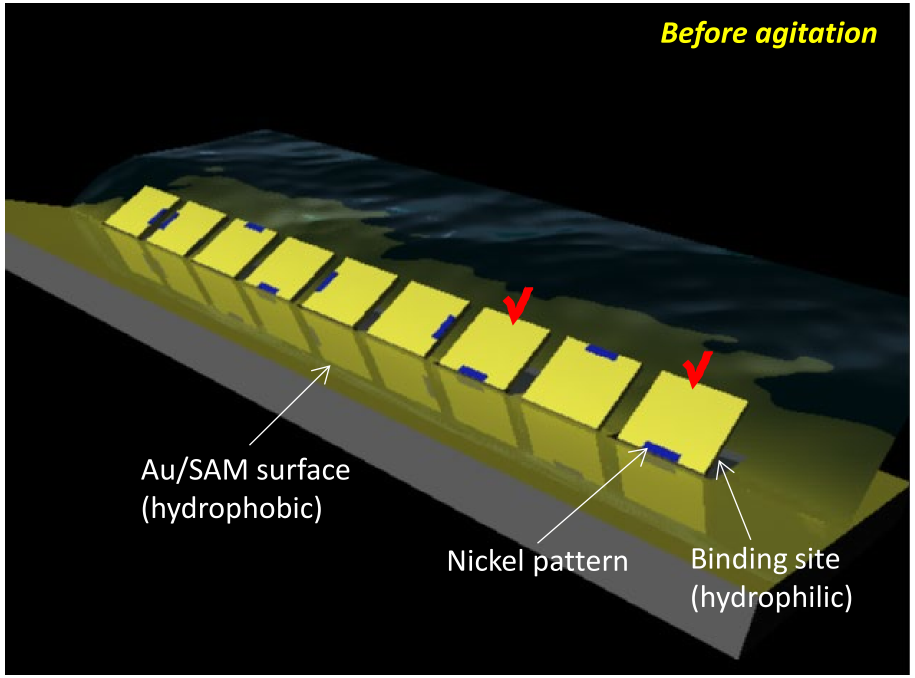


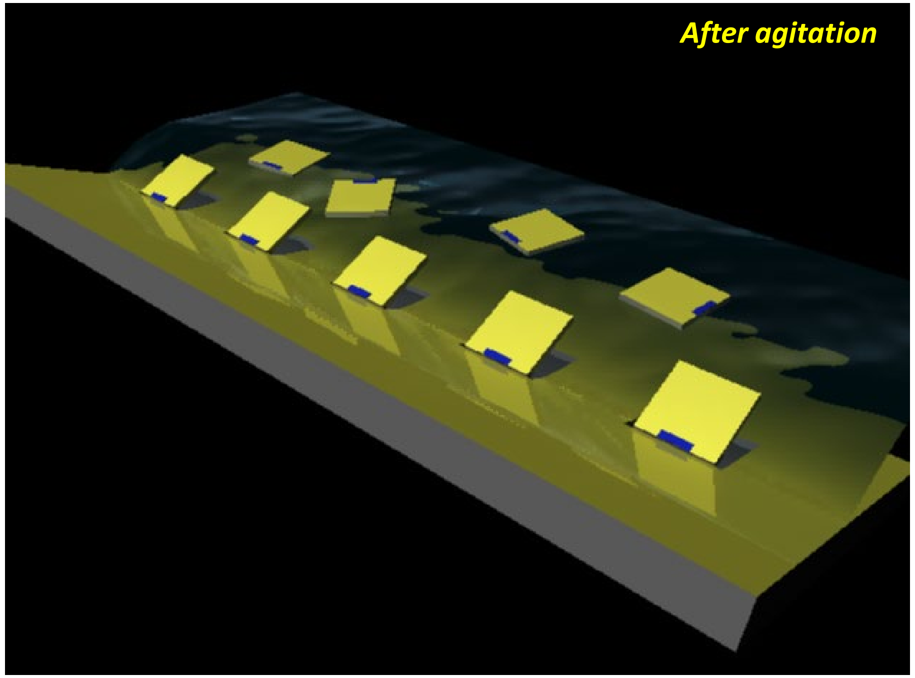
Nickel pattern provides unique orientation.

Fluidic Self-assembly at Air-water-solid Interface

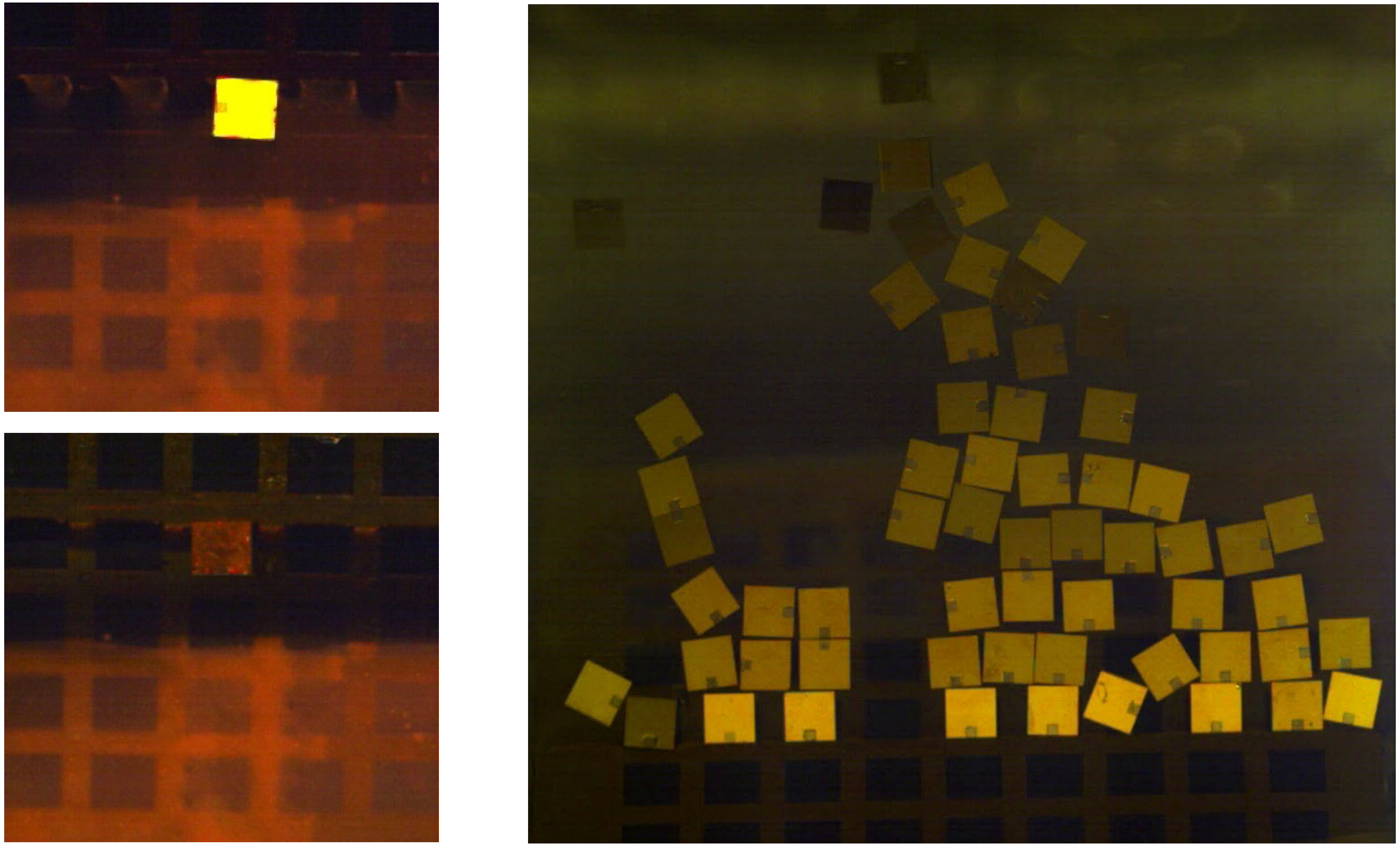
Fluidic Self-assembly at Air-water-solid Interface

Agitation with Faraday waves breaks up incorrect assemblies:





Fluidic Self-assembly at Air-water-solid Interface



Assembling Thin Chips of Various Shapes

Rectangular parts (1.5 x 3.0 mm)

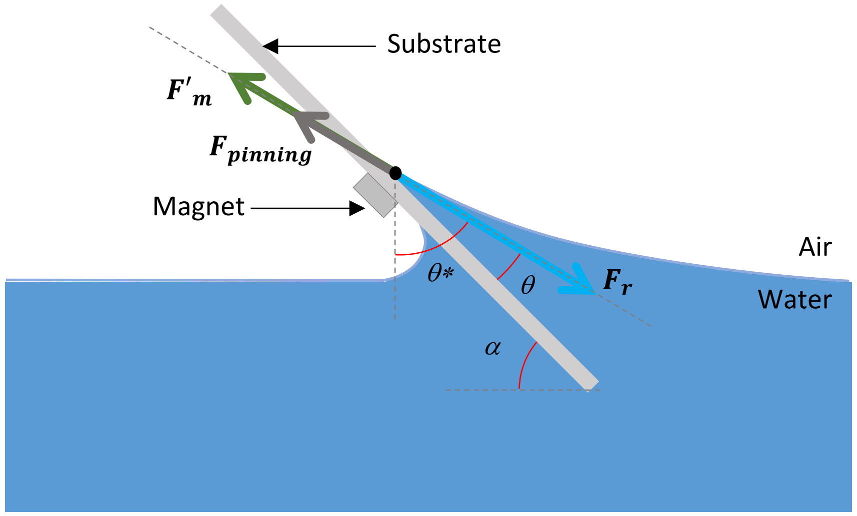
77 rectangular parts in 2-3 min
→ 0.5 chips/s

90 circular parts in 1 min
→ 1.5 chips/s

Today's pick-and-place machines with 6 to 20 individual robots (example: Assembléon's A-Series)

- **Assembly speed: up to 1.5 chips/s per robot**
- Component range : 0.4 x 0.2 mm (01005) to 45 x 45 mm

Modeling of Assembly Forces



F'_m magnetic force
F_r gravity
(tangential components)

Condition for assembly:

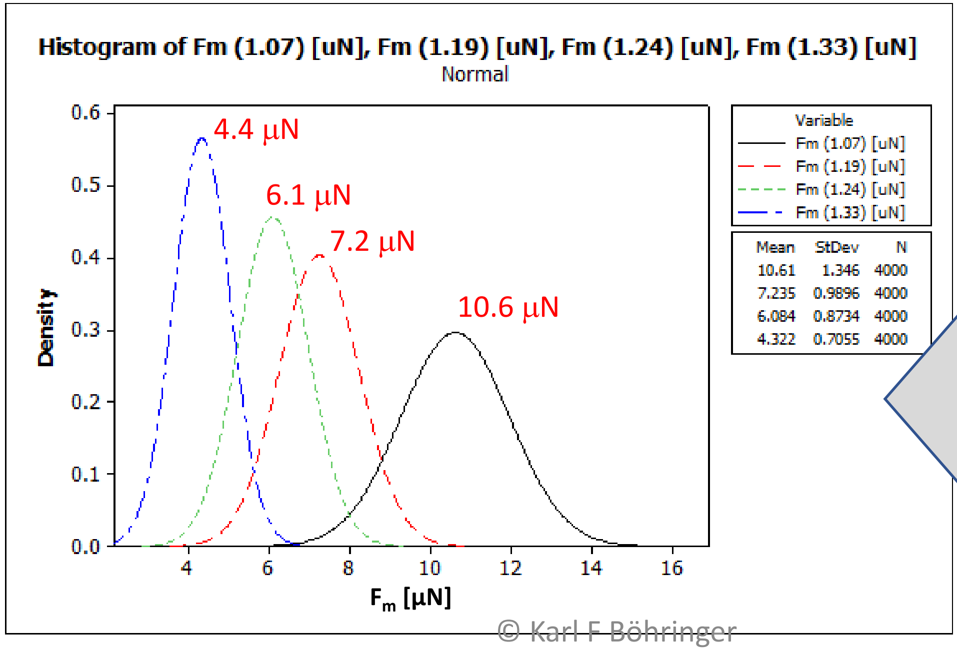
$$F_{net} = F'_m + F_{pinning} - F_r > 0$$

Design choices influence yield, i.e. system parameters determine performance parameters.

Analysis of Experiments

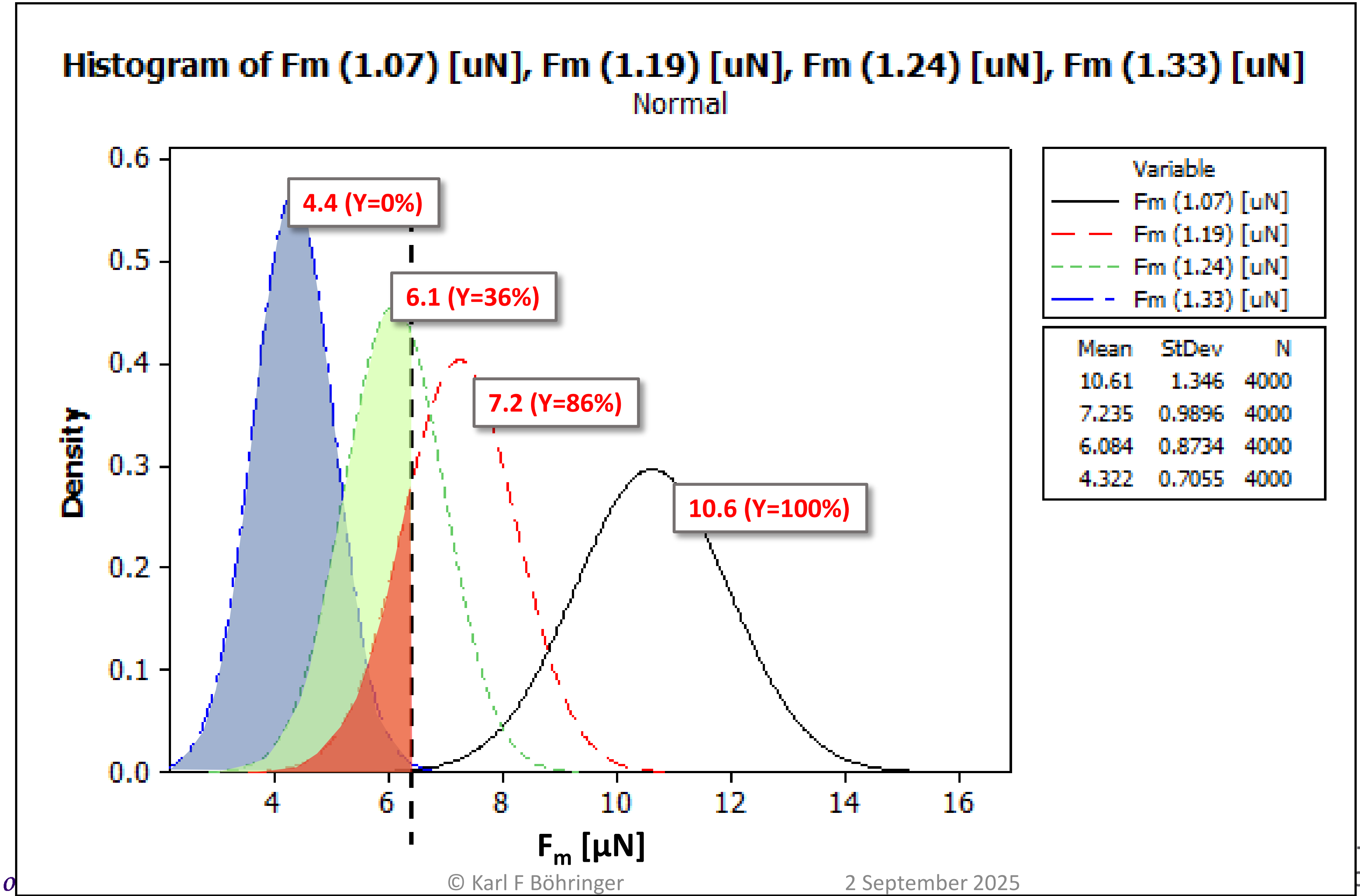
Gap [mm]	Yield		F_m [μN] (Simulation)	
	Experiment	(Simulation)		
0.87	100%	(30/30)	20.3	(12.7-27.9)
1.07	90%	(30/30)	10.6	(6.5-14.6)
1.19	67%	(27/30)	7.2	(4.2-10.1)
1.24	37%	(11/30)	6.1	(3.4-8.7)
1.33	0%	(0/30)	4.4	(2.3-6.4)

(±3 sigma)



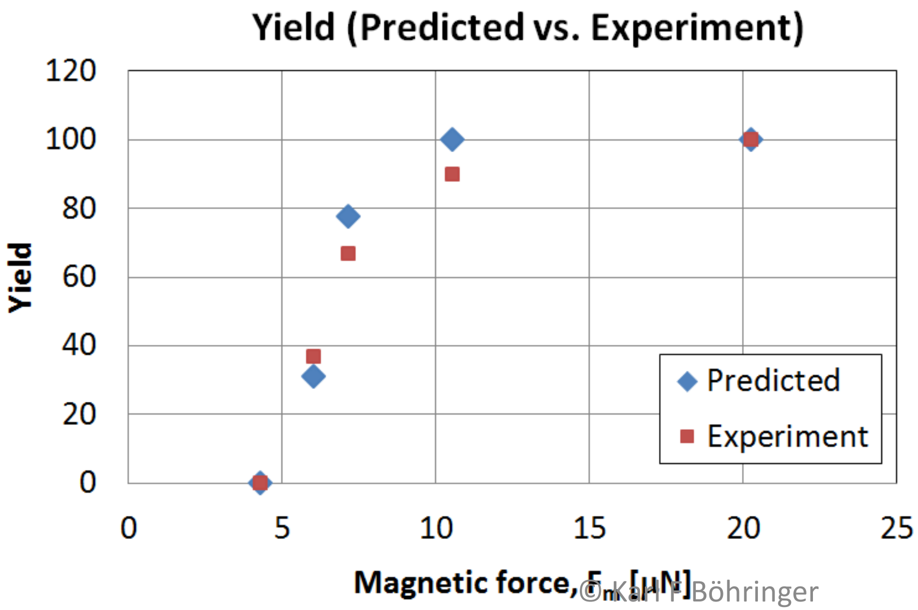
- measurement error
- alignment error using Monte-Carlo simulation

Analysis of Experiments



Analysis of Experiments

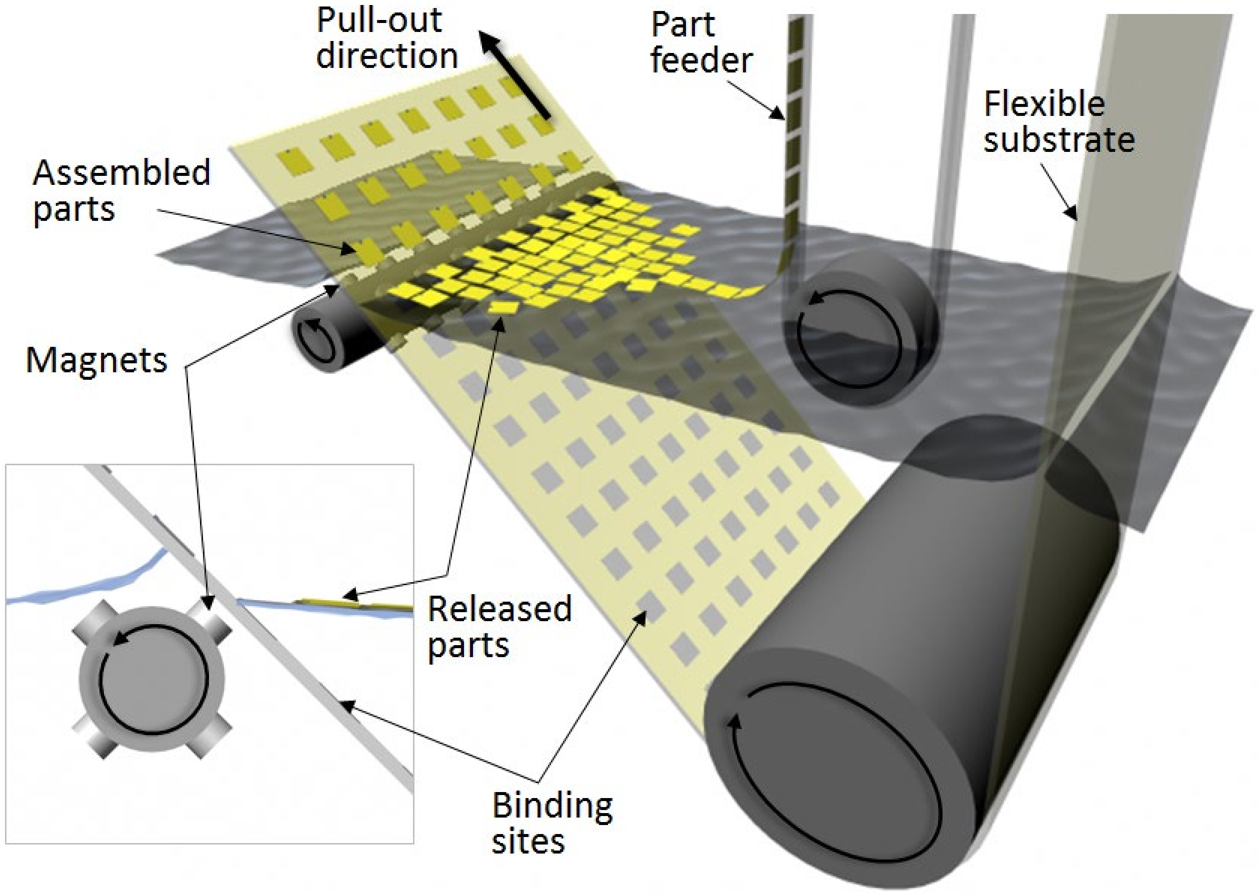
Gap [mm]	Yield			F_m [μN] (Simulation)	
	Experiment	(Simulation)	Predicted		
0.87	100%	(30/30)	100%	20.3	(12.7-27.9)
1.07	90%	(30/30)	100%	10.6	(6.5-14.6)
1.19	67%	(27/30)	86%	7.2	(4.2-10.1)
1.24	37%	(11/30)	36%	6.1	(3.4-8.7)
1.33	0%	(0/30)	0%	4.4	(2.3-6.4)



Critical F_m from statistical analysis of experimental results: 6.4 μN

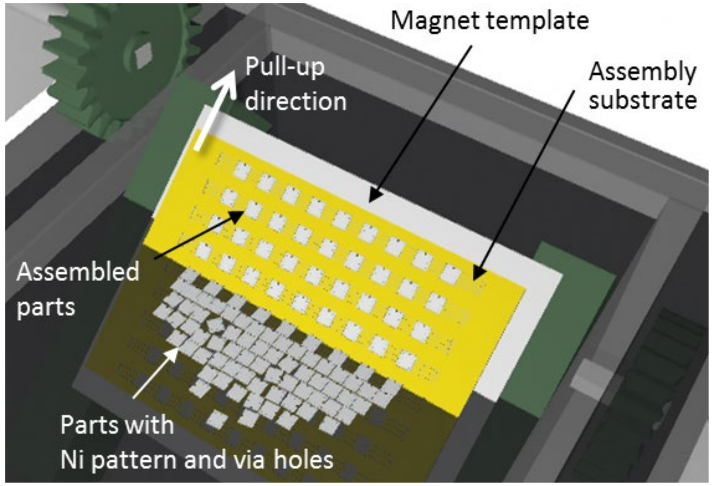
(RMS error = 11%, Max. error = 17%)

Roll-to-Roll Assembly

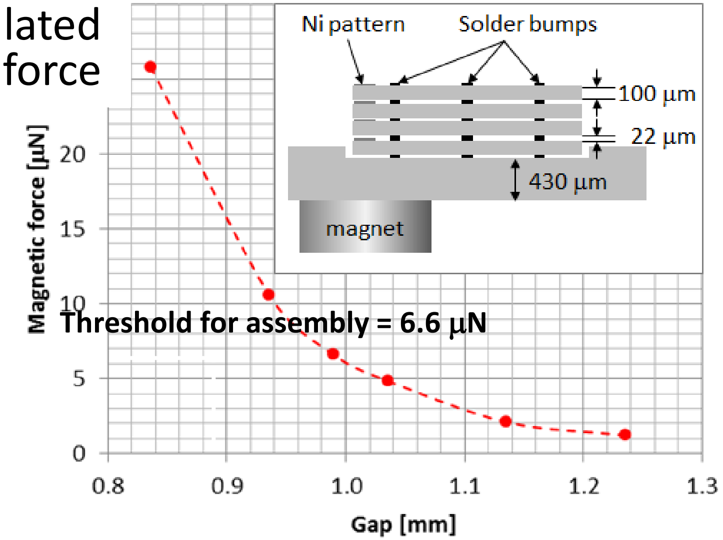


3D Integration Using Self-assembly at Air-water-solid Interface

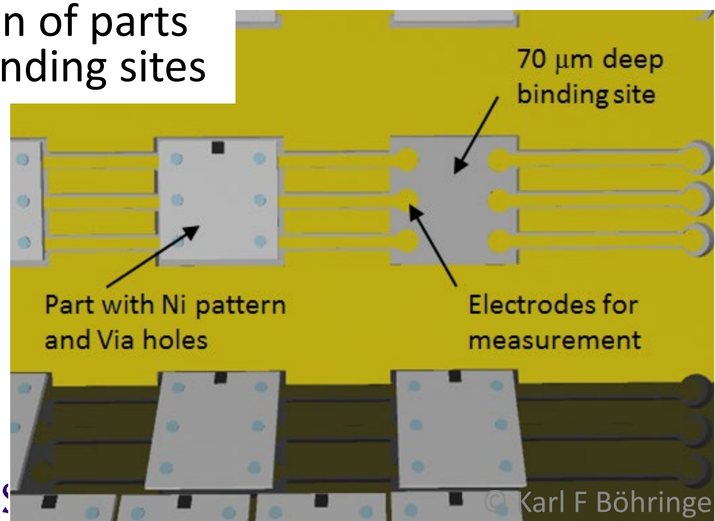
Experimental setup



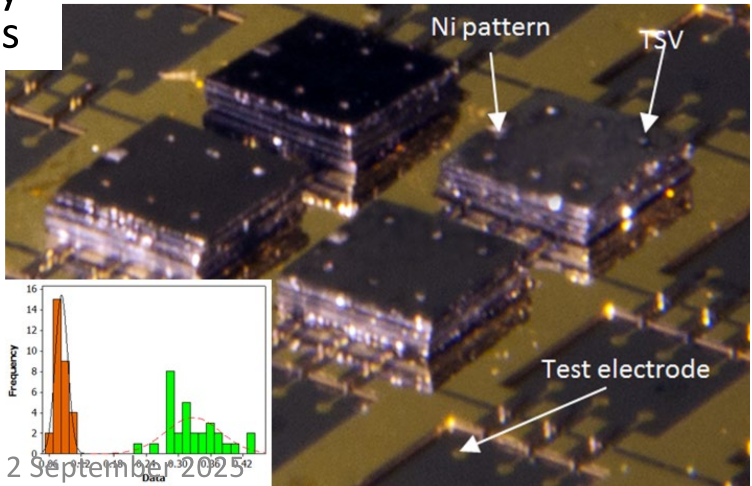
Simulated magnetic force



Design of parts and binding sites



Assembly results

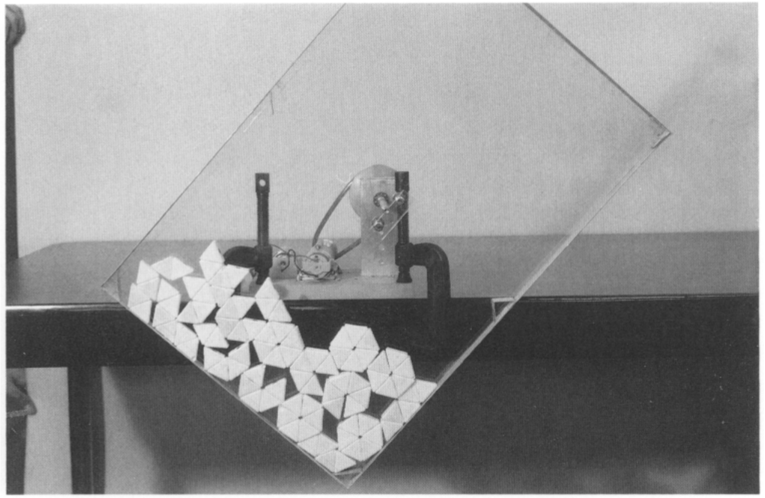


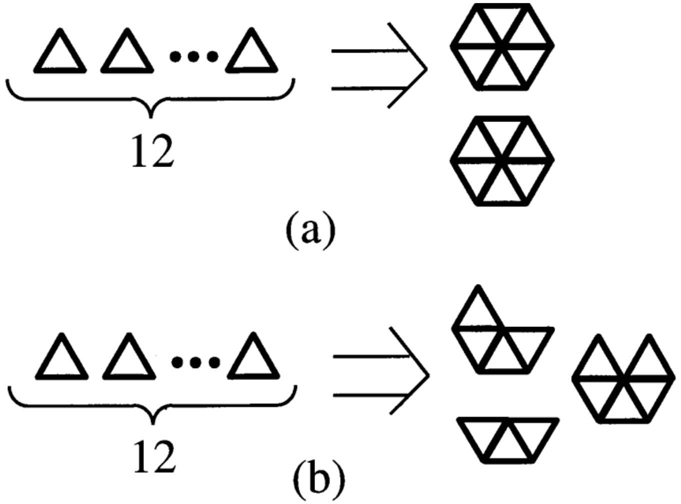
Part IV:
Computational Aspects of Self-assembly

Models for deterministic and stochastic assembly; analogy to chemical reaction kinetics; equivalence between computation and self-assembly; DNA computation, Turing machines and Wang tiles

Self-assembly and Chemical Reactions

- Hosokawa, Shimoyama and Miura observed in 1994 the analogy between self-assembling systems and chemical reactions.
  - They modeled self-assembly with equations for reaction kinetics.
  - This approach provides the means to generate the time evolution of a self-assembling system, and to determine its equilibrium state(s).





Hosokawa *et al.*, *Artificial Life* 1:413-427, 1995

Self-assembly Reactions (1)

- Chemical reaction:

  $3\ SiH_4 + 6\ N_2O \rightarrow 3\ SiO_2 + 4\ NH_3 + 4\ N_2$

- Industrial assembly:

  ICs + resistors + capacitors + … → iPhone

  Obviously, there are limitations to this approach.

Self-assembly Reactions (2)

- Consider a system with two types of components A and B that join one-on-one to form assembly C:

$$A + B \rightarrow C$$

with a forward reaction rate constant k_f

- If there is the possibility of disassembly, we write:

$$A + B \leftrightarrow C$$

with a reverse reaction rate constant k_r

Self-assembly Reactions (3)

- If we have very large numbers of components:

$$\frac{dA}{dt} = -k_f A \cdot B + k_r C$$

$$\frac{dB}{dt} = -k_f A \cdot B + k_r C$$

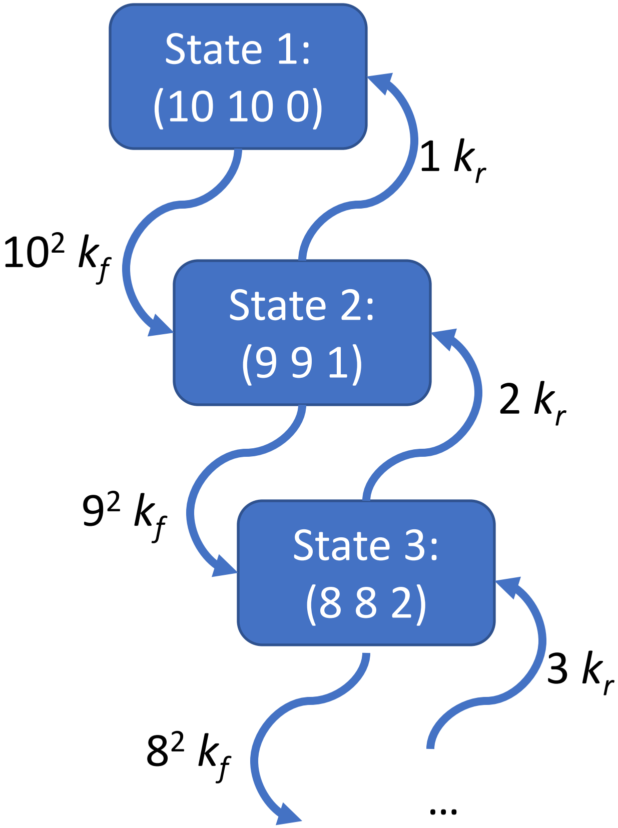
$$\frac{dC}{dt} = k_f A \cdot B - k_r C$$

- System of ordinary differential equations.

  Steady state when $(A \cdot B)/C = k_r/k_f$

Self-assembly Reactions (4)

- If we have a smaller number of components:



State 1:
(10 10 0)

State 2:
(9 9 1)

State 3:
(8 8 2)

$10^2\ k_f$

$1\ k_r$

$9^2\ k_f$

$2\ k_r$

$8^2\ k_f$

$3\ k_r$

…

Markov process

Matrix of transition rates:

$$\begin{pmatrix} . & k_r & . & \cdots \\ 10^2 k_f & . & 2kr & \\ . & 9^2 k_f & . & \\ \vdots & & & \ddots \end{pmatrix}$$

Steady states are eigenvectors of matrix.

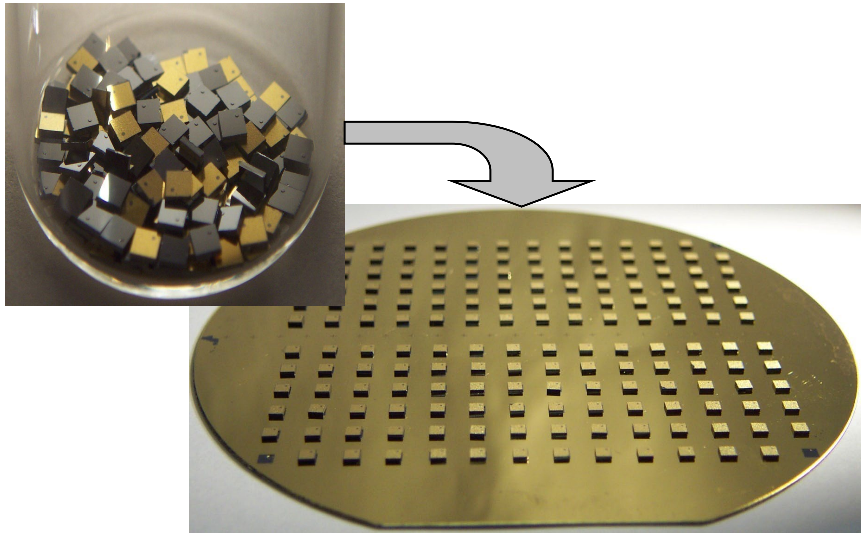
Chemical Reaction Kinetics

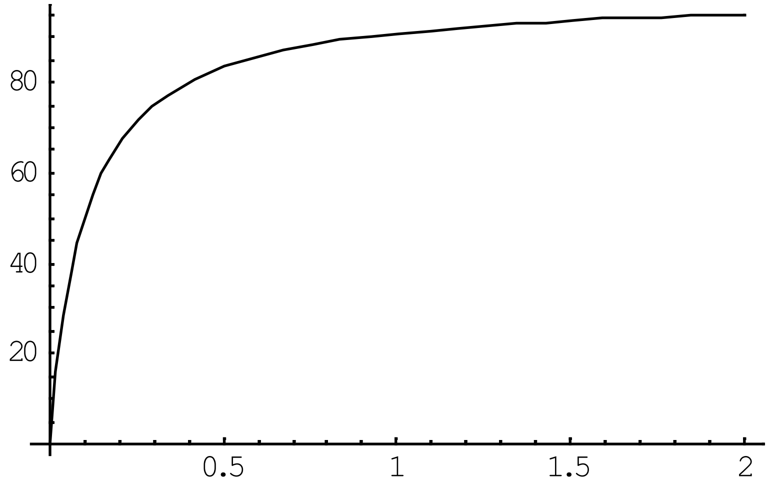
- There are two mathematical formalisms to describe behavior of a chemical system:
  - "Reaction rate equations" are coupled ordinary differential equations that provide a deterministic time evolution of the system.
  - The "master equation" is a single differential-difference equation that captures the stochastic behavior of chemical kinetics.
    - $P(X_1,X_2,\ldots,X_N;t)$ = probability that at time t, there will be X_1 molecules of species S_1, X_2 molecules of species S_2, …
- It can be shown that as the number of reactants goes towards infinity, the two formalisms converge.
- Daniel Gillespie developed an algorithm for exact stochastic simulation in 1977.

Deterministic Solution for Reaction Kinetics

Assume we have n components A and n sites B.

- Initially, the rate of reaction is $k\, n^2$.
- If there are x complete assemblies, then the rate of reaction is $k\,(n - x)^2$.
- This leads to a differential equation for $x(t)$:
  $dx/dt = k\,(n - x)^2$
- Equilibrium: $dx/dt = 0 \rightarrow x = n$
- Solution of this differential equation:
  $x(t) = k\, n^2\, t\, /\, (1 + k\, n\, t)$



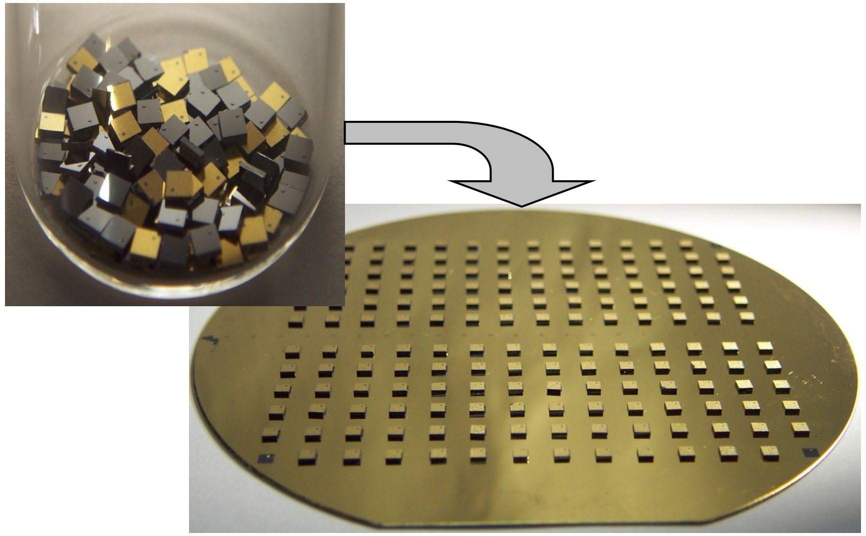


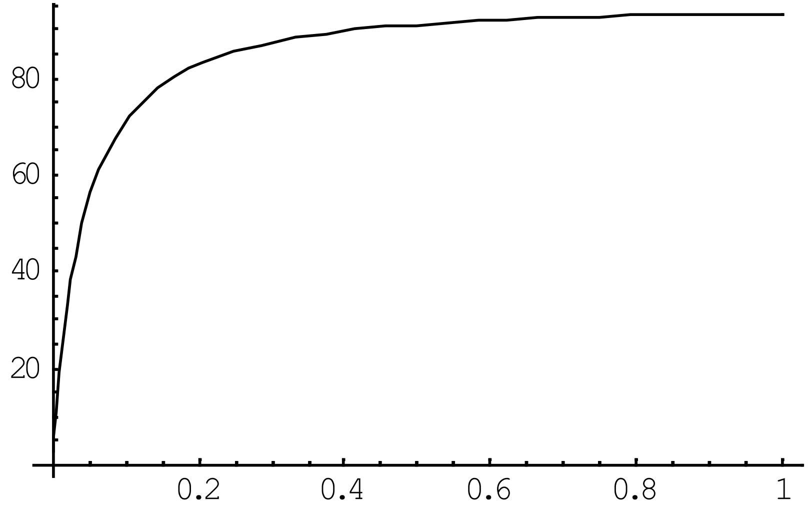
Kinetics with Reverse Reaction

Assume we have n components A and n sites B.

- Forward rate of reaction is $k_f\,[A]\,[B]$.
- Reverse rate of reaction is $k_r\,[A{\cdot}B]$.
- If there are x complete assemblies then the forward rate of reaction is $k_f\,(n-x)^2$ and the reverse rate of reaction is $k_r\,x$.
- This leads to a new differential equation for $x(t)$: $dx/dt = k_f\,(n-x)^2 - k_r\,x$.

$$x(t) = \frac{2k_f n^2}{k_r + 2k_f n + \sqrt{k_r}\sqrt{k_r + k_f n}\cosh\left(\frac{1}{2}\sqrt{k_r}\sqrt{k_r + k_f n t}\right)}$$





Limitations to the Analogy with Chemical Reaction Kinetics

- The number of components is finite, may not be assumed as infinite.
- Self-assembly components are geometrically and physically more complex than atoms and molecules.
- Deriving reaction rate constants from first principles is very difficult.
  - What is “temperature” in a self-assembly system?
- Describing a self-assembly system is a multi-physics problem.
  - Models may require techniques spanning from molecular dynamics to robotics to computational geometry.

Self-assembly: the Big Picture

- >> 100 years ago:

  “energy = mass”

  - Einstein 1905 (Nobel Prize Physics 1921)

- >> 10 years ago:

  “assembly = computation”

  - Adleman 1994 (Turing Award 2002)
  - DNA computation of NP-hard combinatorial problems

- Proposition:
  - This equation not only applies to DNA, but in particular also to assemblies of micro and nano systems

Self-assembly: the Big Picture

“assembly = computation”

Direction of equations is important for practical engineering purposes:

- energy = mass:
  - “→” esoteric physics
  - “←” most powerful known source of energy
- assembly = computation:
  - “→” esoteric computers
  - “←” most powerful known method of manufacturing
    - from CAD to VLSI
    - from DNA to living organisms

Self-assembly: the Big Picture

Thus, “assembly = computation” means:

If I can create a (data) structure with some algorithm then I can create a corresponding (physical) structure by self-assembly

Assembly and Computation

- Background
  - NP-hard problems
  - Turing machines
  - Wang tilings

- Adleman: DNA strands compute solutions to combinatorial problems
- Winfree: DNA tiles perform arithmetic calculations

DNA Computing

- In 1994, Leonard M. Adleman showed that hard computational problems can be solved by self-assembly:
  - The problem is encoded in DNA.
  - The solution is found by processing the DNA.
- Why is this important?
  - A new way for nano-scale, massively parallel computing.
  - If self-assembly can simulate any algorithm, then any structure that can be described by an algorithm can also be realized with self-assembly.

Background: NP-hard Problems

- NP-hard problems are problems that are very difficult to solve with a computer (or without one).
- NP stands for nondeterministic polynomial-time.

- An NP-hard problem is a decision problem:
  - yes/no answer.
- If a possible solution is found, it is “easy” to check whether the solution is correct:
  - “easy” means “with a polynomial-time algorithm”.
- But it is “difficult” to find a solution:
  - “difficult” means “combinatorically many”.

Background: NP-hard Problems

- Example: “SUBSET-SUM”
  - Given a set S of n integers, does any non-empty subset of S add up to zero?
  - It is easy to verify a given solution S_0:
    - Check whether S_0 is a subset of S.
    - Check whether S_0 adds up to zero.
  - It is difficult to find a solution:
    - To find a solution, or to prove that there is none, we have to enumerate (more or less) all possible subsets.
    - This leads to a “combinatorial explosion”, i.e., an algorithm that is exponential in n.

Background: NP-hard Problems

- There exist many such problems.
  - Another example: “KNAPSACK”
    Given n items with cost c_i and value v_i, are there items of value at least V without exceeding cost C ?

- Interestingly, all these problems are similarly hard.
  - If I can find an efficient algorithm for KNAPSACK then I can also find an efficient algorithm for SUBSET-ZERO, and vice versa.
  - These problems are “NP-hard”, they are the most difficult ones that can be solved nondeterministically in polynomial time.

Hamiltonian Path

- Another NP-hard problem:
  - Traces back to 19th century Irish mathematician W. R. Hamilton, who invented a game: find a path along the edges of a dodecahedron that visits each vertex exactly once.
- In a general graph, a Hamiltonian path is a path that connects all vertices via edges without visiting any vertex twice.

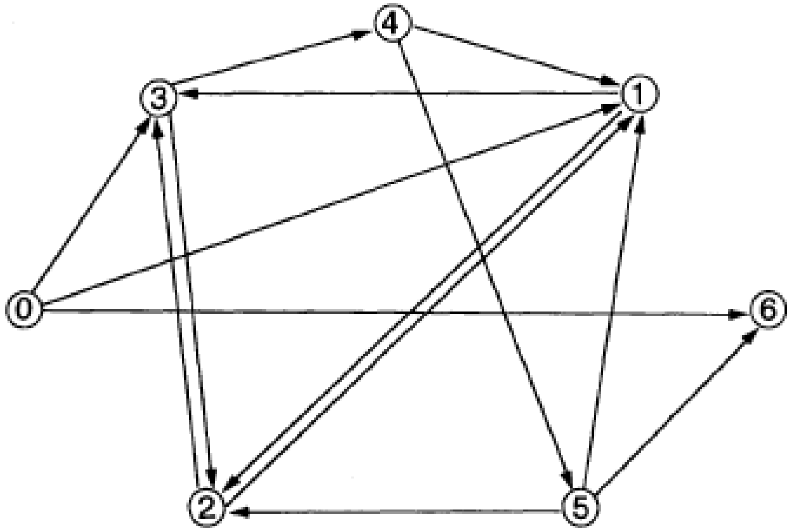


Fig. 1. Directed graph. When $v_{in} = 0$ and $v_{out} = 6$, a unique Hamiltonian path exists: 0→1, 1→2, 2→3, 3→4, 4→5, 5→6.

Finding a Hamiltonian Path

A nondeterministic algorithm for a Hamiltonian path of a graph with n vertices from v_{in} to v_{out} :

1. Generate random paths through graph (i.e., random sequences of vertices).
2. Delete all paths that do not start with v_{in} or do not end with v_{out} .
3. Delete all paths of length not equal to n.
4. Delete all paths that visit a vertex more than once.

If there is a path left over, then it is a Hamiltonian path.

Adleman realized all these steps with DNA processing for the graph with 7 vertices on the previous slide.

1. Encoding a Graph in DNA

- Each vertex v_i is represented by a 20-base sequence (20-mer) of DNA.
- Each directed edge (v_i, v_j) is represented by the last 10-mer of v_i and the first 10-mer of v_j .
  - Exception 1: all edges (v_{in}, v_j) use the entire 20-mer of v_{in} and the first 10-mer of v_j .
  - Exception 2: all edges (v_i, v_{out}) use the last 10-mer of v_j and the entire 20-mer of v_{out} .
- Experiment:
  - 50pmol of complementary DNA for each vertex.
  - 50pmol of DNA for each edge.
  - The complementary strands bind and thus represent random paths in the graph.

1. Encoding a Graph in DNA

- There were about 3 10^{13} oligonucleotides for each vertex and edge in the solution.
- How many different paths exist?
  - Infinitely many, but very long paths (i.e., very long DNA sequences) are unlikely to be created since v_{in} and v_{out} terminate the DNA sequence.
  - Count all possible sequences up to length 14:
    7^{14} = 6.8 10^{11}.
  - It is very likely that the solution is among the self-assembled DNA sequences.

2. Select Paths from v_{in} to v_{out}

- DNA amplification with polymerase chain reaction (PCR):
  - PCR splits DNA between two markers and duplicates it in each cycle.
  - Here, we use markers for v_{in} and v_{out} such that only DNA representing paths from v_{in} to v_{out} are amplified.

3. Select Paths of Length *n*

- Run DNA through agarose gel:
  - Separation of DNA molecules by length: the mobility of the DNA molecule is directly proportional to its size.
  - Extract the DNA sequences with $20n = 140$ base pairs, representing paths with exactly 7 vertices.
  - PCR amplification to improve purity.

4. Delete Missing-Vertex Paths

- Create single stranded DNA.
- For i = 0 to n
  - Add complementary DNA sequence representing v_i with biotin-avidin bound magnetic beads.
  - Hybridization.
  - Separate labeled DNA from unlabeled DNA.
  - Repeat
- Here, we are left only with paths that include all vertices.
- … and we have solved the Hamiltonian Path.

Pro’s and Con’s

- Massively parallel computing.
- High density (theoretically, 1 molecule = 1 data structure).
- Energy efficiency (near thermodynamic optimum).
- Linear in number of vertices (as opposed to exponential).

- Demo for a trivial problem size. Ultimately, combinatorial explosion is unavoidable.
- Lengthy lab procedure.
- …

Turing Machine

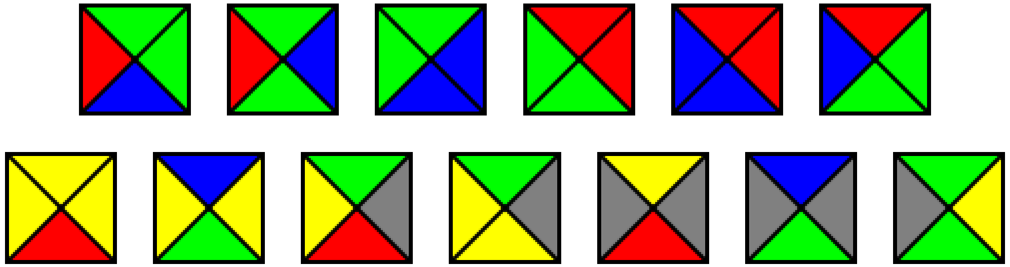
- Proposed 1936 by English mathematician Alan Turing.
- An extremely simple machine that can perform computation.
- Various versions of Turing Machines exist; a typical configuration consists of
  - an endless tape,
  - a head that can read and write symbols on the tape,
  - a look-up table that decides
    - whether to move the tape left of right,
    - whether to read or what to write on the tape,
    - what "state" to transition to.

Turing Machines

- It has been shown that computations with modern computers / programming languages can also be performed by Turing Machines.
- It is generally agreed that *any* computation can be performed by a Turing Machine.
- In fact, one way to define what is meant by "computation" is a program executed by a Turing Machine.

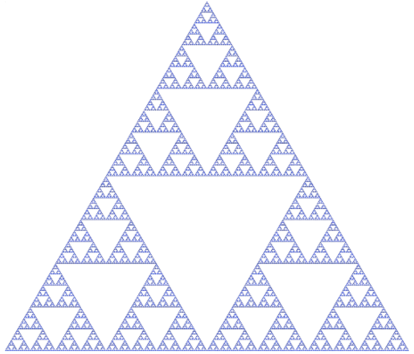
Wang Tiles

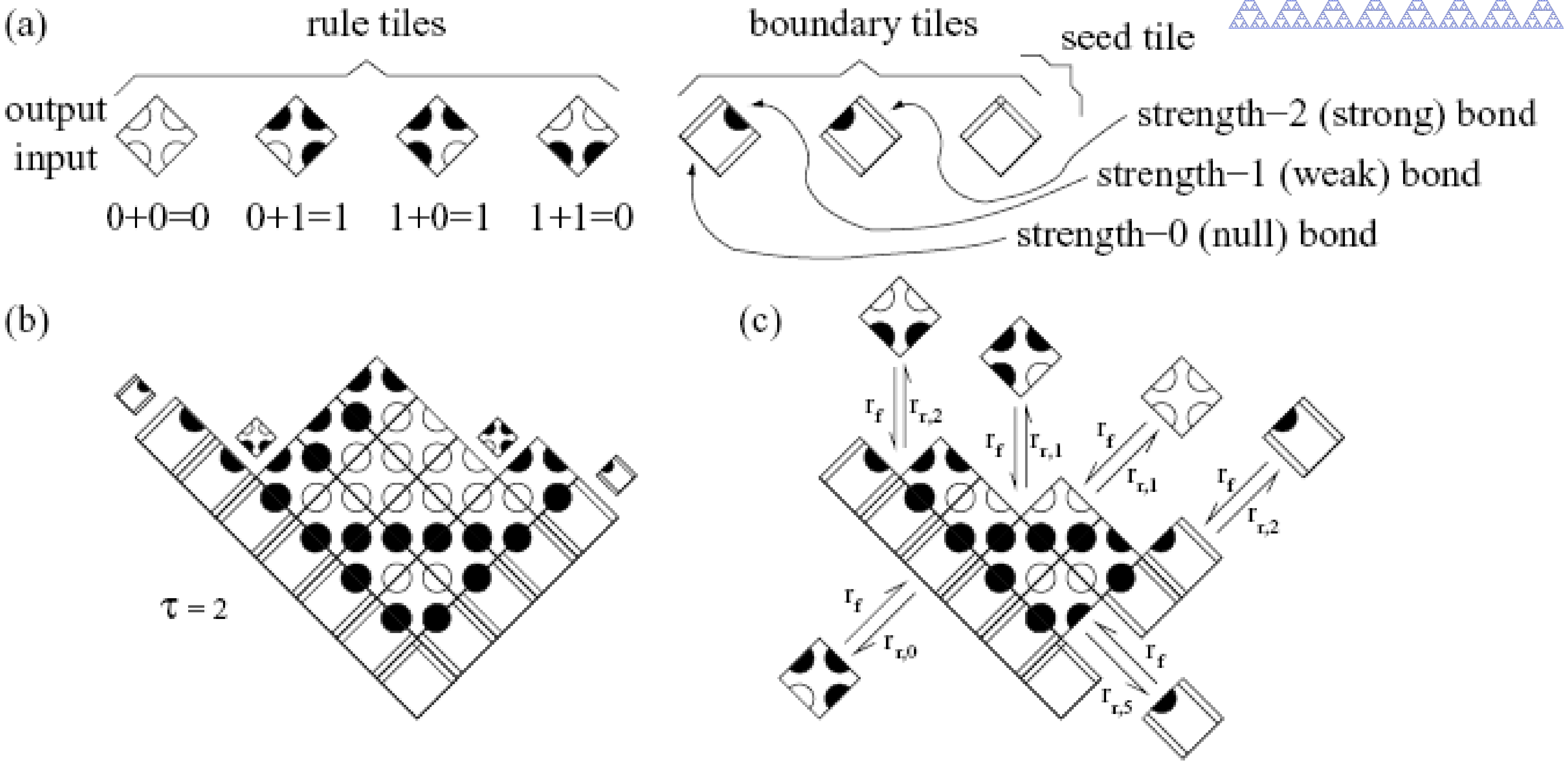
- Introduced by Chinese-American mathematician and philosopher Hao Wang in 1961.
  - Wang gave an algorithm to decide whether a given tile set can cover the plane (adjacent colors must match, and tiles cannot be rotated).
  - Robert Berger (his student) proved in 1966 that this algorithm was wrong. In fact, no such algorithm can exist.



- It has been shown that Wang tiles are equivalent to Turing machines.
  - This means that any computational problem can be represented with Wang tiles.

Example: Sierpinski Triangle





DNA Tiles

- Double cross-over (DX) molecules are ideal to implement Wang tiles at the molecular level.
  - DX provide stiffness for 2D assembly.
  - 4 sticky ends connect to neighbor tiles.
  - ssDNA on sticky ends provide a high degree of programmability.