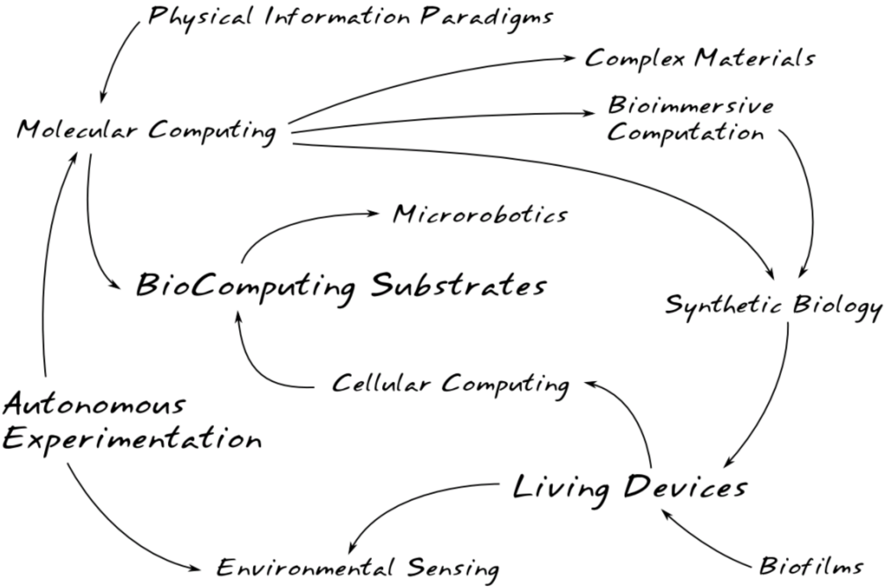
Enzymatic Computing

Klaus-Peter Zauner
Science and Engineering of Natural Systems
School of Electronics and Computer Science
University of Southampton, U.K.

Biological Computing Substrates



Physical Information Paradigms

Complex Materials

Molecular Computing

Bioimmersive Computation

Microrobotics

BioComputing Substrates

Synthetic Biology

Cellular Computing

Autonomous Experimentation

Living Devices

Environmental Sensing

Biofilms

Outline

Motivation
- The Past

Biological Substrates
- What can biology contribute?
- Macromolecules
- Cells

Towards Implementation

Outline

Motivation
    The Past

Biological Substrates
    What can biology contribute?
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    Cells

Towards Implementation

The origin of the present computing paradigm

Access to a 19th century database…

The origin of the present computing paradigm

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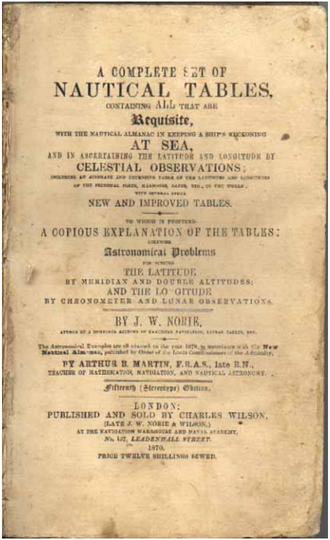


A COMPLETE SET OF
NAUTICAL TABLES,
CONTAINING ALL THAT ARE
Requisite,
WITH THE NAUTICAL ALMANAC IN KEEPING A SHIP'S RECKONING
AT SEA,
AND IN ASCERTAINING THE LATITUDE AND LONGITUDE BY
CELESTIAL OBSERVATIONS;
INCLUDING AN ACCURATE AND EXTENSIVE TABLE OF THE LATITUDES AND LONGITUDES
OF THE PRINCIPAL PORTS, HARBOURS, CAPES, ETC., IN THE WORLD,
WITH SEVERAL OTHER
NEW AND IMPROVED TABLES.

TO WHICH IS PREFIXED
A COPIOUS EXPLANATION OF THE TABLES:
LIKEWISE
Astronomical Problems
FOR FINDING
THE LATITUDE
BY MERIDIAN AND DOUBLE ALTITUDES;
AND THE LONGITUDE
BY CHRONOMETER AND LUNAR OBSERVATIONS.

BY J. W. NORIE,
AUTHOR OF A COMPLETE EPITOME OF PRACTICAL NAVIGATION, LUNAR TABLES, ETC.

The Astronomical Examples are all adapted to the year 1870, in accordance with the New Nautical Almanac, published by Order of the Lords Commissioners of the Admiralty,
BY ARTHUR B. MARTIN, F.R.A.S., late R.N.,
TEACHER OF MATHEMATICS, NAVIGATION, AND NAUTICAL ASTRONOMY.

Fifteenth (Stereotype) Edition.

LONDON:
PUBLISHED AND SOLD BY CHARLES WILSON,
(LATE J. W. NORIE & WILSON,)
AT THE NAVIGATION WAREHOUSE AND NAVAL ACADEMY,
No. 157, LEADENHALL STREET.
1870.
PRICE TWELVE SHILLINGS SEWED.

The idea of the computer as we know it has been conceived in face of an intense need for tables:

- Astronomical tables
- Barometrical tables
- Nautical tables
- Trigonometrical tables
- ⋮

The origin of the present computational paradigm

A computer in the 1940s (on the chair—not on the table!)

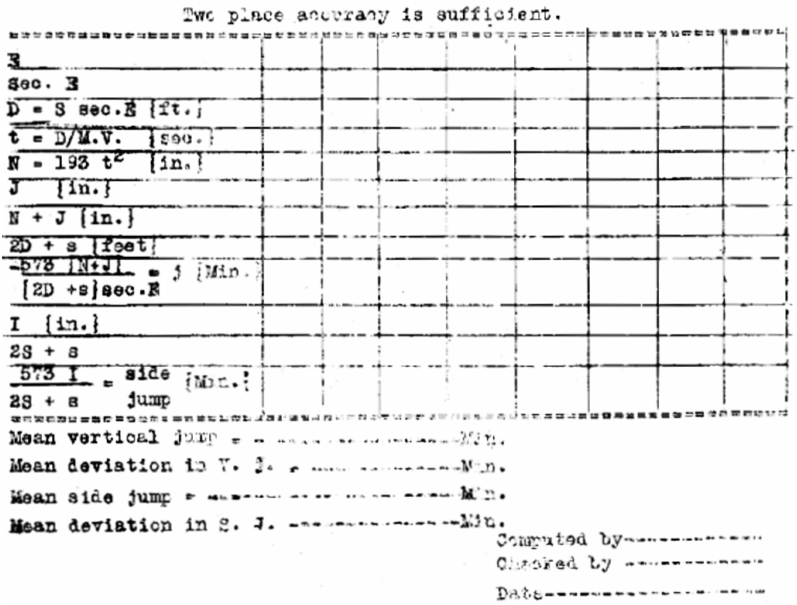
The origin of the present computational paradigm

A computer in the 1940s (on the chair—not on the table!)

The origin of the present computing paradigm

The equivalent of a server room…

The origin of the present computational paradigm



Two place accuracy is sufficient.

E								
Sec. E								
D = S sec.E {ft.}								
t = D/M.V. {sec.}								
N = 193 t^2 {in.}								
J {in.}								
N + J {in.}								
2D + s {feet}								
$\frac{573 \{N+J\}}{\{2D+s\} \sec . E}$ = j {Min.}								
I {in.}								
2S + s								
$\frac{573\ I}{2S+s}$ = side jump {Min.}								

Mean vertical jump = ---------------------------Min.

Mean deviation in V. J. = ----------------------Min.

Mean side jump = -----------------------------Min.

Mean deviation in S. J. ----------------------Min.

Computed by-------------

Checked by -------------

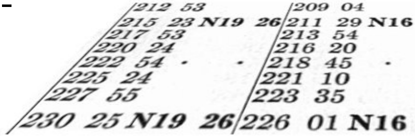
Date--------------------

The Present Computing Paradigm

Mechanisation of table calculation

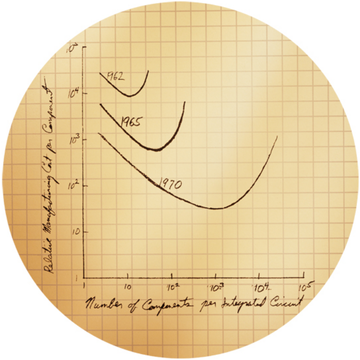
- Fast, simple operations
- Large cycle numbers

Universal Computation…
→ Computer Science focused almost exclusively on processing *time* and memory *space*.



212	53			209	04		
215	23	N19	26	211	29	N16	
217	53			213	54		
220	24			216	20		
222	54	·	·	218	45	·	
225	24			221	10		
227	55			223	35		
230	25	N19	26	226	01	N16	

The present computing paradigm: A GEAT SUCCESS!



Gordon Moore 1965

Exponential progress over 30 years with essentially same operational principle and device structure.

No doubt, this will end.

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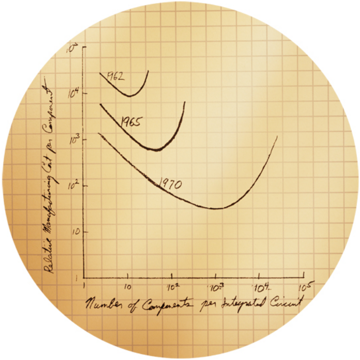

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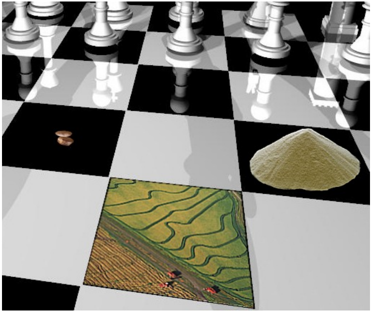

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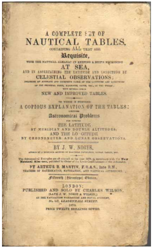
Mechanisation of Table Calculation



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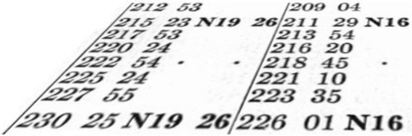
Right approach for any kind of information processing?

Suitable for any computational substrate?



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Why look for other paradigms?

Efficiency

- Turing computable $\neq$ real-time with a realisable device
- Programmability has high cost

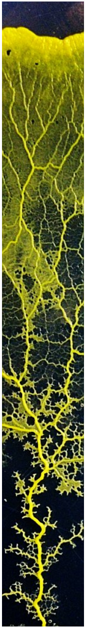
Scope

Programming is limited to compressible maps

Density

Driven my material properties

"It is not at all certain that in this domain a real object might not constitute the simplest description of itself, that is, any attempt to describe it by the usual literary or formal-logical method may lead to something less manageable and more involved." John von Neumann, 1948



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Biological Substrates

- What can biology contribute?
- Macromolecules
- Cells

Towards Implementation

Life needs Information Processing

- From the very outset living matter had to defend its intricate organisation against the onslaught of entropy.
- Subsequently the need to compete with rivalling life forms required evermore refined information processing.

→ *As a consequence organisms exhibit an intriguing sophistication in overcoming computationally difficult challenges.*

Nature vs. Engineering

Our paradigm

Machines designed to precisely enact a formalism that is arbitrary with regard to the computing substrate.

- Physics of the machine is hidden from the programmer
- Requires high energy barriers to enforce precise control over machine states

Nature's paradigm

No need for predictable behaviour of components and component interaction (but of course repeatability).

- Large number of component interactions
- Course of computation driven by physics and chemistry
- Small amounts of matter sufficient to implement function

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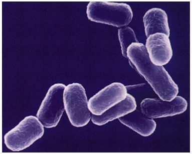
Nature's Molecular Computers

Seed germination: Complex, ambiguous sensor information has to be evaluated to make a crucial decision: to grow or not to grow.

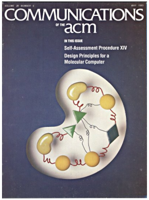


Bacterial chemotaxis: Molecular motors are controlled according to the fused information from a large number of sensors.

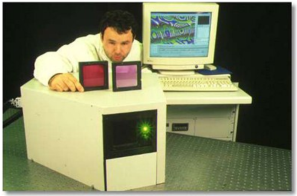
Single cells → all information is processed on the molecular level

A Very Brief History of Molecular Computing

1970s	First ideas (M. Conrad, 1972; E. Liberman, 1972)
1980s	Many conceptual architectures, first experiments, Biophysical Institute at Puchino
1990s	Several prototypes, DNA Computing (R. Birge, 1992; L. Adlemann, 1994; Winfree & Seeman, 1998)
2000	First commercial application (N. Hampp)



ACM 1985



Bacteriorhodopsin, 2000

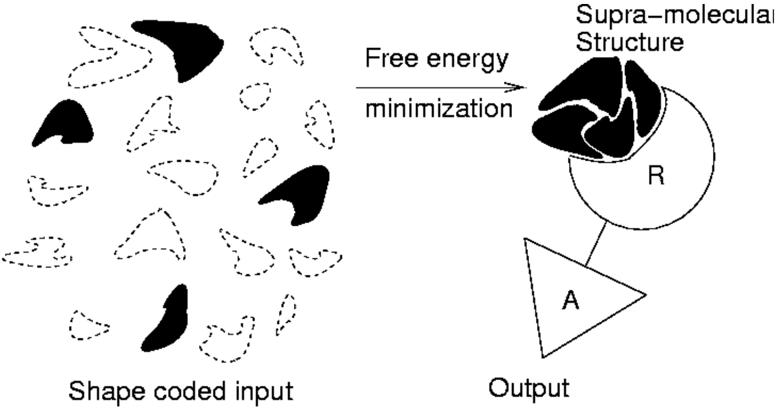
Molecules offer:

- Reproducable nonlinearity
- Self-assembly (defined shape, additive weak forces)
- High integration density of complex I/O mappings

Self-Assemby Computing

- Molecules are large enough to possess specific shape features.
- Molecules are small enough to explore each other by diffusion.
- Molecules interact through short range, additive electrostatic forces.
- If the shapes of two molecules are complementary, the numerous close contacts allow for potential energy to overcome entropy at relatively high temperature.

Self-Assembly Computing



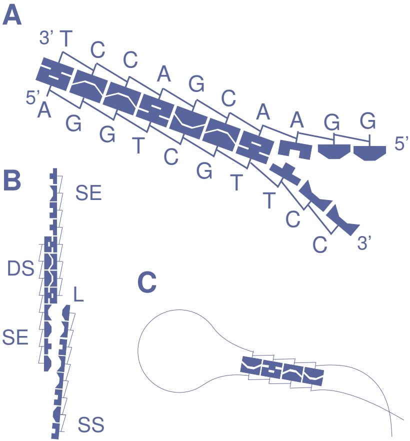
Abstract model of self-assembly processing

M. Conrad, 1989

Self-Assembly Computing

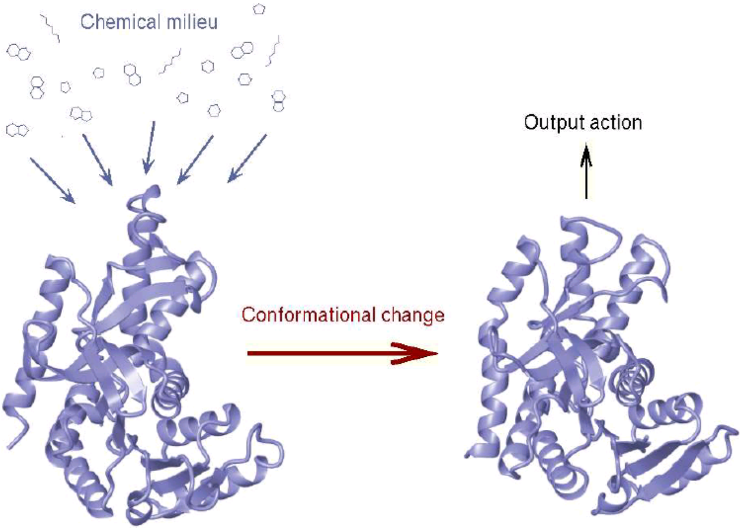
- Symbolic pattern recognition → free-energy minimisation
- Protein, RNA, DNA or organic molecules can be employed
- Problem: diffusion does not scale up

(Adam & Delbrück 1968)



The self-assembly properties of DNA oligonucleotides are relatively easy to predict.

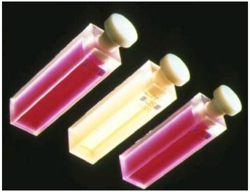
Conformation-based computing

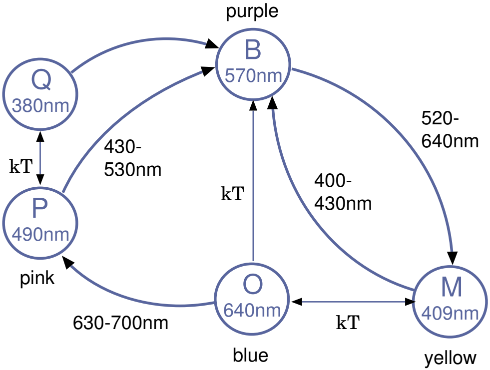


Conformation fuses signals form the chemical context.

Bacteriorhodopsin: A Photonic Automaton

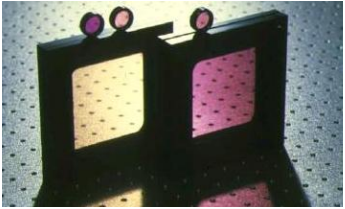
- Photocycle comprises at least 8 states
- B → M transition produces photocurrent
- Fastest transition: ≈ 50 ps





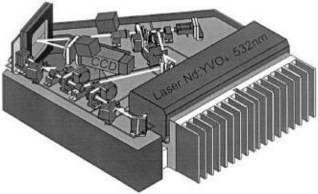
Transition scheme for BR states commonly employed in information processing applications.

Bacteriorhodopsin: Application



- Commercial application: holographic real-time image processing
- BR films with 90 × 90 mm aperture
- Resolution: 5000 lp/mm

- BR can x support processing speed at video frame rate (30 f/s)
- The optical computation in the joint transfrom correlator corresponds to 900 000 × 900 000 pixels



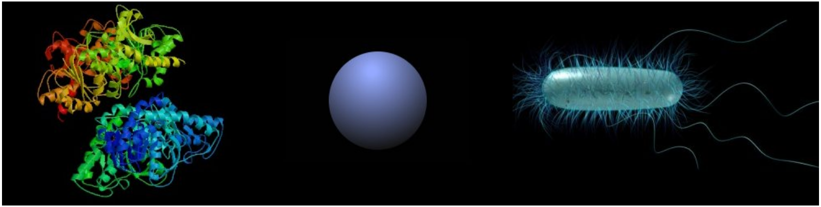
Juchem & Hampp 2000

Cells offer:

- Cheap and fast nano-engineering (self-reproduction)
- QA build in (testing at point of assembly)
- Replenishment of components
- Self-reconfiguration and self-repair

Vision (50+ years)

Molecular information technology at the border between inanimate and animate matter.



inanimate *animate*

Future
Information
Processors

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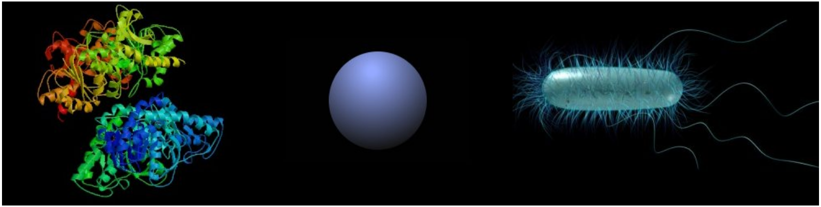
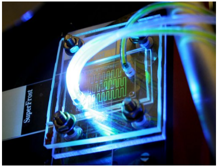


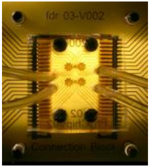
inanimate *animate*

Lab-on-chip →



Future Information Processors

← Living devices



Potential Benefits

- Robotics at mm^2-scale
- Bioimmersive devices
- Complexification of matter

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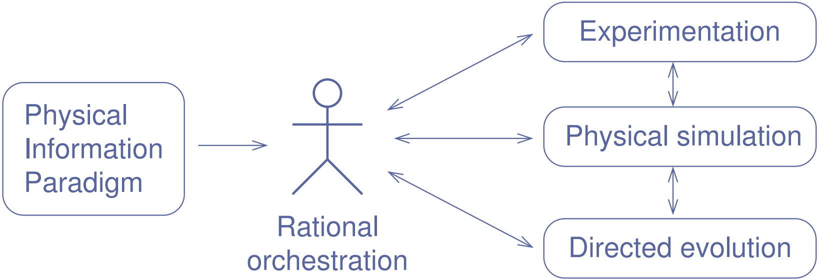
Orchestration of Informed Matter



Physical Information Paradigm

Rational orchestration

Experimentation

Physical simulation

Directed evolution

Computer Science needs to be expanded from formal to physical paradigms

Outline

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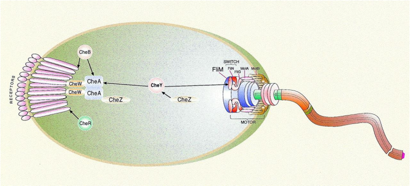
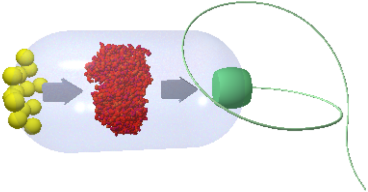
- What can biology contribute?
- Macromolecules
- Cells

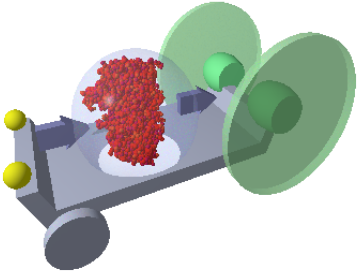
Towards Implementation

Towards artificial devices

Bacterial chemotaxis—sensory signals are processed on the molecular level to control a molecular motor.





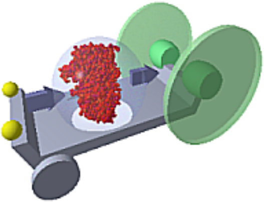


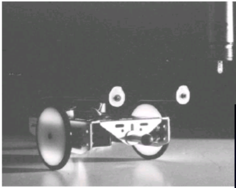
We need:

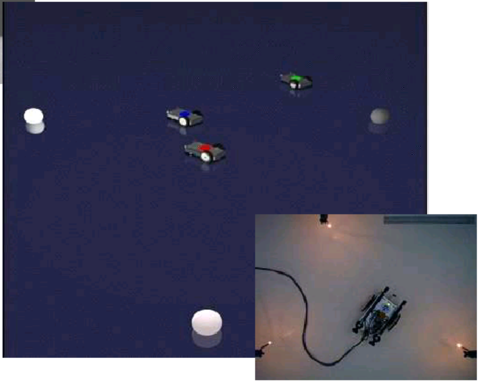
1. a Robot
2. a Molecular Controller
3. an Interface

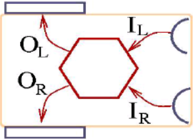
Molecular Robot Control

1. The robot: A Braitenberg Vehicle







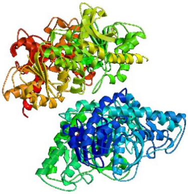


V. Braitenberg: Experiments in Synthetic Psychology, MIT Press, 1984

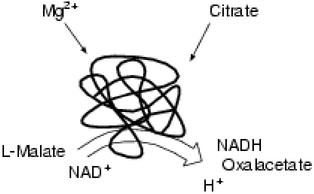
Malate Dehydrogenase (MDH)

2. The Molecular Controller

$$\text{L-malate} + \text{NAD}^+ \xleftrightarrow{MDH} \text{oxalacetate} + \text{NADH} + \text{H}^+$$



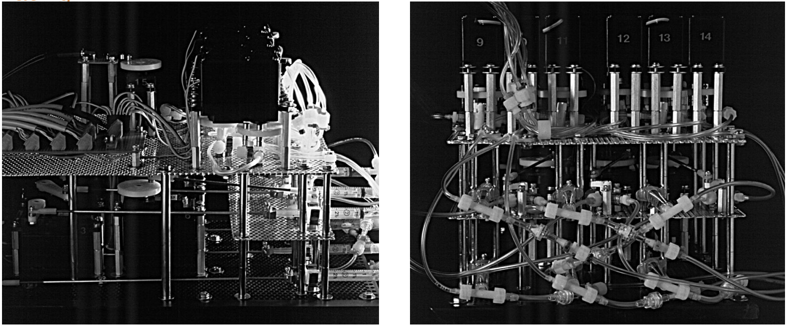
Malate dehydrogenase



Malate dehydrogenase is an enzyme that occurs in a wide variety of species including the microbial world and plants.

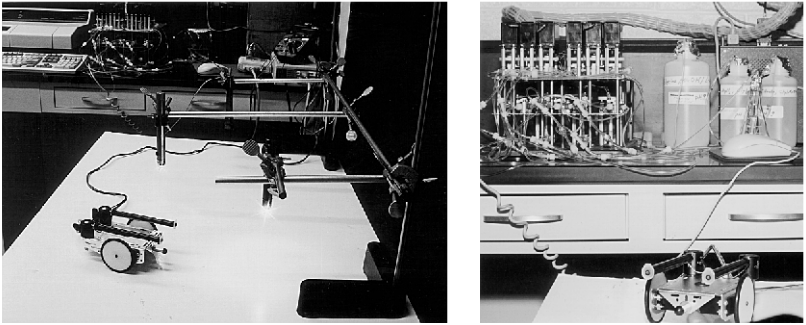
Molecular Robot Control

3. Interfacing



Computer controlled fluidics to transduce signals from the robot’s light sensors to chemical signals (“second messengers”).

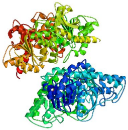
Molecular Robot Control



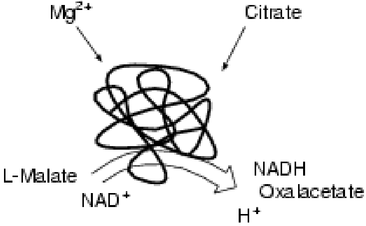
The chemical signals from the robot’s light sensors are processed by the enzyme malate dehydrogenase. The resulting output is detected with a spectrophotometer and used to control the wheels of the robot.

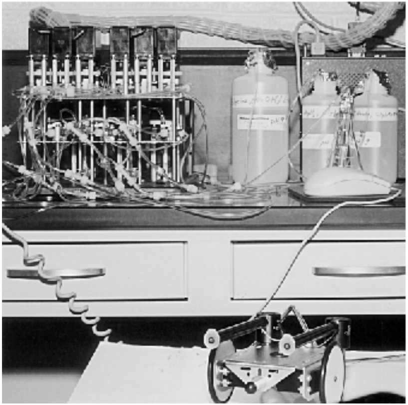
with Naoki Matsumaru and Jeff Pfaffmann

Molecular Robot Control: MDH



Malate dehydrogenase (MDH)

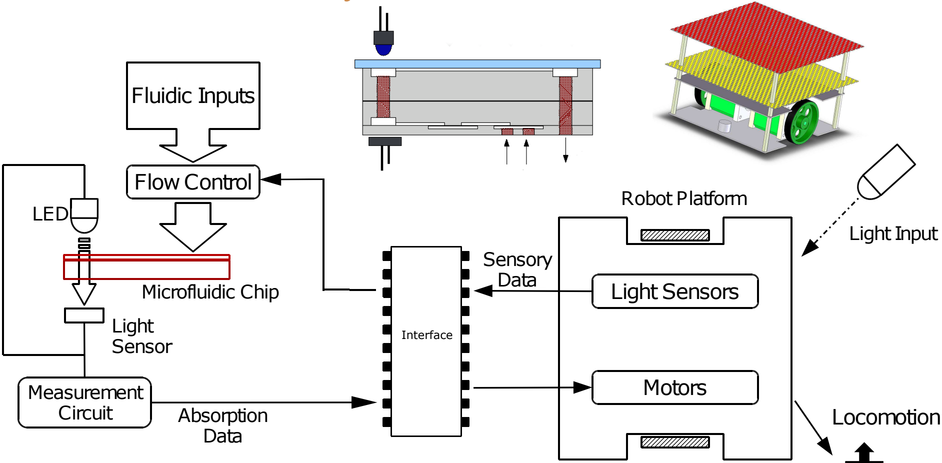


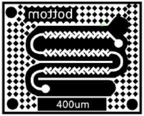


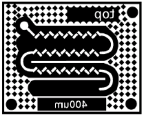
Phototaxis of a Braitenberg Vehicle controlled by malate dehydrogenase activity. The nonlinear response of MDH allows the robot to remain within a zone of intermediate light level.

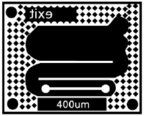
with Naoki Matsumaru and Jeff Pfaffmann

Microfluidics for Enzymatic Robot Control





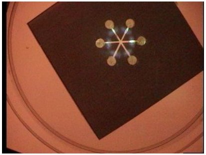




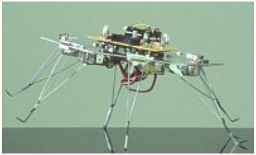
From Cells to Circuits and back I

- Single cell (Plasmodium)
- Very robust
- Distributed, parallel, molecular information processing
- Cells can be shaped into circuits of coupled oscillators

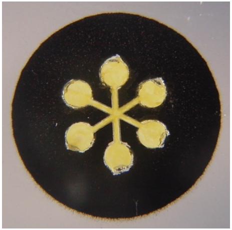
Physarum polycephalum



Optical interfacing



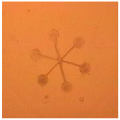
Cellular robot control

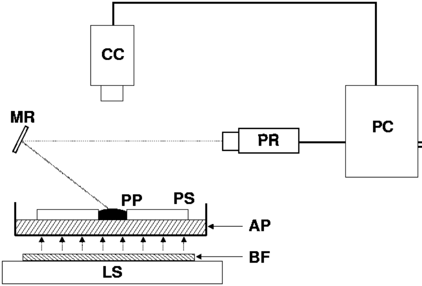


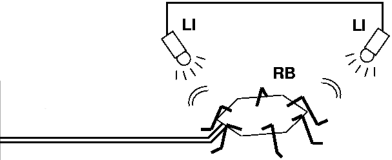
Grown in desired shape

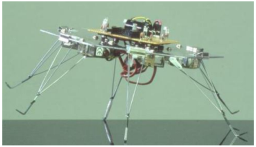
Robot Control With a Cell

Signals from the robot's light sensors are projected onto the channels of the *Physarum* circuit. The oscillations of the cell are mapped onto the robot legs.





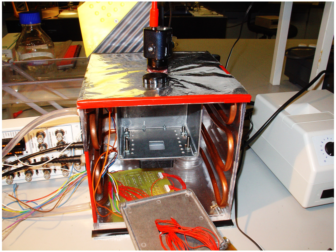




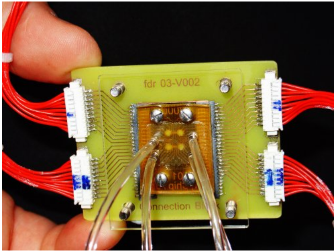
Tsuda, Zauner & Gunji, 2005

Miniaturisation

Original setup (2005)

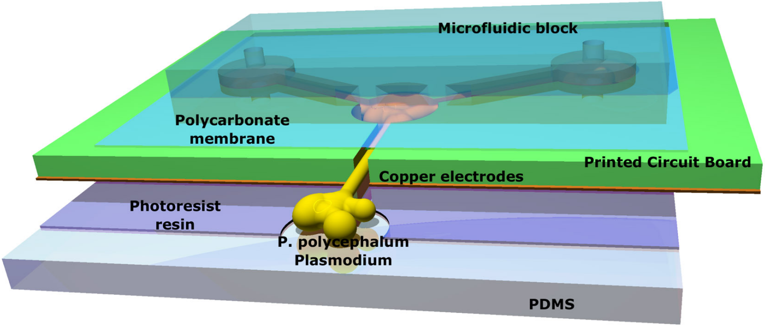


Electronic interfacing (2006)



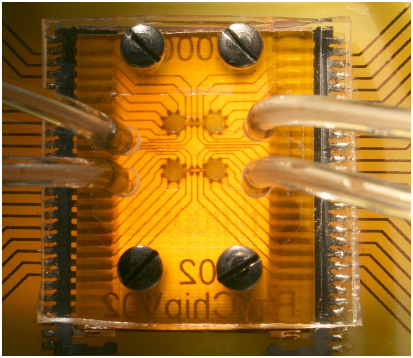
Integration in chip (2007)

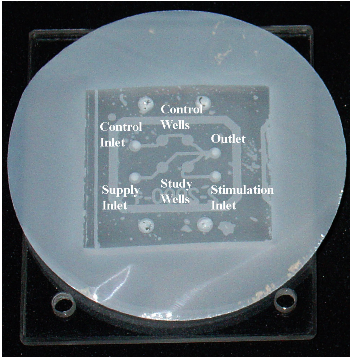
Physarum on a chip



with Ferran Revilla and Hywel Morgan

Physarum on a chip





- Impedance Measurements at 100kHz to 1 MHz
- Supply of water and nutriants
- Optically tarnsparent

with Ferran Revilla and Hywel Morgan

Slimsvamps skræk styrer robot

En klar gul slimsvamp, der kan blive flere meter bred er sat til at kontrollere en kravlende, seks-benet robot.

Robot napędzany strachem śluzorośli.

LICHTSCHUWE SLIJMBOT

Szenzáció: működik nyálkagomba irányítású robot!

Slime mould used to create first robot run by living cells

VISIONEN

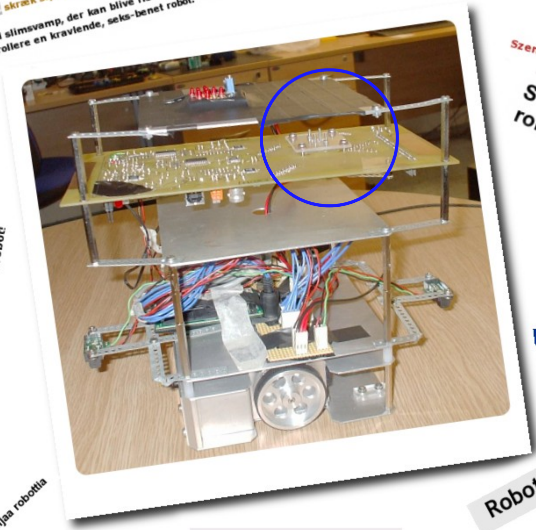
Roboter mit Pilzsteuerung

Current News

Slime Mold Incites Motion in Robot

Slim styrer robot

Une moisissure pouvant contrôler un robot!



Robot ovládaný strachem hlenky

Robô com cérebro de ameba foge da luz

Limasieni ohjaa robottia

Robot Takut Cahaya

Беспокойная слизь
загоняет робота в
тёмный угол

Robot
moved by a slime mould's fears 靠粘液菌的害怕
移动的机器人

Pilz im Roboterhirn

Concluding Remarks

1. Interfacing with biological substrates is now becoming feasible in small devices
2. We *need new computing paradigms* to elicit efficient computation from the novel bio- and nano-materials that are becoming available
3. We need to learn to engineer systems that contain both "programmable" and "non-programmable" components.

Many Thanks to:
MICHAEL CONRAD
YUKIO GUNJI,GARETH JONES, TOBIAS KLEEMAN,
PAUL MACEY, NAOKI MATSUMARU, HYWEL MORGAN,
JEFF PFAFFMANN, EFFIRUL RAMLAN, FERRAN REVILLA,
ROBERT SPANTON, SOICHIRO TSUDA

NASA
Microsoft Research Cambridge

Publications are available at:
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