POWER LAWS
SOME EXAMPLES

Addendum
Gutenberg-Richter Law

There are more small earthquakes than large ones. But there is no apparent cut-off in the possible size of an earthquake; earthquakes of all sizes are possible.

If the probability distribution were of the form $\exp(-E/E_0)$, then there would be a well defined cut-off at the energy $E_0$ such that the probability for an earthquake of size $E$ much greater than $E_0$ is exponentially small.

- Natural ($100B)
- Technological ($10B)

Slope = -1 (α=1)

Log(rank) vs. Log(size)

Median
Distribution of City Sizes

Data for US cities (g ~ 0.8)
[Source: Oxford University Press]

<table>
<thead>
<tr>
<th>City</th>
<th>Pop. (thousands)</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York</td>
<td>7333</td>
<td>1</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>3449</td>
<td>2</td>
</tr>
<tr>
<td>Chicago</td>
<td>2732</td>
<td>3</td>
</tr>
<tr>
<td>Houston</td>
<td>1702</td>
<td>4</td>
</tr>
<tr>
<td>Philadelphia</td>
<td>1524</td>
<td>5</td>
</tr>
<tr>
<td>San Diego</td>
<td>1152</td>
<td>6</td>
</tr>
<tr>
<td>Phoenix</td>
<td>1049</td>
<td>7</td>
</tr>
<tr>
<td>Dallas</td>
<td>1023</td>
<td>8</td>
</tr>
<tr>
<td>San Antonio</td>
<td>999</td>
<td>9</td>
</tr>
<tr>
<td>Detroit</td>
<td>992</td>
<td>10</td>
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</tbody>
</table>

...
## Distribution of City Sizes

How about Chinese cities? \( g \approx 0.5 \)

<table>
<thead>
<tr>
<th>Cities</th>
<th>Pop. (thousands)</th>
<th>Rank</th>
</tr>
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<tbody>
<tr>
<td>Shanghai</td>
<td>8206</td>
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<tr>
<td>Beijing</td>
<td>7362</td>
<td>2</td>
</tr>
<tr>
<td>Hong Kong</td>
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<td>3</td>
</tr>
<tr>
<td>Tianjin</td>
<td>5804</td>
<td>4</td>
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<td>6</td>
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<tr>
<td>Guangzhou</td>
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<td>7</td>
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<tr>
<td>Wuhan</td>
<td>3833</td>
<td>8</td>
</tr>
<tr>
<td>Tai'an</td>
<td>3825</td>
<td>9</td>
</tr>
<tr>
<td>Harbin</td>
<td>3597</td>
<td>10</td>
</tr>
</tbody>
</table>

Why is the exponent for the size distribution of the Chinese cities different from that of the US cities? What social-economic dynamics gives rise to the difference?
Power Laws are Ubiquitous

Cumulative distributions

<table>
<thead>
<tr>
<th>quantity</th>
<th>$x_{min}$</th>
<th>exponent</th>
</tr>
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<tbody>
<tr>
<td>frequency of use of words</td>
<td>1</td>
<td>2.20(1)</td>
</tr>
<tr>
<td>number of citations to papers</td>
<td>100</td>
<td>3.04(2)</td>
</tr>
<tr>
<td>number of hits on web sites</td>
<td>1</td>
<td>2.40(1)</td>
</tr>
<tr>
<td>copies of books sold in the US</td>
<td>2000000</td>
<td>3.51(16)</td>
</tr>
<tr>
<td>telephone calls received</td>
<td>10</td>
<td>2.22(1)</td>
</tr>
<tr>
<td>magnitude of earthquakes</td>
<td>3.8</td>
<td>3.04(4)</td>
</tr>
<tr>
<td>diameter of moon craters</td>
<td>0.01</td>
<td>3.14(5)</td>
</tr>
<tr>
<td>intensity of solar flares</td>
<td>200</td>
<td>1.83(2)</td>
</tr>
<tr>
<td>intensity of wars</td>
<td>3</td>
<td>1.80(9)</td>
</tr>
<tr>
<td>net worth of Americans</td>
<td>$600m</td>
<td>2.09(4)</td>
</tr>
<tr>
<td>frequency of family names</td>
<td>10000</td>
<td>1.94(1)</td>
</tr>
<tr>
<td>population of US cities</td>
<td>40000</td>
<td>2.30(5)</td>
</tr>
</tbody>
</table>

TABLE I Parameters for the distributions shown in Fig. 4. The labels on the left refer to the panels in the figure. Exponent values were calculated using the maximum likelihood method of Eq. (5) and Appendix B, except for the moon craters (g), for which only cumulative data were available. For this case the exponent quoted is from a simple least-squares fit and should be treated with caution. Numbers in parentheses give the standard error on the trailing figures.
R E C H E N B E R G ' S  T U B I N G  P R O B L E M

Addendum
The “Tubing Problem”

- Evolution of a 90 degree bend
- Fuel flows in from the left
- Fuel should leave the tube such that resistance of the fluid is minimized
- Six manually adjustable shafts determine the form of the pipe
- What is the shape of the connecting tube?

Ingo Rechenberg, TU Berlin
The “Tubing Problem”

- Evolution of a 180 degree bend
- 10 robot-controlled cable-drives alter the 180° pipe bend
- What is the shape of the connecting tube?
INTRODUCTION TO MORPHOLOGICAL COMPUTING

December 6, 2013
Rolf Pfeifer
Rudolf M. Füchslin
MORPHOLOGICAL COMPUTING: FUNDAMENTAL CONSIDERATIONS
What is a Computation?
Recap: Conventional (Binary) Computation

- A **binary computation** is a mapping from a set
  \[ X \subset \{0,1\}^* \] to a set \( Y \subset \{0,1\}^* \).

  \[ S^* \] denotes the Kleene-star of a set \( S \).

- It is sufficient to study **decision problems**:
  \[ X \subset \{0,1\}^* \rightarrow \{0,1\} \]

  All binary computations can be reduced to sets of questions with yes/no-answer.

- A computation is a mapping in the above sense but not all conceivable mappings are computations. There are different **models of computation**, the most important is the one given by Turing (up to equivalence, such as lambda – calculus).
Turing provided a specific model of computation, the Turing-machine. By the term “conventional computation”, we refer to computations that can be performed by a Turing-machine.
Control

• Is there a difference between control and computation?
Computation and Control

• **The goal of a computation** is to provide a yes/no – answer to a well-defined problem, given by a binary input string that is **completely known at the start of the computation**.

• **The goal of a control process** is the generation of a continued stream of signals which are provided as input for some form of actuator. The signals are in general a function of some sensory input.

• Control usually involves some form of computation (and some computers)

Note: This distinction of computation and control neither produces deep insights nor is it generally made, nor is it that strict. Most control processes are resolved into many short computations.
The concept of control differs from that of a computation:

1. Control: Input not completely known at begin of process.

2. Success: A computation is successful, when it reaches a halting state. There is no comparable concept for control.

3. Output-Input relation:
   - Computation: Output does not influence the input.
   - Control: Output at time $t$ can (should) influence the input that will be gathered at later times.
Control

- How do you control a robot?
In “conventional control”, sensory input is translated into finite binary strings, which are then processed by a Turing machine and back-translated into signals for the control of actuators.
Conventional Control

Our computers are Turing machines: Programs are (in principle) fully portable between two different realizations of a Turing machine.

- The physics of the realization of the TM is of no importance for the outcome (maybe for the speed, but not for the outcome as such).

- If one desires to solve a problem that involves physics, all the necessary physics has to be provided by the program, the physics of the machine must not interfere.
Abstraction: Pros and Cons

- Abstraction: Definition of conventional computation is as independent as possible of the nature of the computing device.

- Morphological computation (to be defined in what follows) is inspired by the suspicion that this independency is not for free.

- Already in conventional computation, dedicated hardware speeds up a calculation at the price of losing portability.
Abstraction vs. Embodiment

To be discussed: Embodiment and portability are antagonistic and seem to correlate with the pair programmability vs. specific function. Morphological computation can be regarded as the attempt to explore the space between the extremes.
Reconfigurable Hardware

Reconfigurable hardware

• Does not need an OS in the usual sense: The computation is directly realized in hardware.

• Takes profit of the connection topology of individual components.

Reconfigurable hardware is an example where morphology facilitates conventional computation.

BTW: Graphic cards, initially designed for 3D geometry only, are used for various types of problems being structurally related to those posed by graphics.
MOTIVATION: ROBOTICS
Embodied Intelligence

Engineered systems

Biological systems
Embodied Intelligence

There is an apparent gap between the success of control exerted by Turing machines in stiff engineered systems and the precision and adaptability of control in compliant biological systems.
Control of Body

- How do you control your body?
Embodied Intelligence

**Embodiment** exploits intrinsic stabilization capabilities of cleverly designed system.

**Control is outsourced to the body!**

Prof. Rolf Pfeifer
Attractors and Basins of Attraction
Attractors and Basins of Attraction
Only Fixed Points?

- Are fixed points the only possible type of attractor?
Limit Cycles

Limit cycle
Transient from the interior
Transient from the exterior
Gait Patterns
Gait Patterns

- **Brain** chooses red or green basin of attraction.
- **Body-dynamics** drives system into attractor (and keeps it there).
Gait Patterns: Picture incomplete

- Transient time should be short.
- Fluctuations: Strong damping
- Attractor landscape can be changed.
Brain & Body: A Recent Result from Robotics

- **Feed-forward neural networks**: Some but not universal computational power.
- **Mechanical mass-spring systems**: Can generate time-dependent signals.

Recent result (H. Hauser et al.): A properly interfaced hybrid system (mass-spring + feed forward neural network) can emulate/compute large classes of filters (functions onto functions).

It's not that our brain is so smart; it's our body that makes walking easy!
Morphological Control

Body as dynamical system with attractors:

- **Brain** chooses red or green basin of attraction.
- **Body-dynamics** chooses attractors.
“Ideal” conventional control: complete abstraction of the control task.
Real conventional control: minimize the effects of the morphology.
Morphological control exploits and optimizes the effects of morphology.
Morphological Control: How?

First step: Shape and material (morphology) make certain patterns of motion to attractors:

- **Conventional control** initiate switches between basins of attraction
- **Morphology** takes over the calibration and stabilization.
- **Programming** by designing attractors
Morphological Control: How?

- **Attractor landscape is determined by the morphology**: It can be autonomously re-shaped as a reaction on external demands (e.g. forces that change the morphology).

- **Morphology needs to be designed such that it adapts optimally to various external demands.**

- A conventional control device (e.g. a neural net) can support the change of morphology such that e.g. stabilization takes place in an optimal manner.
Morphological Control: Dynamic Attractors

• Example: Bending and twisting of body under load.
• If we have to carry a heavy load, we learnt how to adapt our morphology such that we can optimally perform the task.
• Experienced skiers and tennis players say that their posture is essential for precise reactions on unexpected bumps or shots (reliable source needed)

Optimize your morphology (shape and internal tension) when exerting difficult/unexpected tasks (left: Led Zeppelin, Stairway to Heaven, right: SUVA brochure)
Morphological Control: Adapting Attractors

Training ➔ Brains learns posture such that specific movements are optimally supported by morphology

Experienced skiers: Posture is essential for precise reactions on unexpected bumps.

Brain & Body: A Recent Result from Robotics

- **Feed-forward neural networks** have some but not universal computational power.
- **Mechanical mass-spring systems** can generate time-dependent signals.
- **Recent result**: A properly interfaced hybrid system (mass-spring + feed forward neural network) can emulate/compute large classes of filters (functions onto functions).


MORPHOLOGICAL CONTROL: CONCEPTUAL ASPECTS
What is Morphology?

Morphology, as we understand it:

**Morphology = Shape + Material properties**

Material properties:

- Elasticity / plasticity / deformability
- Weight
- Friction coefficients
- ...


A workshop at the first International conference on Morphological Computing in Venice 2007 (lead by Packard and Pfeifer) called a process a **morphological computation** if

- **There it be a clearly identifiable input and output.** This rules out systems which cannot be prepared or read out because they are continuous and chaotic.

- **The process must be programmable:** The choice of the input and maybe some parameters should allow to reach a big range of outputs.

- **There is a teleological embedding:** A river flowing downhill does not perform a computation.

Note: This definition is not complementary to Turing-computation, but renders a concept of computation not restricted to TM.
Lorenz-System: Morphological Computation?
Lorenz-system: Impossible to reproduce specific outcome, because initial conditions cannot be reproduced.
CA: Initial conditions are easy to reproduce and output can be read.

Discrete, CA-like systems can be used for morphological computation, but not Lorenz-systems.
The Hidden Charm of Nature

1. Nature is indifferent towards the problems of numerical analysis:
   a. Whether a system exhibits a simple linear or a complex chaotic dynamics is of no importance for whatever type of speed of the system.
   b. Nature implicitly deals with complicated boundary conditions, e.g. shape of objects.

2. Nature is inherently parallel: You don't have to care about transferring information about mutual positions of, say, hard spheres, they care after themselves.

3. The physics is already there: You haven't to code it, but you also cannot go beyond it.

4. Morphological control is evolvable.

5. Temperature delivers random numbers for free.
Nature and Numerical Analysis

Nature doesn’t care about numerical analysis: There is no slow-down in nature when the problems gets numerically tough.
Complex boundary conditions are implicitly treated.
Boundary conditions are an example for the problem of translating reality into (binary) representations. We most often have no efficient way of expressing boundary conditions, even if the dynamics as such is simple.
Boundary Conditions: A (Simple) Example

A tentacle: Five actuators, five sensors, ➔ full flexibility
Boundary Conditions: A (Simple) Example

Five actuators, five sensors, $\Rightarrow$ full flexibility
Boundary Conditions: A (Simple) Example

Only one parameter (cable offset), no actuators in joints. Bending angles become correlated and are a function of cable offset.
Gripping is still possible: Morphology of tentacle correlates angles with structure of object to be gripped.
Boundary Conditions: A (Simple) Example

- Gripping with tentacle without springs/cables requires the control of five parameters.
- Doing the same with a tentacle with springs/cables requires the control of one parameter.

⇒ The morphology of the tentacle (springs, joints, cable) takes over a part of the control.
The tentacle with springs **adapts to the object to be gripped**. But: Without an object to be gripped, only limited configurations of the tentacle can be achieved.

**Morphology correlates internal degrees of freedom under inclusion of the environment.**
Programming Morphological Control

- Programming the simulation of a physical process requires to code the physics.
- Using morphology as part of computation, one relies on the fact that the physics is always there: **One has not to care about it, but in turn cannot go beyond it.**
- A MC-program is not anymore an algorithm that is fully defined but resembles a recipe, where not all details are explained.
- Programming process may necessarily require evolutionary means (one may rely on not completely known systems).

Note: Cooking a potato soup requires one page of instruction and weakly standardized pots, oven and spices. Simulating the cooking of a potato soup is probably beyond present technology.
Natural vs Morphological Computing

There is a research area called **natural computing**:

1. In natural computing, **non-electronic means are used to perform basically conventional computations**.

2. Examples are: DNA-computing, membrane computing (P-systems), chemical tagging systems, some branches of quantum computing.

3. Full programmability with the intention to actually perform real conventional computations is a major goal of natural computing.

4. The border between natural and morphological computing is not sharp.
The **MC – program** for cooking a potato soup requires
- one page of instruction
- and weakly standardized pots, oven and spices.

**Conventionally simulating** the cooking of a potato soup is probably beyond present technology.
Natural vs. Morphological Computing

Morphological Computing:
• Control oriented.
• Efficiency of computation is in focus.
• Universality is of interest, but not primary goal.
• Embodiment plays the central role: Exploiting material properties and organization schemes is a core issue.

Natural Computing:
• Computation oriented
• Efficiency is relevant.
• Universality is a core interest.
• One searches for instances of computation in nature; exploiting embodiment is relevant, but not central.
Morphological Control vs. Control Theory

- Morphological computation overlaps with control theory.
- Control theory: Crucial notion is that of the “reference”, which provides an exact specification of the way system parameters should behave.
- In morphological control no reference is explicitly required.
MORPHOLOGICAL CONTROL: CASE STUDIES IN ROBOTICS
A flying insect must avoid an obstacle $R$, means keeping a distance $d > d_{\text{min}}$. Assume that an insect eye consists of several sensors, each able to detect the obstacle but only with a small aperture and at different orientations. Usually, the arrangement of the sensors is fixed and a neural network for optimal obstacle avoidance is evolved.

Evolving the Morphology of a Compound Eye on a Robot
Lukas Lichtensteiger and Peter Eggenberger
Lichtensteiger and Eggenberger took a **simple fixed neural network** and evolved the optimal sensor distribution. Using simple morphology requires the calculation of sine-functions by the neural net, optimized morphologies only require linear functions.

*The morphology computes!*

Light sensors with small aperture

\[
\rho = k \frac{1}{\sin^2 \alpha}
\]
The concept: By proper arrangement of the sensors, keeping proper distance can be achieved by keeping constant the „optical flow“ (Time the object to be avoided can be seen by one individual sensor).

T. Lundh (Chalmers) recently suggested a measure for the amount of computation performed by morphology.

Stumpy: A „Simple“ Systems Dances!

The robot “Stumpy” walks surprisingly reliable and with different movement patterns.

Stumpy:
- Only two actuated joints.
- Elastic „feet“ are crucial
- „Dancing“ is achieved by actuating horizontal rotation of „shoulder“ and bending of „waist“.
- The morphology facilitates the problem.

Raja Dravid, Chananda Paul, Fumiya Iida, Max Lungarella
Puppy, MiniDog, Geoff et al.

- Iida et al. constructed a dog-like robot with elastic limbs.
- Pressure sensors in feet.
The robot only „experiences“ pressure signals.

The gaits are attractors ➔ complex coordinated pattern emerges without conventionally computing according internal representation.
Self-Organized Gait Patterns

- Robot is able of walking and **self-organizes its movement into gait patterns**.
- These gaits depend on the texture of the ground.
TENDON DRIVEN ROBOTS
SOFT ROBOTS
AILabs's Roboy

Tendon driven humanoid robot
Soft Robots

Soft robots at the lab of G. Whitesides

Project Octopus (partner: AI Lab)
**Real conventional control**: minimize the effects of the morphology.
Why Are Robots Stiff and Heavy?
Why Are Robots Stiff and Heavy?

Physics matters:

- **Stiffness**: Easy to localize in real space
- **Heavy weight**: Easy to localize in momentum space.

robot's state should have as few degrees of freedom as possible \(\Rightarrow\) stiff

Heavy weight: Interaction with objects to handle changes in momentum only a bit.
Morphological control exploits and optimizes the effects of morphology.
Soft Robots

Physics matters:
• Stiffness: Easy to localize in real space
• Heavy weight: Easy to localize in momentum space.

With MC, no complete representation is necessary ➔ Robots can be soft and light.
MC ON SMALL SCALES: STATISTICAL INSTEAD OF CLASSICAL MECHANICS
Many applications of morphological computation are found in the realm of mechanical control and exploit mechanical properties of macroscopic systems.

**Embodied process management (EPM)** aims to apply the concept of and lessons learnt from robotic embodied intelligence to chemical processing.

**Slogan:**

\[
\text{Embodied Intelligence in Robotics} \quad \text{Classical Mechanics} = \quad \text{Embodied Process Management in Chemistry} \quad \text{Statistical Mechanics}
\]
Morphological Control and Chemistry

- Do you know a chemical system subject to MC?
Cells
Macrophages

Typical size: 20 micrometers
Centralized external control

Robust, self-organized control. Chemical kinetics and statistical mechanics of e.g. lipid phases regulate cell behavior.
Cells are More Than Containers

Cellular processes cannot be understood with simple kinetics: The interaction between molecules, supra-molecular structures and membranes controls the processes in the cell, see e.g. endocytosis.

Note that e.g. the stabilization of processes in the context of cellular process management requires the handling of non-equilibrium processes and is not restricted to stationary situations or even thermodynamic equilibria.
The Search for “Primitives”

Digital computing primitives proved to be a basis for efficient design of microelectronics.

**Motion primitives** will form a basis for MC in robotics (Maass, Hauser, Pfeifer, Ijspeert).

**Reaction primitives**, basic chemical modules that can be combined will be necessary for MC in cell-like process management.

**Functional motives** in networks

„Primitives“: Basic functional building blocks that can be combined. Such primitives are enable modular engineering and probably necessary if MC shall be part of a novel methodology in construction and design of technological components.
MORPHOLOGICAL CONTROL AS GUIDING PRINCIPLE IN PHYSIOLOGY AND MEDICAL APPLICATIONS
REJUVENATING ATTRACTORS
Elderly patients sometimes suffer from a decrease of control over movement patterns, especially walking.

Why?
Elderly patients sometimes suffer from a decrease of control over movement patterns, especially walking.

Conventional explanation:

Aging ➔ decrease of neural performance ➔ loss of control
Aging changes mechanical properties of the body

- Attractor landscape less suited for support of movement patterns (less efficient damping, longer transients, etc.)
Aging: Loss of Morphological Control

**Vision:** External mechanical means “reshape” the parameterized attractor landscape

- No local repair of sinews, ligaments
- Goal: Re-establish morpho-computation power of the body.
- Attractor landscapes and parameterization are made more functional.
Support Systems: Exoskeleton

Bleex

Hulc™

eLEGS

50 best inventions 2010
Time magazine
Synergetic combination of an airbeam with conventional cables and struts.

Tensairity® = Tension + Air + Integrity

Rolf Luchsinger, EMPA Dübendorf
- 8m span, 2 tons max. load
- Fits in the trunk of a car
- Set up time < 30 min (two persons)
- Weight 70 kg (one girder)
Tensairity actuator
First Steps Towards Support System

Test system for supporting and stabilizing knee dynamics: Not a servo!

A. Dzyakanchuk, Kenneth Hunt, R. Füchslin, R. Luchsinger, M. Muster
Advantages of actuated inflatable elements:

1. **Low weight.**
2. Inflatable structures may exert significant total forces but can’t apply strong local forces ➔ **Generic safety.**
3. Tensairity structures as well as the signals administered by them can easily be **personalized.**
4. **Actuated tensairity opens novel therapeutic strategies** and higher levels of personalization.
5. Vibratory signals need **not to be generated at its point of their administration.**
6. Forces/Signals are applied over broad areas ➔ **Reduction of local stress.**
Why Tensairity?

Soft robots are safe(r) robots!
DO IT LIKE A CELL: CONTROLLING THE SYNTHESIS OF BRANCHED POLYMERS
Spatial structuring is programmable and can increase yield rates in the synthesis of branched polymers.
Programmable Chemical Microfabs

Conditions have to be suitable for all reactions. Each branch of the reaction can take place in an optimal environment.
Optimization by Compartmentalization

- **Pro:** Compartmentalization ➔ optimization by branch-specific choice of chemical conditions.
- **Con:** Matter and information has to be transported between the compartments.
Programming by Arranging

- Matter and signal transport takes place between adjacent containers.
- The arrangement influences the overall reaction.

Optimization by compartmentalization  Control by influencing matter transport
SHCμR

Programmable Self-Assembling Spatially Heterogeneous Micro-Reactors

A Theoretical Investigation of an Example of Embodied Process Control

Benedikt Reller

Synthetizing branched molecules in self-assembled reactors.
Artificial Branched Molecules
Artificial Branched Molecules

Monomer: Up to 3 linkers
Artificial Branched Molecules

Multiple use of monomers

Monomer: Up to 3 linkers
Artificial Branched Molecules

Same linkers allow wrong assembly

Multiple use of monomers

Monomer: Up to 3 linkers
Reactors

- Reactors assemble on 2-dim substrate.
- Two different linkages: containers and monomers
- Types of reactors.
  - Specific external linkers to other containers
  - Specific internal linkage reaction
Running SHCµR

Simulation run

Self-assembly of the grid

- Algorithms for self-assembly
  - Two container models
  - Two association models

Predefined grid

- Fixed-Grid definition

Polymerization: reaction-transfer cycle

- Algorithms:
  - Binding and Decomposition
  - Transfer of polymers between containers
Synthesis: Stochastic Reactors

- Each type of container performs a specific synthesis step.
- Containers arranged by stochastic self-assembly.

Benedikt Reller, R. Füchslin (MATCHIT)
Synthesizing Branched Molecules
Fixed Grids

Improvement of yield rate improved up to three orders of magnitude.
Chemical Compilers – An Example

- In case of an FSArealized with DNA,
  - Takes the formal description of a specific FSA as input.
  - Renders as output:
    - The structure of the DNA-strands necessary for implementing the given FSA
    - Instructions, what to do with these DNA-strands in a standardized lab.

<table>
<thead>
<tr>
<th>q0</th>
<th>a</th>
<th>b</th>
<th>c</th>
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</tr>
<tr>
<td>q3</td>
<td>q3</td>
<td>q3</td>
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</tr>
</tbody>
</table>
Chemical Compilers – Another Example

- Compiler takes chemical reaction as input and delivers
  - Linkers and types of containers
  - Relative number of containers
  - Instructions for setting up the SHCmuR
MATCHIT Automaton

- FP 7 Project MAtrix for CHeMical IT

1 dim channel
- So called chemtainers (e.g. vesicles) interact with channel and each other.
- Control by DNA – computing
- Mathias Weyland and Harold Fellermann developed compiler for synthesis of branched polymers.
Evolution vs. Compilation

1. a) b)

2. a) b)

Evolved

Compiled
Non-Interacting, Non-Controlled Reactions

Chemical reactions produce a grammar tree of sequences.
Non-Interacting Controlled Reactions

Chemical reactions and control produce a "weighted grammar tree" of sequences.
Controlled Reactions

Chemical reactions, interaction of intermediates and control produce something complicated.
Can reactions as we study them be understood as formal languages, as grammars constructing molecules?

In case of Benny's FSA, this is possible!
## Languages and Problems

<table>
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<tr>
<th>Type</th>
<th>Recognition</th>
<th>Emptiness</th>
<th>Equivalence</th>
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<tr>
<td>3</td>
<td>yes</td>
<td>Yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

- Relevant to us: We have a set of chemical prmitives represented in a language.
- We have to restrict our chemistry such that the grammar is not of level 0, otherwise we can't build a compiler!
The Hidden Benefit of Small Size

Macroscopic processes: Metastable substances can only be used with considerable effort.
On the micrometer – scale, a few seconds life time are sufficient for diffusive transport.

Macroscopic Catalysts: Need efficiency and stability
Microscopic Catalysts: Efficiency is sufficient!
Golgi Apparatus

Pictures from http://jennarever.weebly.com/index.html

Production of oligosaccharides (among other things)
Cells as dynamical systems

- Consequences to therapy optimization
THE MC – VIEW OF THE MOLECULAR BIOLOGY OF THE CELL
Multi – Scale Processes: Endocytosis

Receptor – mediated endocytosis:
• Chemical reactions
• Supramolecular self – assembly
• Membrane physics

Endocytosis is an attractor of a non – equilibrium system.
Lesson learnt: Molecular pathways have to be complemented by multi-scale dynamics.


Visualization: N. Mennes and T. Maeke
The Network Picture

Cell as a dynamical network of physico-chemical interaction
Properties of Networks

- Every (most) functions are distributed over many nodes and every (most) nodes contribute to many functions.
- Network is result of an evolutionary process → some structural properties can be derived in broad generality.
- Evolution selects networks with some appropriate attractors.
Two Types of Diseases

One or several nodes are dysfunctional → network functionality may be affected.

All system components are functional, but system is in wrong basin of attraction.
Two Types of Diseases

- Ventricular fibrillation
- (Some forms of) cancer?
- (Some forms of) depression?
Two Types of Diseases

- Network has to be mended
- Dysfunctional node has to be substituted.

- Network has to be pushed in proper basin of attraction.
- Proper basins of attraction have to be fortified.
- Environmental conditions have to be changed
Evolutionary Medicine

OPINION

Darwinian medicine: a case for cancer

Mel Greaves

Abstract | Epidemiological, genetic and molecular biological studies have collectively provided us with a rich source of data that underpins our current understanding of the aetiology and molecular pathogenesis of cancer. But this perspective focuses on proximate mechanisms, and does not provide an adequate explanation for the prevalence of tumours and cancer in animal species or what seems to be the striking vulnerability of Homo sapiens. The central precept of Darwinian medicine is that vulnerability to cancer, and other major diseases, arises at least in part as a consequence of the ‘design’ limitations, compromises and trade-offs that characterize evolutionary processes.

"These data suggest that a propensity to develop benign tumours and malignant cancer is a common feature of multicellular animals and that, although intrinsic risk or actual spontaneous rates might be expected to escalate with increasing complexity and longevity, these features alone do not adequately account for the vulnerability of Homo sapiens, which seems substantially greater than that seen in other mammals including the great apes."

Vulnerability to Cancer

Potential explanations:

• More mutagenic stress

• Present life style / environment parameters drives cells into "spurious attractors".

Spurious attractors:

• Evolution is blind. In a given environment, useful attractors are positively selected.

• The system may exhibit further attractors. If they occur under unusual environmental conditions, they are not subject to negative selection.
Cells as Dynamical Systems

• Understanding cellular dynamics in terms of dynamical systems sounds plausible.
• But where is the clinical benefit?
How to Profit from Models

• Sometimes, models are predictive

• Humans:
  • Perform well in recognizing static structures.
  • Perform poorly in estimating dynamic consequences.

• Models may reveal effectively low – dimensional dynamic structure

• ➔ personalization of treatment by use of more advanced statistical methods.

• ➔ estimates for synergistic effects.
"Phenomenological" Modeling

- Model with few parameters.
- Assumption: There is semantics on a supra-molecular level.

**Evolution:**
- Variation affects the genotype. → Molecular level
- Selection happens to the phenotype → Semantics occurs on the phenotypic level → May or may not be the molecular one.

**Cellular control is evolved:**
- If we build a model, we have to consider its evolutionary construction
Conundrum: Reaction of cells to irradiation highly non-linear. "The more intensity, the more (long-term) damage" does not hold (Fig. by S. Scheidegger).
Combination Therapy

- Apply multiple stresses to cells:
  - hyperthermia (43°C)
  - radiation
- Taken alone, stresses are not lethal
- Their combination is chosen such that healthy cells are not affected too strongly
Dose Equivalent Models (HT – RT)

\[ \frac{dN_i}{dt} = f(N_i, N_k, \ldots, \Gamma, \Lambda) \quad \frac{dN_k}{dt} = g(N_i, N_k, \ldots, \Gamma, \Lambda) \]

\[ \frac{d\Gamma}{dt} = R - h(\Gamma) \quad \frac{d\Lambda}{dt} = u(\Lambda) - w(\Lambda) \]

\[ N_i \, : \, \text{Tumor cells not damaged by heat or radiation} \]
\[ N_k \, : \, \text{Tumor cells lethally damaged by heat or radiation} \]
\[ \Gamma \, : \, \text{Radiation-related dose equivalent} \]
\[ \Lambda \, : \, \text{Heat related dose equivalent} \]
\[ R \, : \, \text{Dose rate} \]
\[ f,g,h \, : \, \text{Functions describing induced death/repair/survival} \]

Phenomenological top-down model of synergistic effect of hyperthermia and radiotherapy.

Four-parameter model
Are Four Parameters Really Enough?

E. Wanker et al. Human protein network
Are Four Parameters Really Enough?

- Why is it possible to map a generically high-dimensional system to a low-dimensional one?
- Are dose equivalents really parameters?
- How to control the dynamics of the observed parameter?
Are Four Parameters Really Enough?

- Why is it possible to map a generically high-dimensional system to a low-dimensional one?

  Evolved system ➔ Easy control is a selection criterion ➔ Effective low – dimensionality is a selective advantage.

- Are dose equivalents really parameters?
- How to control the dynamics of the observed parameter?

Describing a complex system by few parameters doesn't work in general.

It may work if the system is evolved.
Are Four Parameters Really Enough?

- Why is it possible to map a generically high-dimensional system to a low-dimensional one?
- **Are dose equivalents really parameters?**

Dynamics can be parameterized in many ways ➔ Every choice is ok, as long as it works.

- How to control the dynamics of the observed parameters?

---

Cartesian coordinates are as correct as polar coordinates!
Are Four Parameters Really Enough?

• Why is it possible to map a generically high-dimensional system to a low-dimensional one?
• Are dose equivalents really parameters?
• **How to control the dynamics of the observed parameters?**

*Obtaining clinically relevant control is the big challenge!*
The Art of Hacking

1. Bring system into non–documented state.
2. Perform some unusual action.
Controlling cells: There is reason to believe in simple models.
IMMUNOLOGY: DETECTING DANGER BY MORPHOLOGY
Detecting danger by morphology

Question (Roland Scholz, ETHZ): Is there a non–enumerative way to detect non-default states in the states of tissues?
Matzinger developed an alternative view: The immune system is activated by general signs of danger, not (only) by foreignness.

Among other things, the model explains:
- Why the immune system can respond to tumors
- Why one needs adjuvants to make vaccines effective.

Detecting Danger by Morphology

- Fact: Chain molecules may fold up and get a non–trivial morphology.
- Fact: This fold is determined by
  - the molecules sequence (proteins: amino acids)
  - the conditions under which the fold takes place.
Detecting Danger by Morphology

Assume a molecule M with a fold that is evolved to be highly susceptible to chemical conditions.

Default fold

“Something is wrong” fold
Epitope D activates IS
Detecting Danger by Morphology

- **Cell ok, Environment ok**: Default fold
  - Immune system remains passive

- **Cell not ok, Environment ok**: Danger fold
  - Immune system activated

- **Cell ok, Environment not ok**: Danger fold
  - Immune system activated
Detecting Danger by Morphology

- Morphology of the molecule is sort of a "checksum".
- We don't claim that the mechanism is present in biological systems, but it may be implemented in artificial evolvable replication systems.

NEUROIMMUNOLOGY: MC AT WORK
The chemical immune systems know that and what is going wrong.

The nervous system knows where it is going wrong.
Hypothesis

- Nervous and immune system are coupled.
- **Rolf Pfeifer:** Find the optimal balance between nervous system and morphological control
Counterargument: Depression

- There is only limited evidence for an influence of the psyche on the immune system.
- **BUT:** Mental processes have, if at all, only indirect influence on chemical processing.
NOISE IS NOT ALWAYS A NUISANCE
Real conventional control: minimize the effects of the morphology.
Kosko Again

It's the "Kosko cube" Kosko!
Effect of Vibrating Insoles on Elderly People

Priplata et al. report that vibrating insoles have a significant effect on several parameters describing balance in elderly people. They hypothesize stochastic resonance to be the underlying cause of this observation.

Vibrating insoles and balance control in elderly people

Attila A Priplata, James B Niemi, Jason D Harry, Lewis A Lipsitz, James J Collins

Somatosensory function declines with age, and such changes have been associated with diminished motor performance. Input noise can enhance sensory and motor function. We asked young and elderly participants to stand quietly on vibrating gel-based insoles, and calculated sway parameters and random-walk variables. In our 27 participants, application of noise resulted in a reduction in seven of eight sway parameters in young participants and all of the sway variables in elderly participants. Elderly participants showed greater improvement than young people in two variables, mediolateral range (p=0.008), and critical mean square displacement (p=0.012). Noise-based devices, such as randomly vibrating insoles, could ameliorate age-related impairments in balance control.

Lancet 2003; 362: 1123–24

Übersichten

Auszerkungen mechanischer Schwingungsreize

Biomechanische und physiologische Effekte mechanischer Schwingungsreize beim Menschen

C.T. Haas, S. Turbansi, I. Kaiser, D. Schmidtbleicher

Biomechanical and physiological effects of oscillating mechanical stimuli in humans

Biomechanische und physiologische Effekte mechanischer Schwingungsreize beim Menschen

Institut für Sportwissenschaften, Johann Wolfgang Goethe-Universität, Frankfurt am Main
Effect of Vibrating Insoles on PD-Patients

Step-synchronized supra-threshold vibratory signals showed improvement of gait parameters in PD-patients (Novak and Novak).
Alternate rhythmic vibratory stimulation of trunk muscles affects walking cadence and velocity in Parkinson’s disease

Alessandro M. De Nunzio a,1, Margherita Grasso b, Antonio Nardone b,c, Marco Godi b, Marco Schieppati a,*

*a Centro Studi e Attività Motorie (CSAM), Fondazione Salvatore Maugeri (IRCCS), Istituto Scientifico di Pavia, and Department of Experimental Medicine, University of Pavia, Pavia, Italy. 

b Posture & Movement Laboratory, Division of Physical Medicine and Rehabilitation, Fondazione Salvatore Maugeri (IRCCS), Istituto Scientifico di Verano, Rome, Italy.

c Department of Clinical and Experimental Medicine, University of Eastern Piedmont, Novara, Italy.

DeNunzio et al. demonstrated that vibratory stimulation of the muscles improves walking quality of PD-patients.
Priplata et al. showed the effects observed in elderly patients also to be present in patients with diabetic neuropathy or stroke.
Jöbges et al. demonstrated an effect of vibratory stimulation of the forearm on the tremor of PD-patients. Sometimes, tremor vanished for a certain time.
What is Stochastic Resonance?

• Fact: Most (all?) sensory systems of the human body are subject to **threshold conditions**. Means: Detection only if signal intensity is above some threshold value.

• Reasonable, because biological systems have to **distinguish between true signals and ubiquitous noise**.

• In linear (most technical) systems, noise always decreases the quality of a measurement.

• In non-linear (biological) systems, situation is more involved ➔ Sometimes, noise increases the ability to interpret a signal.
Dithering

…[O]ne of the earliest [applications] of dither came in World War II. Airplane bombers used mechanical computers to perform navigation and bomb trajectory calculations. Curiously, these computers (boxes filled with hundreds of gears and cogs) performed more accurately when flying on board the aircraft, and less well on ground. Engineers realized that the vibration from the aircraft reduced the error from sticky moving parts. Instead of moving in short jerks, they moved more continuously. Small vibrating motors were built into the computers, and their vibration was called dither from the Middle English verb "didderen," meaning "to tremble." Today, when you tap a mechanical meter to increase its accuracy, you are applying dither, and modern dictionaries define dither as a highly nervous, confused, or agitated state. In minute quantities, dither successfully makes a digitization system a little more analog in the good sense of the word.

What is Stochastic Resonance?

Arc de Triomphe, black and white. Shown are BW-pictures with various levels of noise.

Arc de Triomphe, gray-level
Noise Can Enhance Visibility

- No noise
- Weak noise
- Medium noise
- Strong noise
Stochastic Resonance

- Measurement of a signal in a healthy patient
Stochastic Resonance

- Neural diseases can increase the threshold

An increase of the threshold makes a signal undetectable.
Adding Noise Makes a Signal Measurable

Medium noise levels make otherwise undetectable signals detectable, though only with decreased quality.

![Graphs showing signal detection with different noise levels.](image)
Apply non-periodic noise with personalized amplitude in order to improve quality of sensory signal processing.
EVOLUTIONARY ASPECTS OF SELF-ASSEMBLY
Problem: Evolving a 4bit x 4bit Multiplier

Each square represent a logical gate (4 input, one output).

The gates as well as the wiring is evolvable.

Totally local approach.

- Tangen et al.
- Miller, J.
Problem: Intelligent Learning

Such arrays of logical gates did not show good evolvability.

They never exhibited structure or could generalize results.
Patterned circuits

A broad class of problems is solved by logical circuits consisting of a regular arrangement of simple logical components.
The „global“ logic of a problem is transformed into the geometry of the arrangement of „local“ logic. Patterns reflect logical structures.

Such patterns are often scalable. Circuit can be extended to handle arbitrarily large inputs.
Self assembly

Scalable patterned structures can be obtained from self-assembling logical blocks (SLB).
Recognition sites for self-assembly

Function generator

The Self-Assembly Process
Evolving SLBs turned out to be difficult. Novel genetic algorithm required.

Self assembly enables structures solutions, novel GA enforces them.
Co-Evolving Test-Vectors

Each individual carries a construction scheme and a test vector, both evolvable.
Tournament is fought by mutual exchange of problems.
Having evolved a “difficult” test-vector is advantageous, at least in the beginning
Having evolved a “difficult” test-vector is advantageous, at least in the beginning
Co-Evolving Test-Vectors

Having evolved a “difficult” test-vector is advantageous, at least in the beginning.

Having evolved a “difficult” test-vector is advantageous, at least in the beginning. The evolutionary dynamics tends towards “difficult” test-vectors. “Difficult” is only defined with respect to the circuits in the population!
Inductive Generalization: 8x8 bit multiplier

As soon as the circuit masters 4bit x 4bit („Das kleine Einmaleins“) multiplication, it can be scaled up to arbitrary size → **inductive generalization.**
1. \[1101 \times 0000\]
   
   0000
   0000
   0000
   0000
   
   00000000

   mult. with zero

2. \[0110 \times 0001\]
   
   0110
   0000
   0000
   
   0000110

   mult. with one

3. \[1010 \times 0100\]
   
   0000
   0000
   0100
   0000
   
   00100000

   mult. with 2^n

4. \[1010 \times 1001\]
   
   0000
   1001
   0000
   1001
   
   1011010

   carryless addition

5. \[1001 \times 1011\]
   
   1011
   0000
   0000
   1011
   
   1100011

   full addition
Fitness

Fitness is given with respect to subtasks. The presented GA rewards solving subtasks and proceeds according to the expected line of increasing difficulty.
Size of Test-Vectors

32 runs for each testvector size, quartile box plots.

EITHER successful evolution of multiplier OR stop after 16 million generations.

For test vectors of size 4 or 64, more than three quarters of the runs didn’t succeed.
Key Point of Test Vectors

- Information is only preserved when regularly tested.
- “Learning” the solution of a specific problem is of limited value; it will be forgotten in the drifting population of test problems.
- “Understanding” how to handle a whole class of problems can be maintained.

If a circuit „stores“ the result of 13*2, the benefit is temporary, if it implements diagonal shifts for the multiplication with powers of two, a permanent gain results.
Evolved Scalable Multiplier

We evolved the answer to infinitely many problems from testing finitely many test cases by exploiting the embodiment of logic by pattern formation.
Is Self-Assembly Versatile?

- multiplier
- ALU
- binary to Gray-code
- Gray-code to binary
- binary in, add, Gray code out
And If There Is Noise?

- No deterministic assembly, Boltzmann-weighted assembly.
- Approach proved to be robust.
Two Typical Cases
Evolution and Self-Assembly

- Self assembly **enables** geometrically structured and scalable solutions for circuit design.
- Co-evolving small sets of test problems **enforces** structured solutions → **inductive generalization without exhaustive testing**: A form of understanding!
- **Robustness** against thermodynamic fluctuations.
Summary

- Static self-assembly is dictated by thermodynamics and relatively well understood.
- Dynamic self-assembly, where systems dissipate energy, is only at its beginning.
- Shifting logical aspects of a problem to geometrical patterns enables inductive generalization..
ALTERNATIVE MODELS OF COMPUTATION
Natural vs Morphological Computing

There is a research area called natural computing:

1. In natural computing, **non-electronic means are used to perform basically conventional computations**.

2. Examples are: DNA-computing, membrane computing (P-systems), chemical tagging systems, some branches of quantum computing.

3. Full programmability with the intention to actually perform real conventional computations is a major goal of natural computing.

4. The boarder between natural and morphological computing is not sharp.
Natural vs. Morphological Computing

**Morphological Computing:**
- Control oriented.
- Efficiency of computation is in focus.
- Universality is of interest, but not primary goal.
- Embodiment plays the central role: Exploiting material properties and organization schemes is a core issue.

**Natural Computing:**
- Computation oriented
- Efficiency is relevant.
- Universality is a core interest.
- One searches for instances of computation in nature; exploiting embodiment is relevant, but not central.
Example: DNA-Computing

- DNA can be regarded as a sequence of symbols from an alphabet $\Sigma = \{\text{Adenin}, \text{Cytosin}, \text{Guanin}, \text{Thymin}\}$.
- Present enzyme technology enables string operations on DNA such as concatenation, cleavage, insertion of substrings etc.
- With such operations, one can emulate a TM.
- There are indications that e.g. plasmids in plant cells perform actual counting.

- One easily can perform $10^{13}$ parallel computations in a test tube.
- Energy consumption is low.
- Reliability is low.
- Generating the solution is one thing, finding it in a test tube another.
These numbers motivate to use DNA as tool for computation. DNA-computing is a well-established field. Especially interesting is probably the implementation of comparably simple algorithms under severe volume restrictions.

<table>
<thead>
<tr>
<th></th>
<th>DNA</th>
<th>Current computer</th>
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<tr>
<td>Information density (bits/nm³)</td>
<td>~1</td>
<td>~10⁻¹¹</td>
</tr>
<tr>
<td>Parallelism (operations/sec)</td>
<td>~10¹⁸</td>
<td>~10¹²</td>
</tr>
<tr>
<td>Energy expenditure (J/operation)</td>
<td>~10⁻¹⁹</td>
<td>~10⁻⁹</td>
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Membrane Computing

Basic idea (many variants possible):
• Hierarchically organized compartments.
• String operations in compartments, realized by chemical processes.
• Transport between compartments.

Membrane computation (P-Systems) has been proven to be equivalent to Turing machines.

Hierarchically organized membranes remind on parsing trees.
Neural Nets and Reservoir Computing

- See lecture by N. Kupuswami (NN and RC are not fundamentally related but will be discussed in Helmut’s talk, that is the reason for appearing on the same slide).
Optical Computing

- Electrons are replaced by photons.
- Photons, or more precise beams of coherent light can interact with each other (interference).
- Logical gates can be built.
- Novel materials, mostly nano-structured are necessary (photonic crystals).
Quantum Computing

- Bits (0 or 1) are replaced by qbits $\exp(i \phi)$
- Instead of two values, all values on the unit circle are possible.
- Quantum processes, especially entanglement are exploited.
- QC is not more powerful than TM, though more efficient.
Also with domino bricks, you can build computers.
Same holds with billiard balls.
Below you see the two gates it takes to build all feed forward logical gates.
One interesting aspect of such physical models is that they show that already in classical physics problems which cannot be solved with present means (build up a computer and ask for the halting problem).
Alternative Models of Computation

- There are many more possibilities
- Always ask whether they are just a non-conventional implementation of conventional discrete computing (Domino/DNA computing) or whether they add something truly new (Quantum computing).
SPECULATIVE ISSUES
Of course, it were nice if we could tackle non-Turing-computable problems.

But going beyond Turing is by no means the only challenge worth to pursue: Not only whether but also how efficient a problem can be solved is of interest.

“Efficiency” is understood in various ways:

- MC may sheds light on the universality of classical computational complexity.
- MC may enable the reliable, decentralized and efficient implementation of control mechanisms for various types of processes.
• Whether a device with computational potential above that of a TM can be built is one question.
• Whether there are more efficient ways of realizing a computation is a different issue.
• **Hypothesis:** Giving up the universality of the Turing model may pay off with respect to efficiency.
• → We have to analyze the structure of conventional computation and search for alternatives.
Relation Between MC- and TM-Computation

Fundamental gain and/or efficiency gain? Whether MC-solvable is truly larger than TM-solvable is a matter of debate.