# SynBioTA

# Assessing and Influencing an Emerging Technology – The Case of Synthetic Biology

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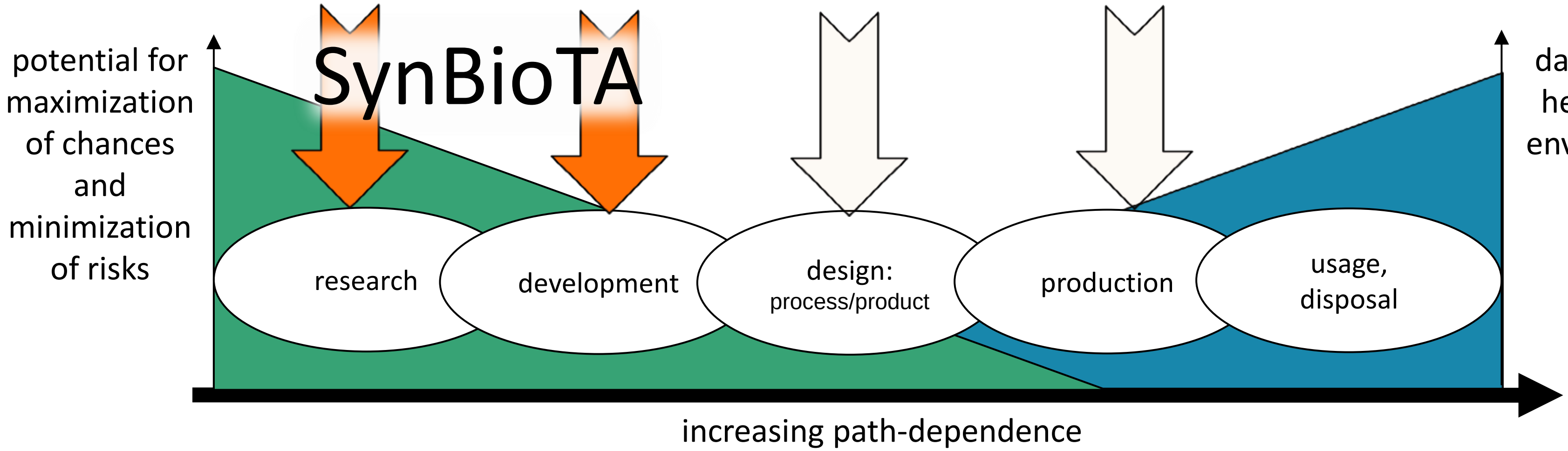
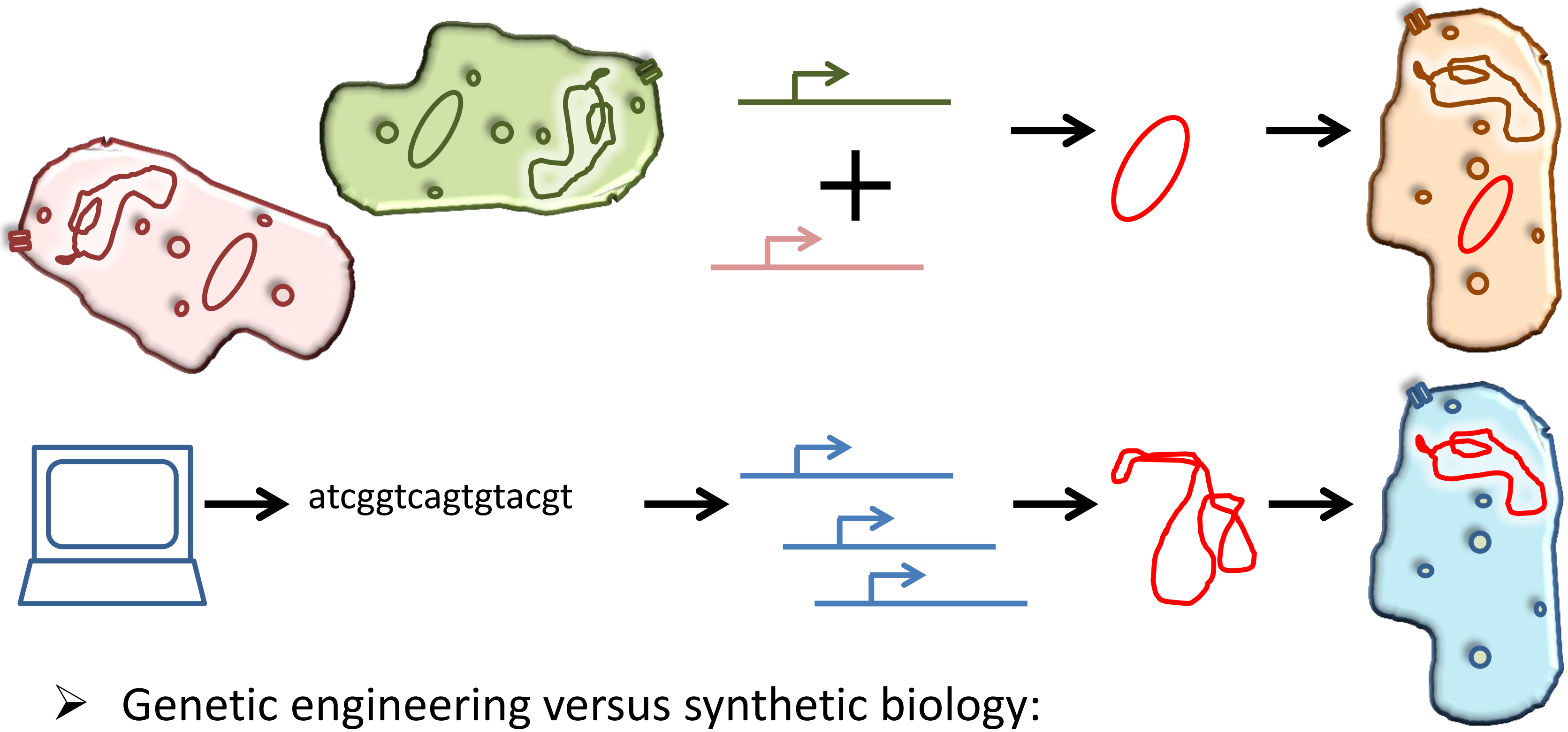
# *Starting Points for Precautionary Systems Design and Minimization of HSE Risks*

1) Paradigms? Contributing research fields?
2) Methodology? Scientific process of abstraction?
3) Functionalities?
4) Potentials and hazards (HSE)?
5) Beneficial technological development with minimized hazards?
6) Recommendations (guiding principles)



# ***Synthetic Biology***

# *From genetic engineering to synthetic biology*




- Genetic engineering versus synthetic biology:

*„From manipulation to creation“*

(Joachim Boldt 2009)

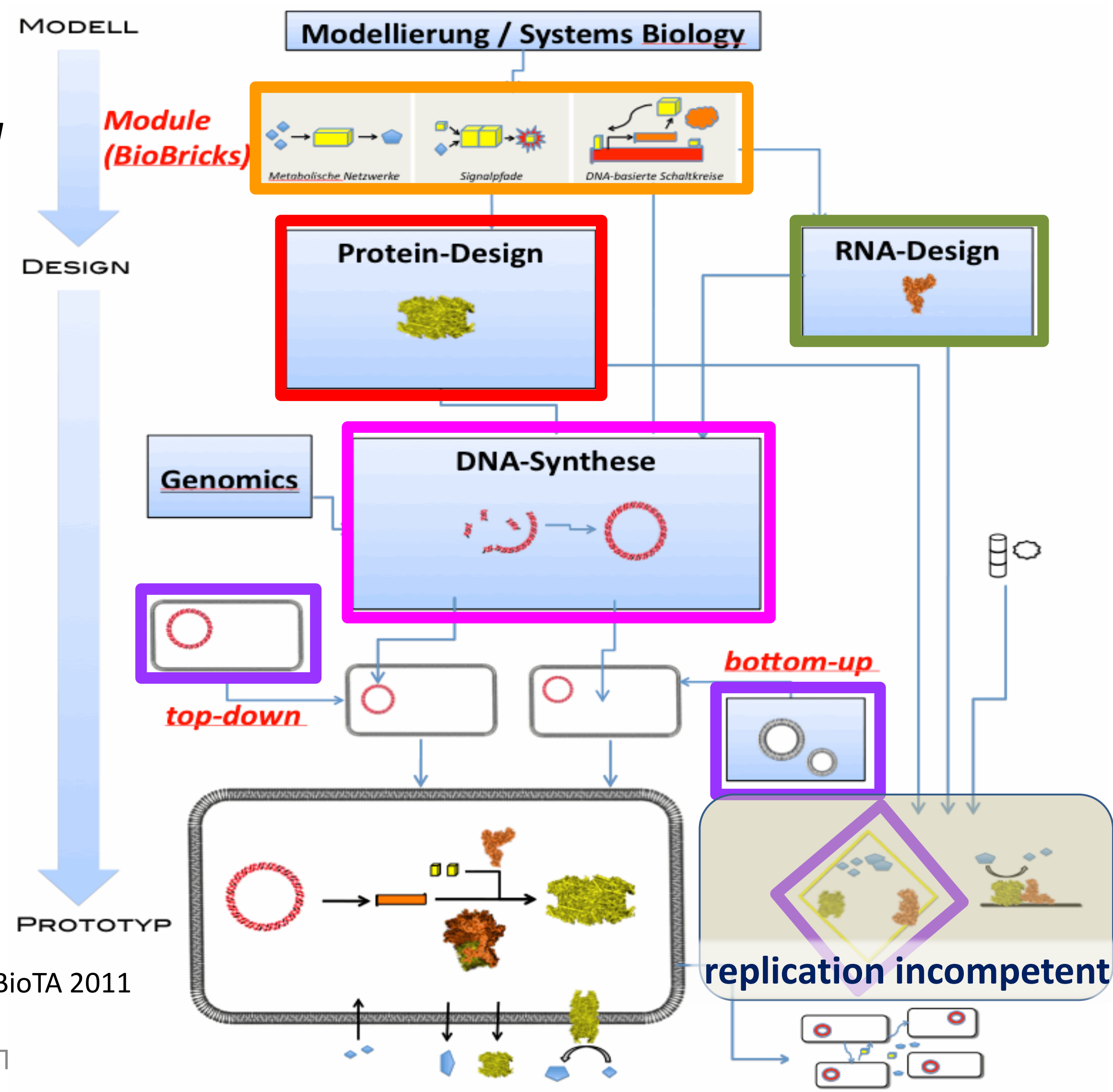
# Subfields of synthetic biology and levels of research objects

***1st level:*** *molecular tools based on proteins or nucleic acids*

***2nd level:*** *genetic modules and circuits*

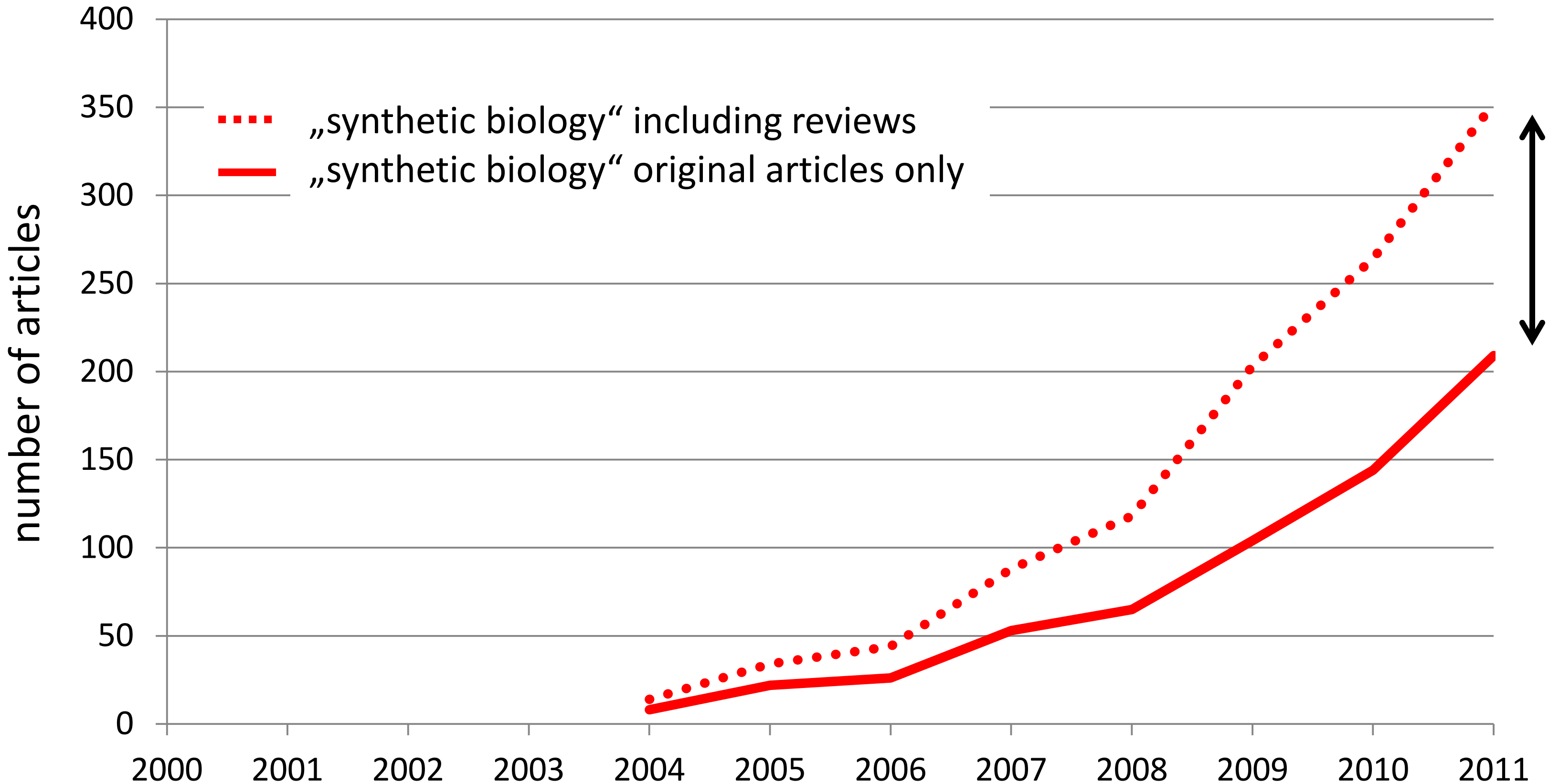
***3rd level:*** *genome*

***4th level:*** *whole cells/microreactors*




Königstein, SynBioTA 2011

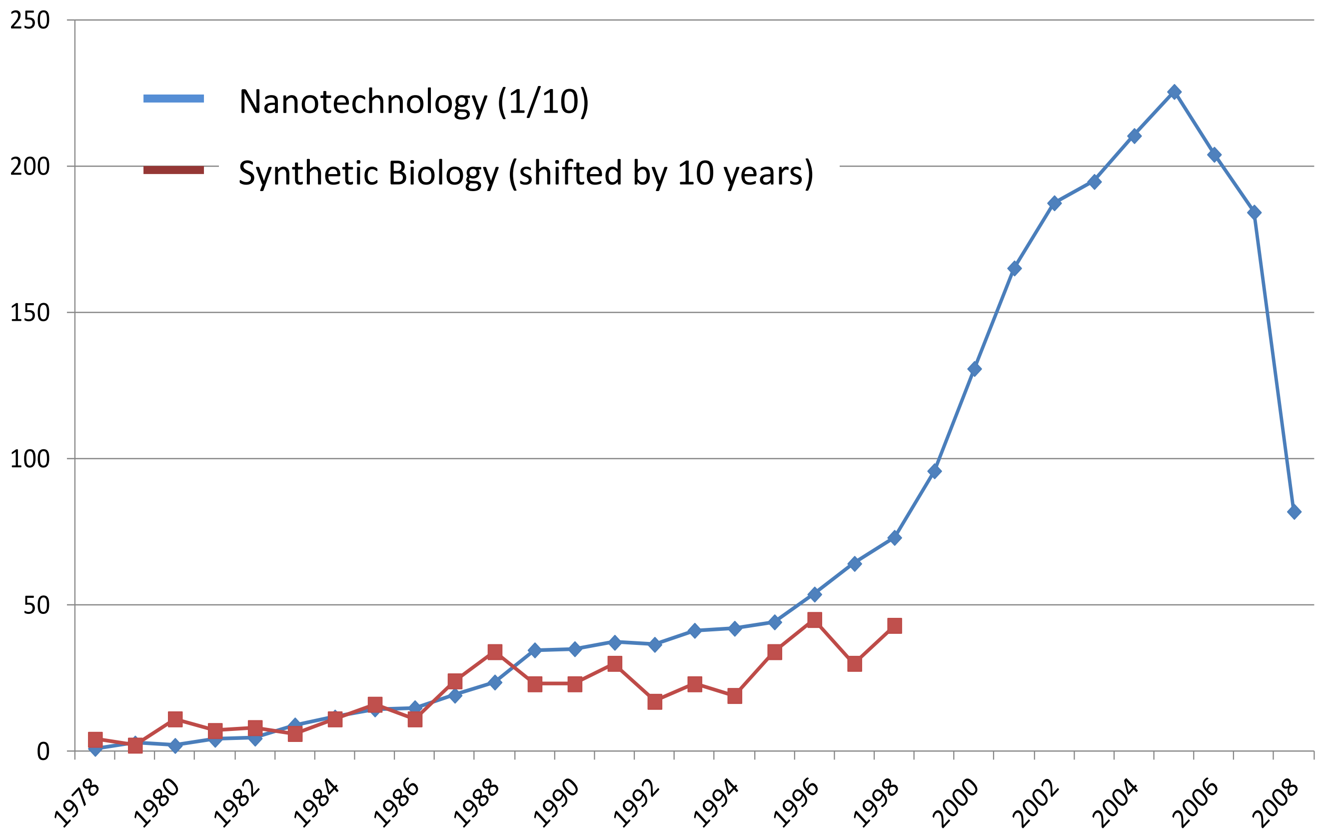
# *Synthetic Biology – in publication numbers*




Source: ISI Web of knowledge January 31, 2012 (own survey)

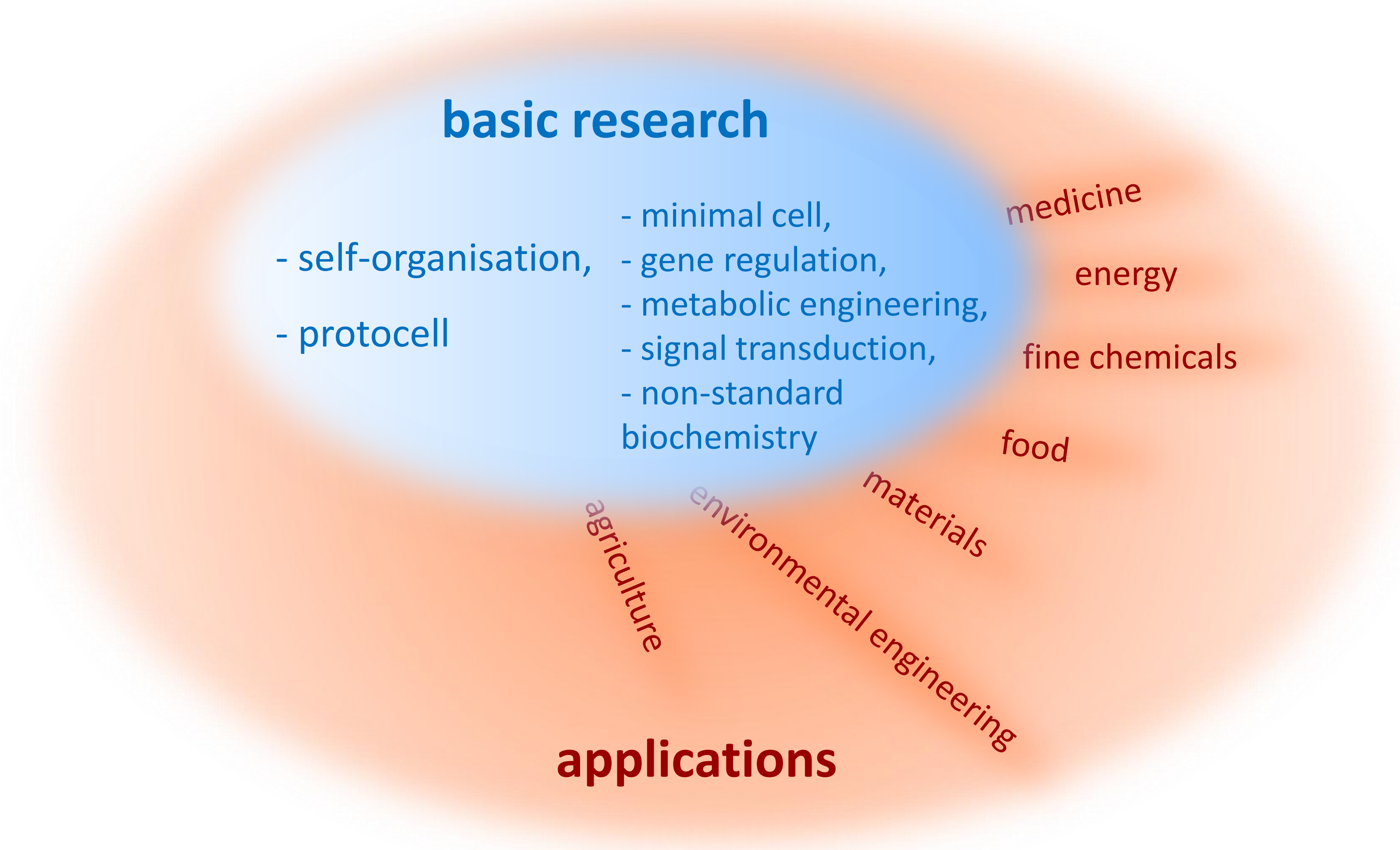
# *Patenting activity – a boom ahead?*

Patents



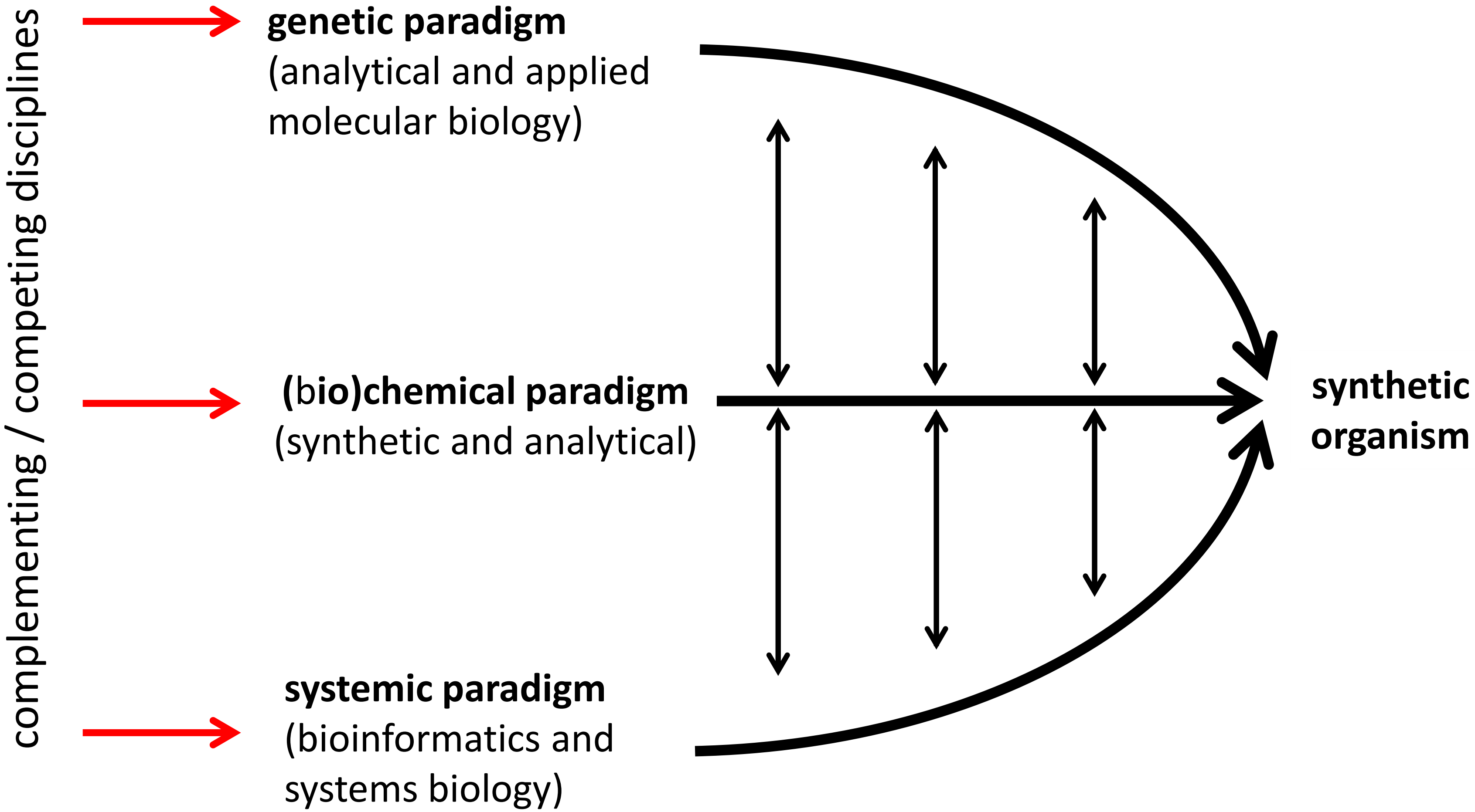

Source: Fraunhofer ISI, Reiss 2012; Reiss und Thielmann 2010

# *Research and application fields*



# *Paradigms/Contributing Disciplines*

# *The roots of synthetic biology*




Source: SynBioTA 2012, based upon the model of Westerhoff and Palsson for systems biology, 2004

# ***Methodology***

# *Common methodological elements*

genetic paradigm

(bio)chemical paradigm →

systemic paradigm

deconstruction

re-design/
re-programming

recombining

→

new objects/
organisms

and functionalities

# *Characteristic elements of abstraction & construction*

**theoretical**

*systems biology, bioinformatics, molecular modeling*

- hierarchical levels
- orthogonality
- modularity
- determinism
- programmability

**practical**

*molecular and cell biology*

- standardisation
- orthogonality
- robustness

**construction**

model → design → prototype

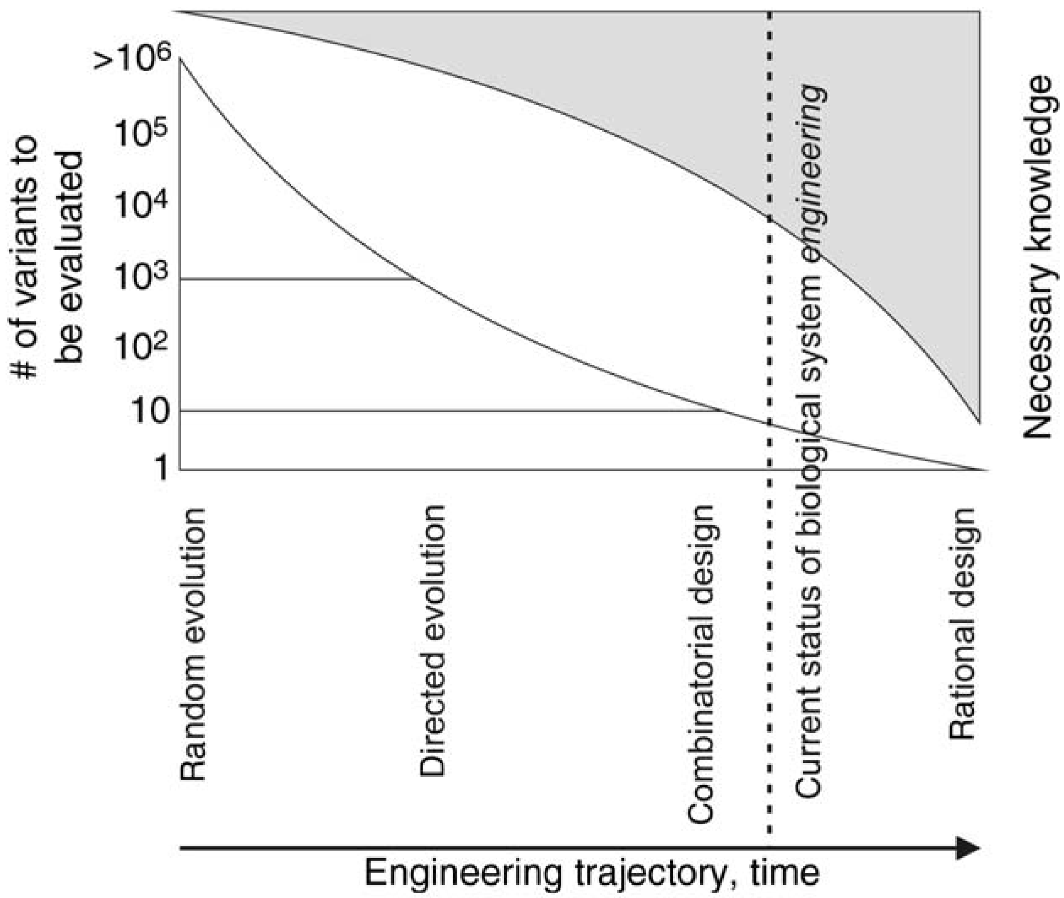
# *Major methodological principles*

a) **rational engineering**

→ predefined synthesis using completely characterized components to avoid any uncertainties

b) **‚tinkering'** (try and error), methods based on **evolutionary** principles

# *Rational design as a central claim*




Source: Bujara & Panke, Current Opinion in Biotechnology 2010, 21:586–591

# *A bibliometric strategy for the investigation of methodological characteristics:*

Level of abstraction
(Parts, Devices, Systems)

↓

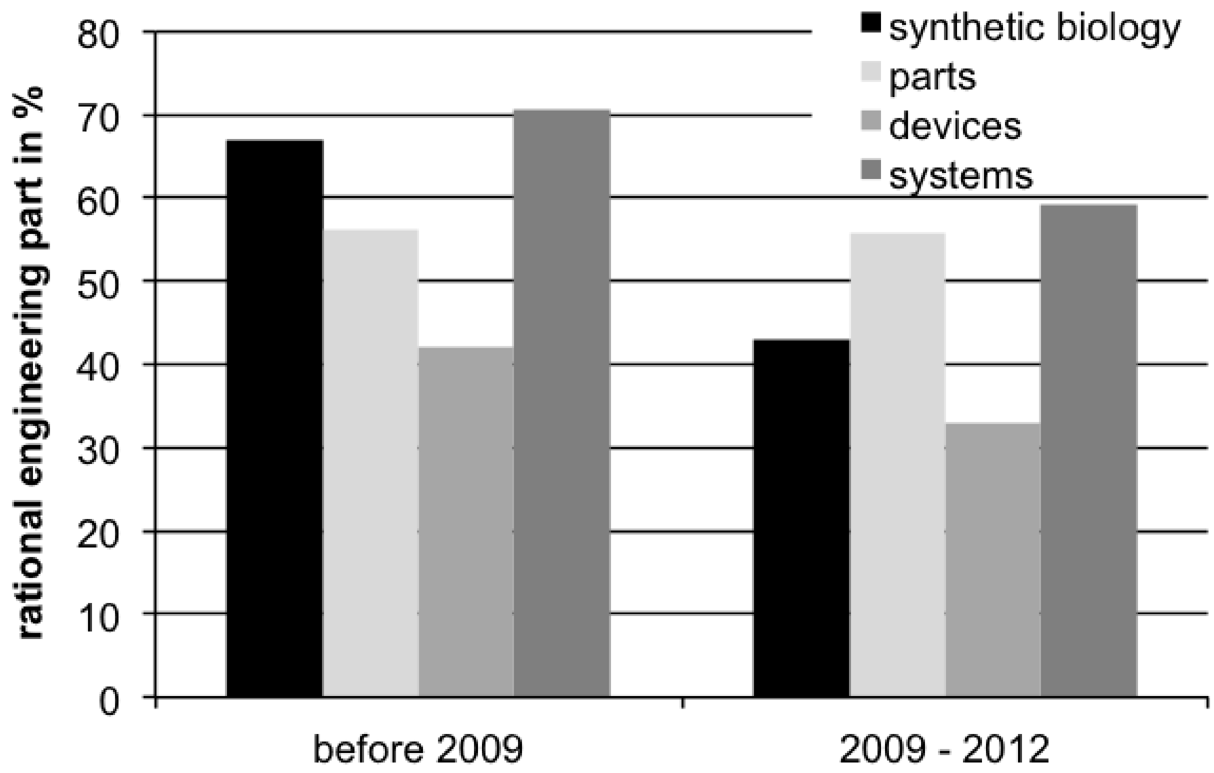
Objects
(DNA, RNA, Proteins, …)

| | | |
|---|---|---|
| search terms for rational engineering | search terms for tinkering | search terms for other methods |

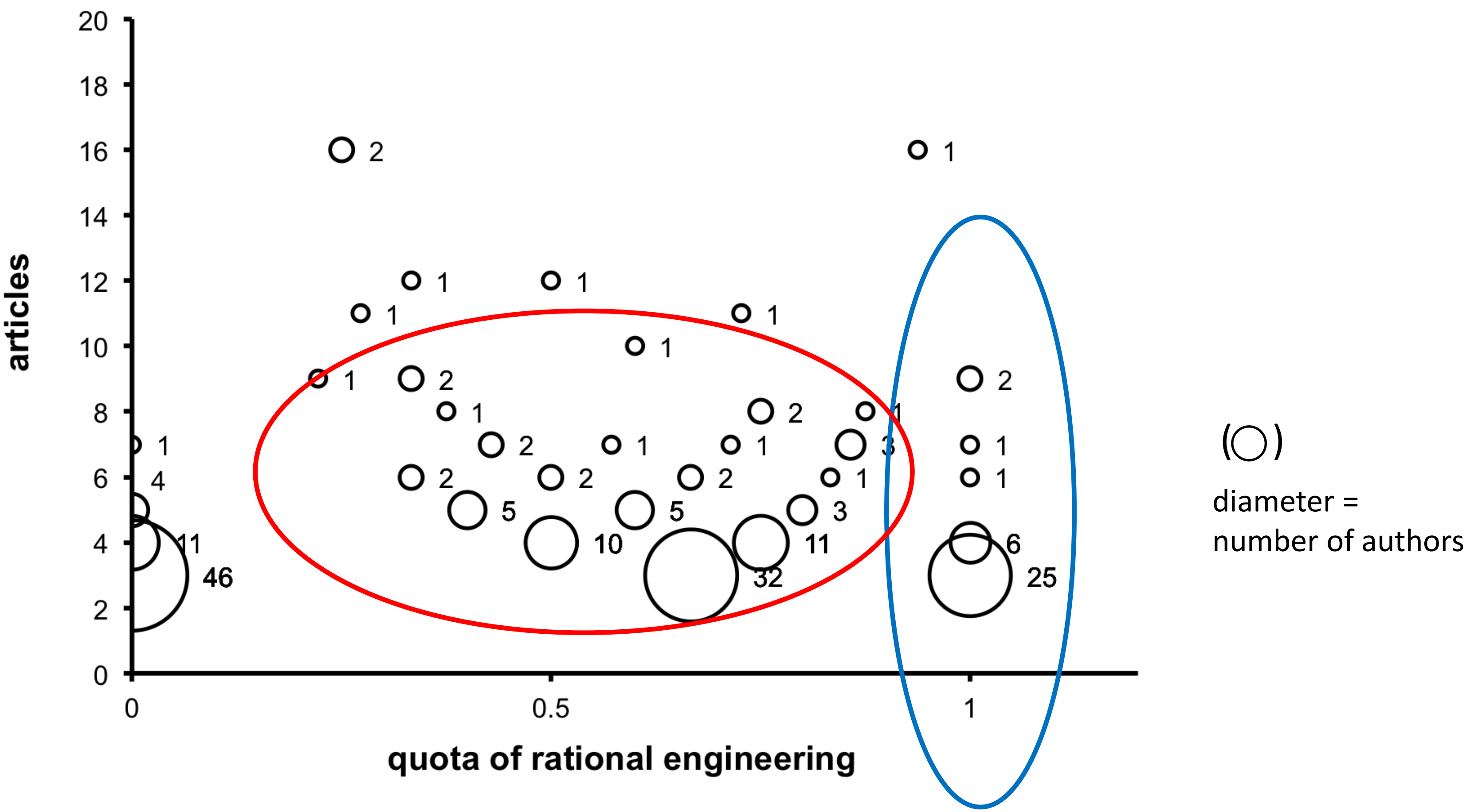
↓

Web of Science query for research articles

# *The extend of rational engineering*



# *Authors and their methodological preferences*




→ Most researchers use a mixture of rational and evolution-based methods.

# *What about pros and cons of …*

## Evolution

(holistic reduction of complexity)

Noise as productive force?

Evolution – but instability?

…

…

## Rational Design

(mechanistic reduction of complexity)

Noise as interfering force?

Directed design – but limited complexity?

…

…

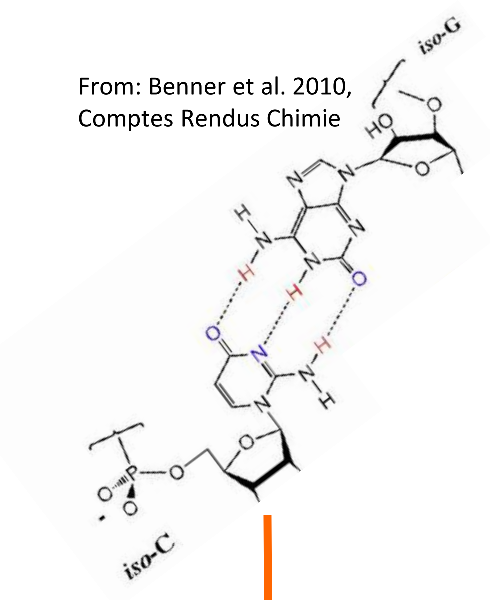
Both strategies seem to become complemented for the engineering-purposes of synthetic biology.

# ***Functionalities***

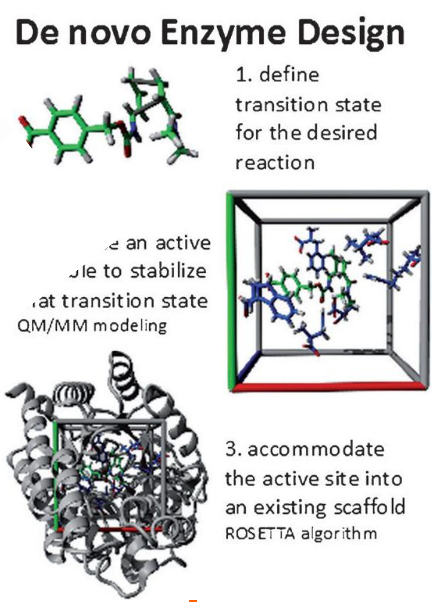
*Free recombination as a central claim*

# *Four levels of recombination*

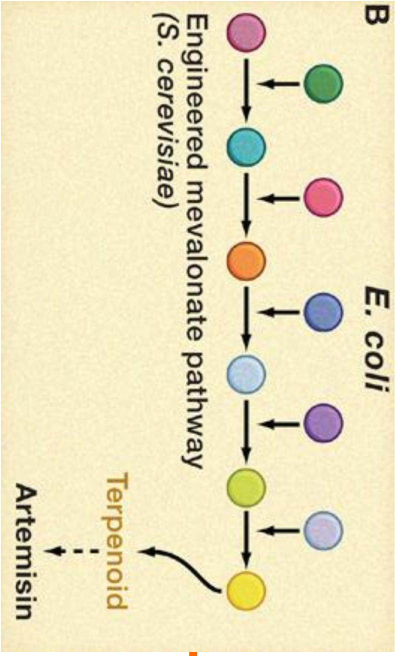
From: Benner et al. 2010, Comptes Rendus Chimie



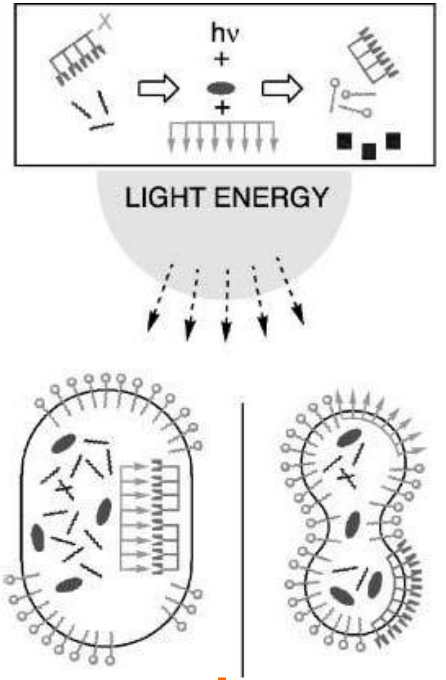

Behrens et al.
Adv. Synth. Catal. 2011, 353, 2191 – 2215




Kiel et al. Cell 140, January 8, 2010 ©2010 Elsevier Inc.




Fellermann et al. Artificial Life 2007, Volume 13, Number 4

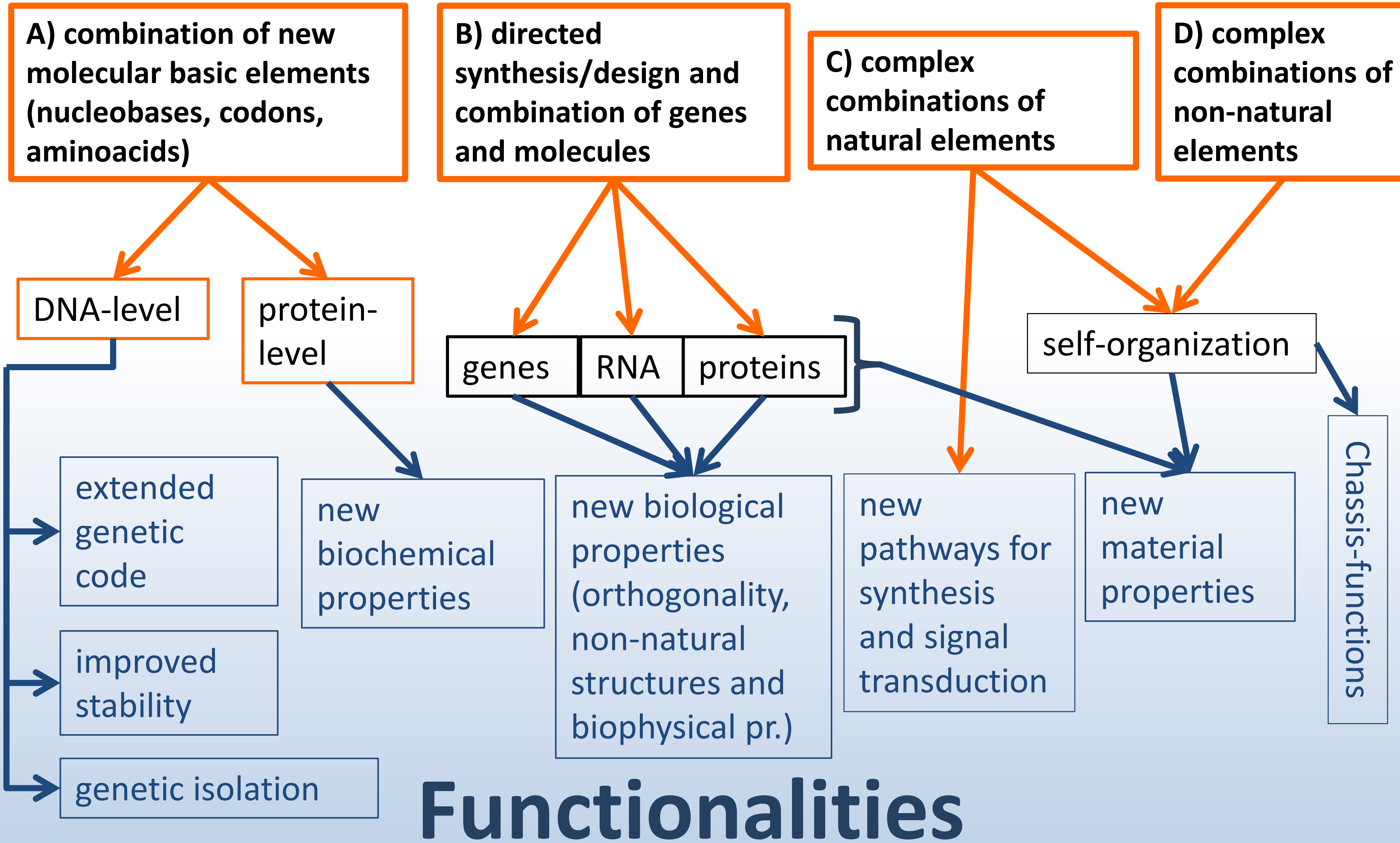



**A) combination of new molecular basic elements (nucleobases, codons, aminoacids)**

**B) directed synthesis/design and combination of genes and molecules**

**C) complex combinations of natural elements**

**D) complex combinations of non-natural elements**




Eigene Abbildung 2012

# *Sources of hazards*

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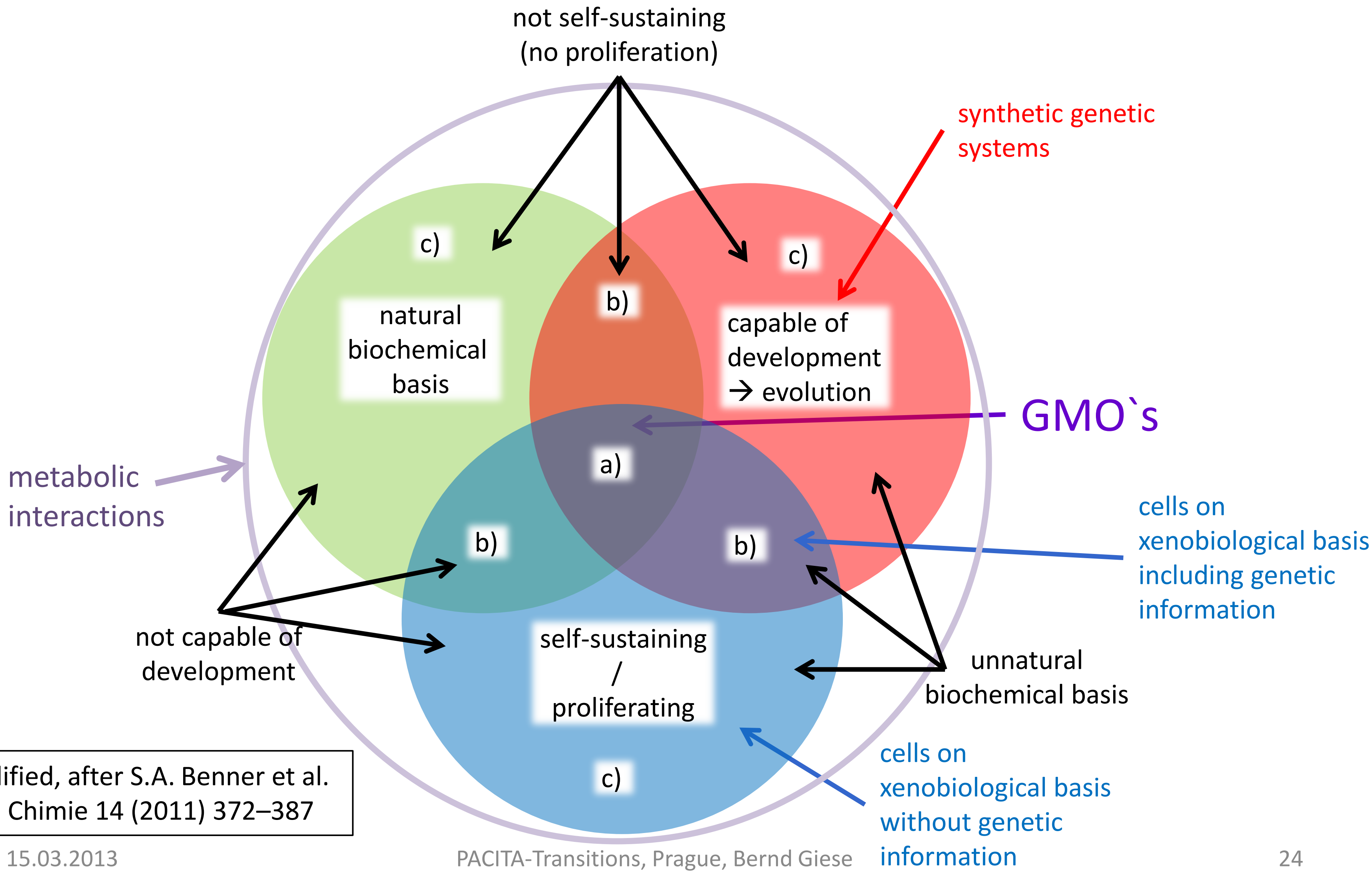
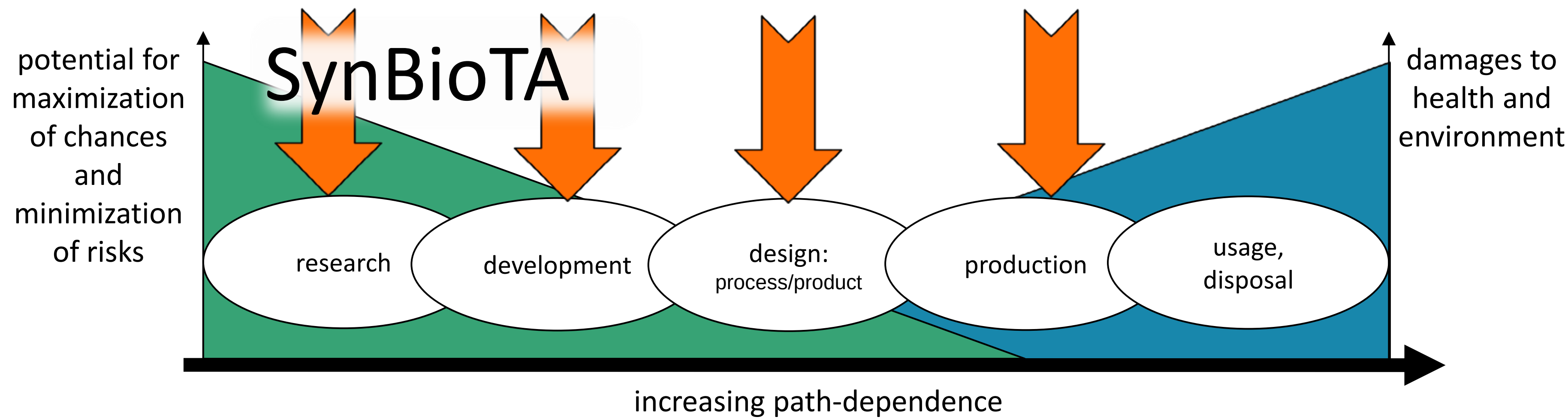



modified, after S.A. Benner et al.
C. R. Chimie 14 (2011) 372–387

# *Options for the **early** integration of hazard-reducing measures*




**Early measures during phase of development/construction:**

→ laborious late stage precautionary measures for containment or elimination would become redundant

# *Strategies for the minimization of hazards*

**trophic containment***

- artificial /modified organisms depending on a xeno-nutrient

**semantic containment***

- genetic cross-talk prevented (e.g. by xeno-nucleic acids)

**function oriented reduction**

- either the potential to evolve or to proliferate or both have to be excluded

*Philippe Marliere, Syst Synth Biol (2009) 3:77–84

**Specialization for improved function by reduction:**

- already a goal for stable expression in biotechnological applications (minimal cells)

→ still required: **reduction for improved safety**

- structurally and functionally reduced systems
  (e.g. analogous to attenuated or killed vaccines for medication)

- **consistent with the claims of synthetic biology** (enabling directed design, less interfering interactions and side effects, improved stability)

## *function-oriented reduction by cell-free systems and microreactors*

**+** improved control and regulation of environmental conditions due to the lack of a plasma-membrane

**+** no interference by evolution

**+** no interference with cellular reactions

**+** precautionary measures according to regulations for GMOs are not required for production facilities

– low yield

– protein aging

– costs for purified components

# *Concluding Recommendations*

# *Recommendations*

- long-term assessment of ecotoxicological effects
  (→ *Dana et al., Nature, March 2012, Vol. 483: long term program for the investigation of physiology, survival, evolution and adaption, gene transfer is immediately needed)*

- function-oriented reduction

- precautionary principle
  → retrievability
  → exposition, persistency and accumulation as critical qualities
  → additionally: criteria of hygiene
  → applications only in small revisable steps

# *The SynBioTA project: workgroup Bremen and partners*

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**University of Bremen**

Technological Design
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# Thank you!

# *Synthetic Biology – in publication numbers*

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