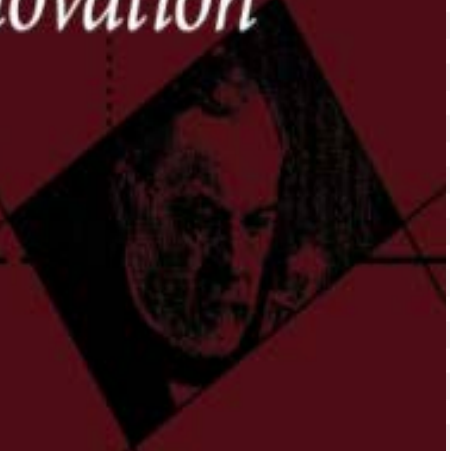
Bioteknologisk FoU – store muligheter for både børs og katedral

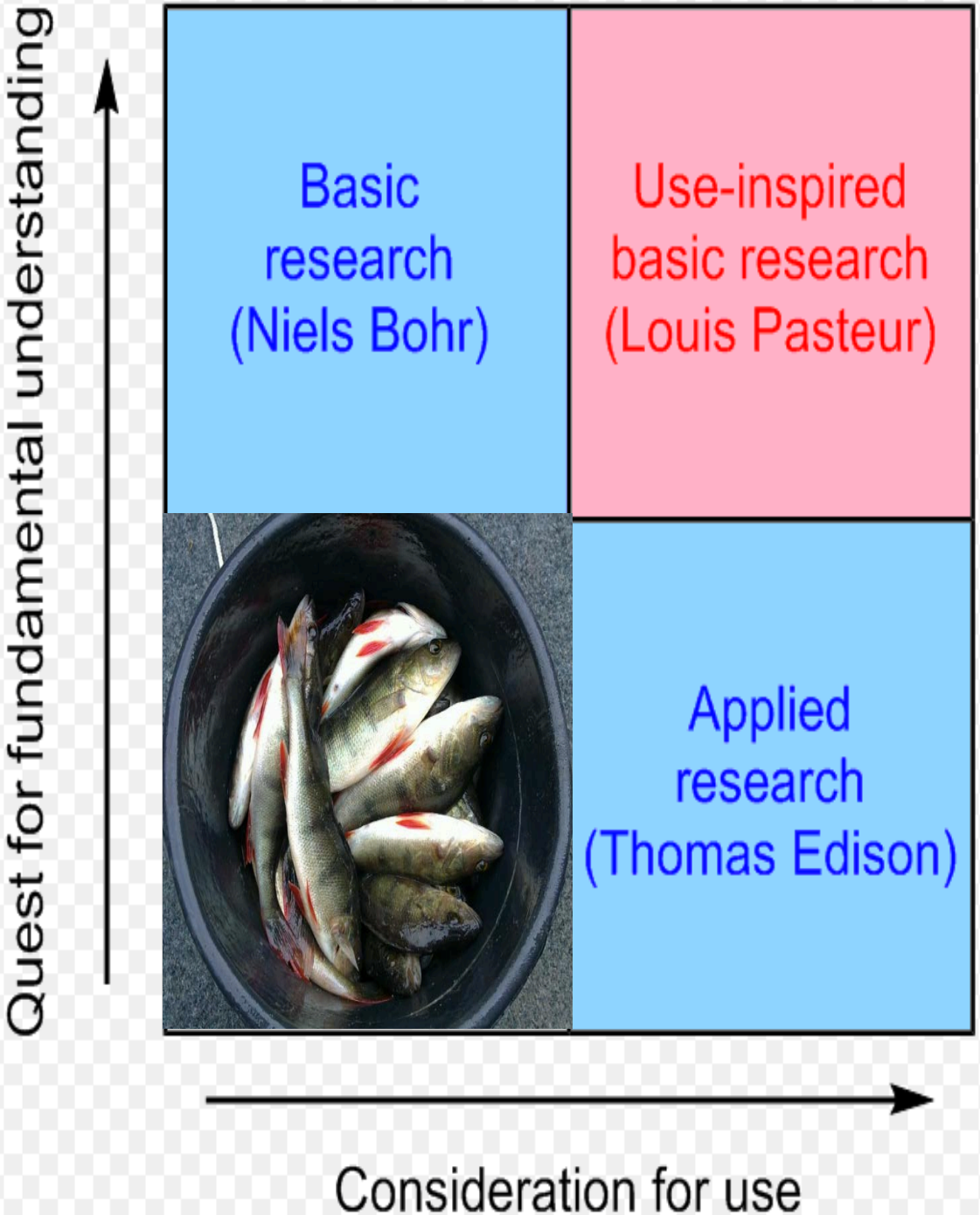
Stig W. Omholt
NTNU Biotechnology: the Confluence of Life Sciences, Mathematical Sciences and Engineering

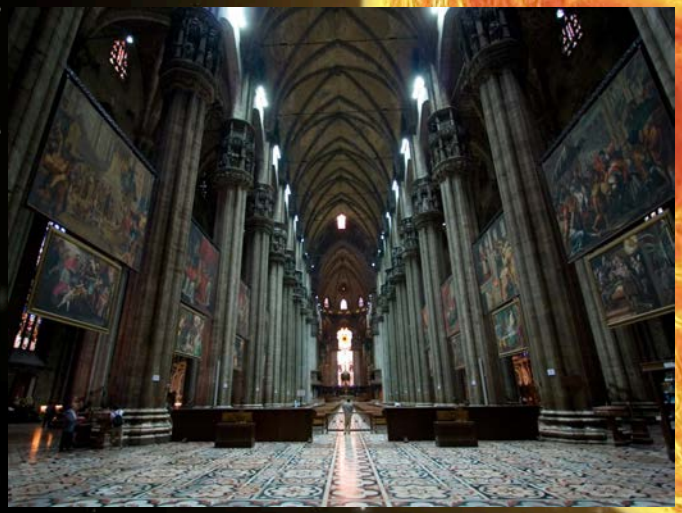
PASTEUR'S QUADRANT

Basic Science and Technological Innovation



Donald E. Stokes

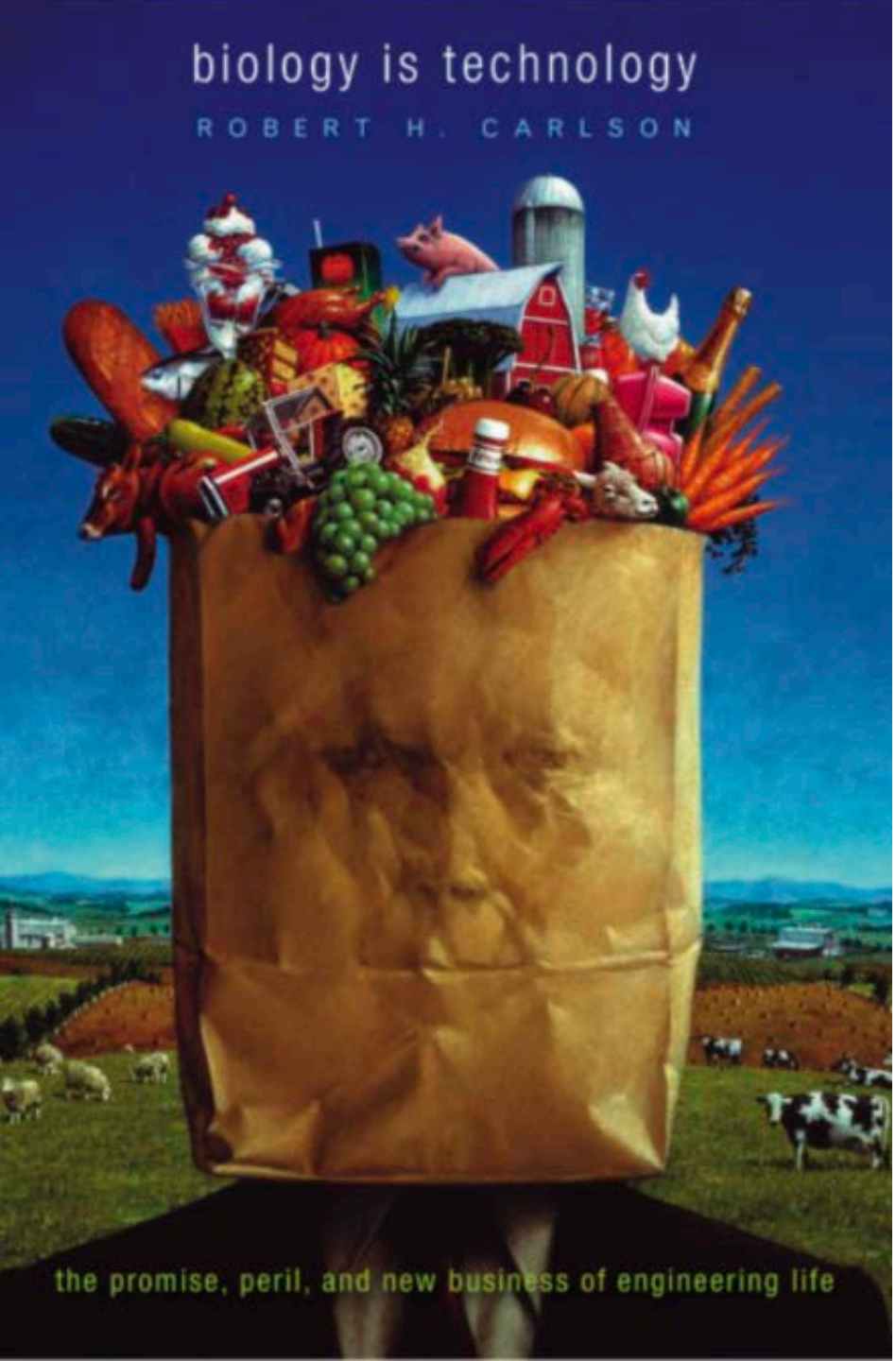




“store muligheter for børs og katedral”

Bioteknologi - definisjon

Anvendelse av naturvitenskap og teknologi
på levende organismer og på deler,
produkter og modeller av disse,
slik at levende eller ikke-levende materialer
endres for å frembringe kunnskap, varer
og tjenester.



“Biology is the oldest technology.”

NTNU Biotechnology
Research & Development
Core facilities
Studies
Sabbatical at NTNU?
Job openings

Research and Development

All R&D activities sorting under the NTNU Biotechnology umbrella stay firmly within the confines of the OECD definition of biotechnology:

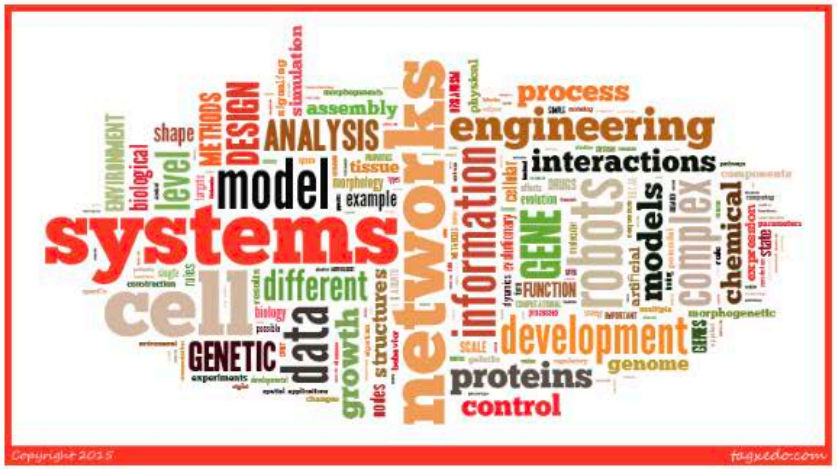
"the application of science and technology to living organisms as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services"

Our R&D streams - emerging from the confluence of life sciences, mathematical sciences and engineering - define the core of the NTNU Biotechnology Programme. Check them out...

ENABLING TECHNOLOGY PROGRAMME 2013-2020

NTNU Biotechnology - the Confluence of Life Sciences, Mathematical Sciences and Engineering

This is the main portal keeping you informed about biotechnology R&D at NTNU, the people involved, and available opportunities to contribute to this vibrant field as a student, PhD, postdoctoral, sabbatical or tenured fellow.



NTNU Biotechnology is one of the three enabling technology programmes at the Norwegian University of Science and Technology. Together they define the strategic core of NTNU's long-term R&D commitment within natural science and technology. The design of NTNU Biotechnology programme reflects the conviction that extensive transdisciplinary interaction between the life sciences, mathematical sciences and engineering is the key to transformative 21st century biotechnology. It is developed in close conjunction with SINTEF, the largest independent research organisation in Scandinavia, and St. Olavs hospital (Trondheim University Hospital), which is tightly integrated with our Faculty of Medicine and Health Sciences .

NTNU is the leading institution of the Norwegian Centre for Digital Life funded by the Research Council of Norway under its BIOTEK2021 programme. The centre's main mission is to become the major vehicle for reorienting and concerting Norwegian R&D on biotechnology in the years to come.

Contact

Stig W. Omholt
Director/Research professor
Phone: +47 90 94 09 85
Email: stig.omholt@ntnu.no

Laila Berg
Coordinator, PhD
Phone: +47 73 41 21 09
Email: laila.berg@ntnu.no

NTNU Biotechnology

The Confluence of Life Sciences, Mathematical Sciences and Engineering

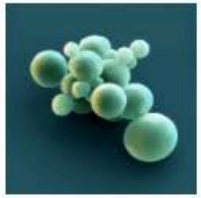
NTNU Human Physiome
The concerted global efforts towards making integrated mathematical descriptions of human physiology. Read more.

NTNU Phenomics Technology
We have a long and successful tradition for blending engineering and biology for developing new measurement technology. Read more.

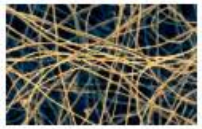
NTNU Tissue Engineering
By merging advanced engineering with molecular and cellular biology we aim to make significant contributions to this technology. Read more.

NTNU Genome Editing
We are in the process of taking advantage of the current revolution in making targeted genome sequence changes. Read more.

NTNU Therapeutic Targeting
In most fields of medicine where therapeutic interventions involve application of drugs there is still tremendous potential for improvement. Read more.



NTNU Analysis, Design and Control of Microbial Systems
Improved methodology for engineering microbes to perform specific tasks is key to industrial biotechnology. Read more.



NTNU Biopolymer Engineering
We have a proven track record in tailoring biopolymers into new biomaterials for numerous application areas within medicine and industry. Read more.

NTNU Aquaculture Biotechnology
Maintaining a profitable and expansive aquaculture industry leaving minimal human footprints is a pressing issue. Read more.

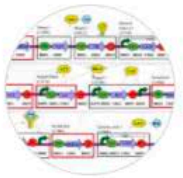
NTNU Synthetic Biology Engineering
Methodology for engineering new complex function in cells is a prerequisite for novel industrial biotechnology. Read more.

NTNU Bioreactor Design and Operation
We aim to contribute to more efficient engineering of devices that support biologically active environments. Read more.

NTNU Morphogenetic Engineering
Novel engineering concepts exploiting nature's capacity for self-organization has numerous applications. Read more.

NTNU Responsible Research and Innovation
Developing methodology and mechanisms for anticipating and assessing the societal implications of our R&D activities. Read more.

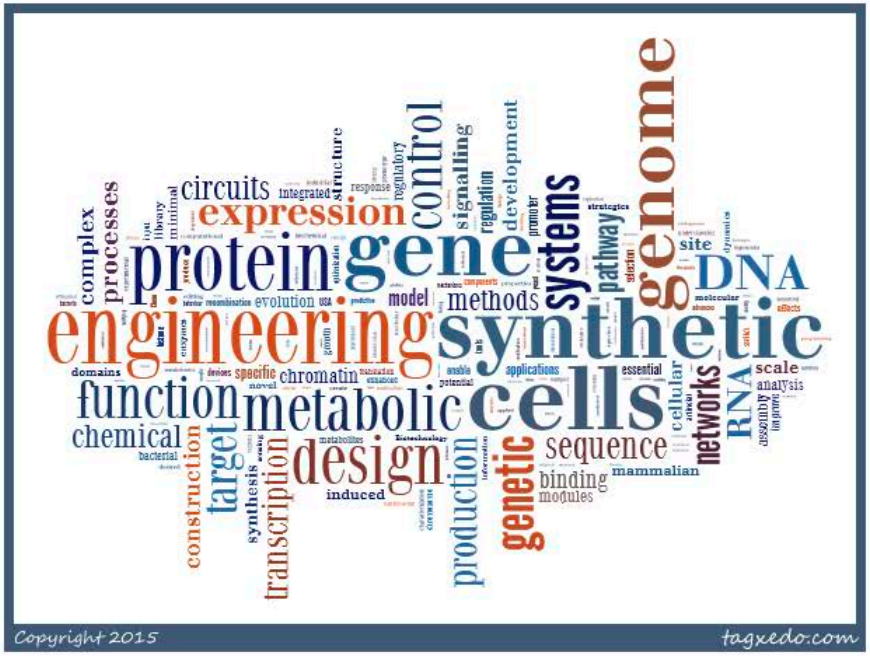
NTNU Synthetic Biology Engineering



Engineering new complex functions in cells is a prerequisite for novel industrial biotechnology.

About | Governance | Publications | Tag cloud | Network | People | Projects

Synthetic biology encompasses the design and construction of new biological parts, devices and systems, as well as the re-design and fabrication of existing biological systems. This involves massive transdisciplinary activity, but in contrast to systems biology, synthetic biology is fundamentally an engineering application of biological science. At NTNU we are actively engaged in a broad range of synthetic biology research. Our main areas of research interest focus on the engineering of energy solutions based on biological systems, the production of medicines and pharmaceuticals using engineered organisms, the engineering of biological systems for the production of high-value chemicals, as well as genetic engineering and computational analyses to understand fundamental design principles in biology. This research stream is tightly linked to NTNU Bioreactor Design and Operation and NTNU Analysis, Design and Control of Microbial Systems.



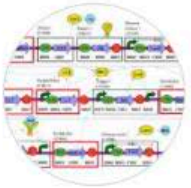
NTNU Synthetic Biology Engineering serves as a nexus for R&D opportunities. For instance, the NTNU iGEM teams have been actively participating in iGEM – the premiere international competition in Synthetic Biology for university students – each year since 2011, receiving many gold medals. Read more about previous NTNU iGEM teams, and about the work of the current team.

NTNU Biotechnology
Research & Development
- NTNU Analysis, Design and Control of Microbial Systems
- NTNU Aquaculture Biotechnology
- NTNU Bioreactor Design and Operation
- NTNU Biopolymer Engineering
- NTNU Genome Editing
- NTNU Human Physiome
- NTNU Morphogenetic Engineering
- NTNU Phenomics Technology
- NTNU Tissue Engineering
- **NTNU Synthetic Biology Engineering**
- NTNU Therapeutic Targeting
- NTNU Responsible Research and Innovation

Core facilities
Studies
Sabbatical at NTNU?
Job openings

NTNU Synthetic Biology Engineering

Engineering new complex functions in cells is a prerequisite for novel industrial biotechnology.



About | Governance | Publications | Tag cloud | Network | People | Projects

NTNU SYNTHETIC BIOLOGY ENGINEERING

Synthetic Biology Engineering Steering Group


Eivind Almaas


Trygve Brautaset


Martin H-Marriot


Rahmi Lale


Håvard Sletta

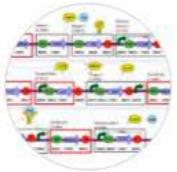

Finn Drabløs

NTNU Biotechnology
Research & Development
- NTNU Analysis, Design and Control of Microbial Systems
- NTNU Aquaculture Biotechnology
- NTNU Bioreactor Design and Operation
- NTNU Biopolymer Engineering
- NTNU Genome Editing
- NTNU Human Physiome
- NTNU Morphogenetic Engineering
- NTNU Phenomics Technology
- NTNU Tissue Engineering
- **NTNU Synthetic Biology Engineering**
- NTNU Therapeutic Targeting
- NTNU Responsible Research and Innovation

Core facilities
Studies
Sabbatical at NTNU?
Job openings

NTNU Synthetic Biology Engineering

Engineering new complex functions in cells is a prerequisite for novel industrial biotechnology.



About Governance Publications Tag cloud Network People Projects

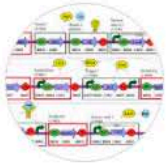
Filter publications

Result 10 of 668

Publications	Authors	Journal	Year
No cancer predisposition or increased spontaneous mutation frequencies in NEIL DNA glycosylases-deficient mice	Veslemøy Rolseth , Luisa Luna , Ann Karin Olsen , Rajikala Suganthan , Katja Scheffler , Christine G. Neurauter , Ying Esbensen , Anna Kuśnierczyk , Gunn A. Hildrestrand , Anne Graupner ...more authors	Scientific Reports	2017
Human chitotriosidase: Catalytic domain or carbohydrate binding module, who's leading HCHT's biological function	Oscar Crasson , Gaston Courtade , Raphaël R. Léonard , Finn Lillelund Aachmann , François Legrand , Raffaella Parente , Denis Baurain , Moreno Galleni , Morten Sørlie , Marylène Vandevenne	Scientific Reports	2017
Dynamic responses to silicon in Thalasiossira pseudonana - Identification, characterisation and classification of signature genes and their corresponding protein motifs	Tore Brembu , Matilde Skogen Chauton , Per Winge , Atle M. Bones , Olav Vadstein	Scientific Reports	2017
The effects of phosphorus limitation on carbon metabolism in diatoms	Tore Brembu , Alice Mühlroth , Leila Alipanah , Atle M. Bones	Philosophical Transactions of the Royal Society B: Biological Sciences	2017

NTNU Synthetic Biology Engineering

Engineering new complex functions in cells is a prerequisite for novel industrial biotechnology.



About Governance Publications Tag cloud Network People Projects

Network

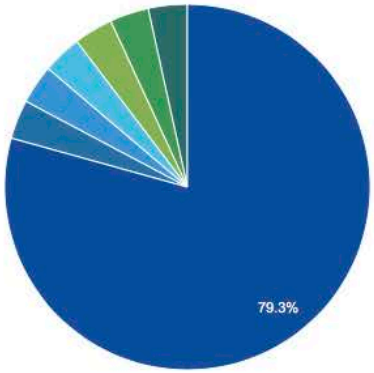
Key metrics

668
Publications

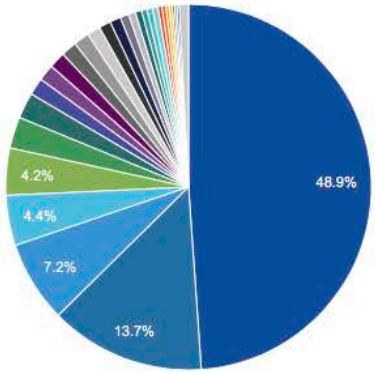
357
Institutions

1360
Persons

Publications for 2017



Co-authors grouped by country



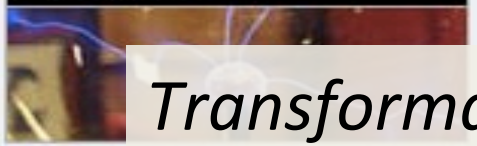
National Science Foundation
WHERE DISCOVERIES BEGIN

QUICK LINKS

SEARCH

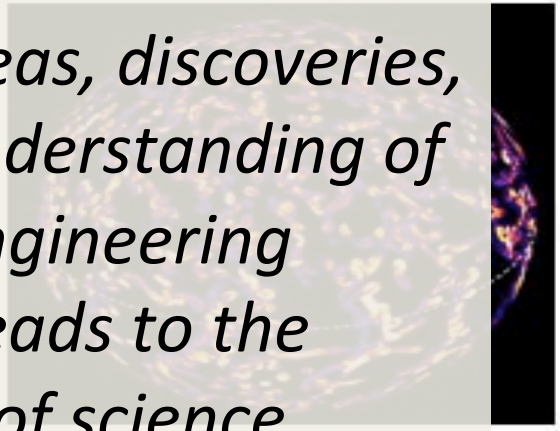
HOME | FUNDING | AWARDS | DISCOVERIES | NEWS | PUBLICATIONS | STATISTICS | ABOUT NSF | FASTLANE

Transformative Research



Introduction
Definitio
Characte
Challeng
Merit Re
Where t
FAQ

Introduction to Transformative Research



Transformative research involves ideas, discoveries, or tools that radically change our understanding of an important existing scientific or engineering concept or educational practice or leads to the creation of a new paradigm or field of science, engineering, or education. Such research challenges current understanding or provides pathways to new frontiers.

and its support at NSF.

Email Print Share

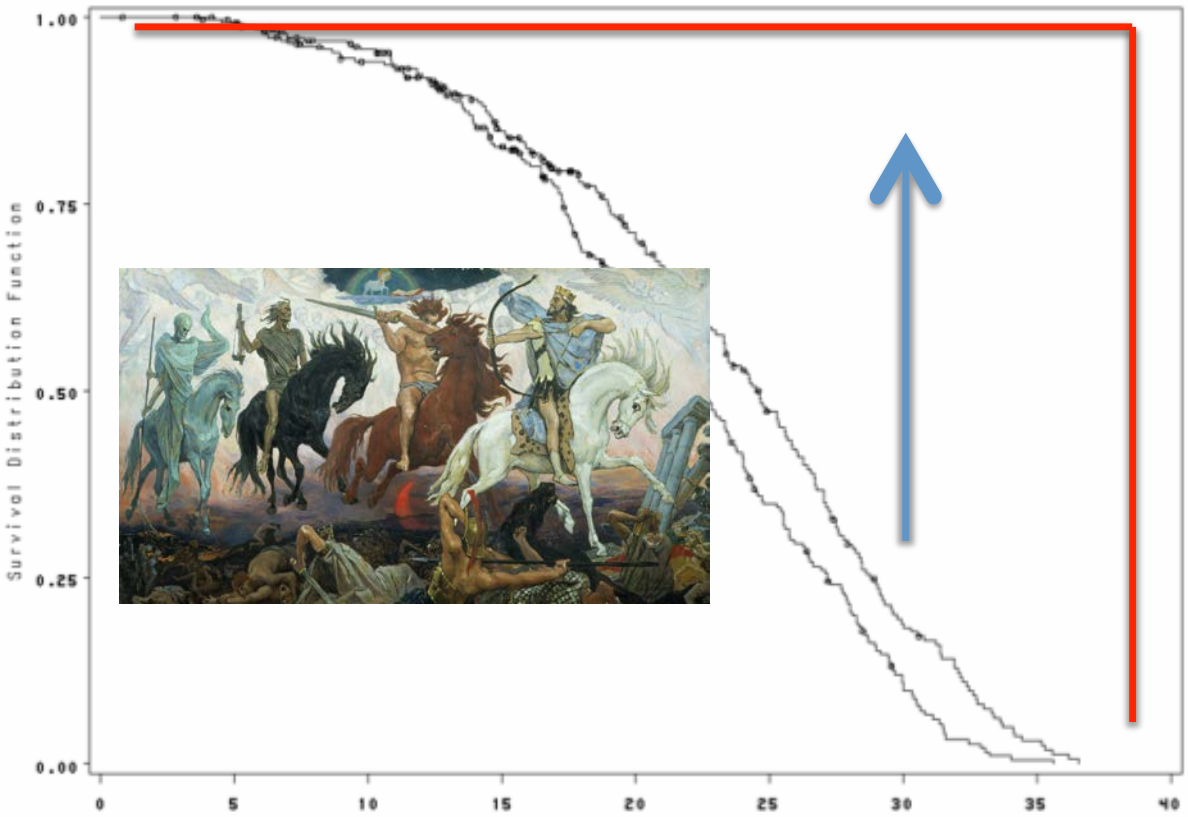
Top

FUNDING | AWARDS | DISCOVERIES | NEWS | PUBLICATIONS | STATISTICS | ABOUT NSF | FASTLANE

Facts do not cease to exist because they are ignored.

Aldous Huxley

Er den rektangulære livskurven oppnåelig?



What is frailty?

Definition: a biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes.

Fysiologi

Studiet av funksjoner og aktviteter til levende materiale (slik som organer, vev og celler) og tilhørende fysiske og kjemiske fenomener

Webster's Third New International Dictionary

IUPS Physiome: Molecular pathways to organ systems

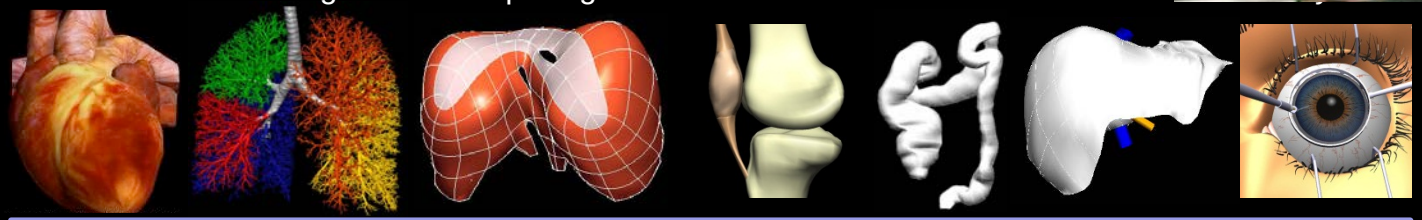
Environment

Organism

Organ system

Organ

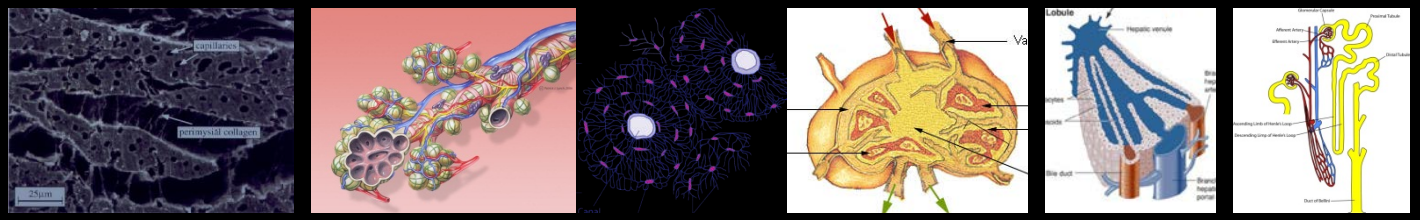
Heart Lungs Diaphragm Knee Colon Liver



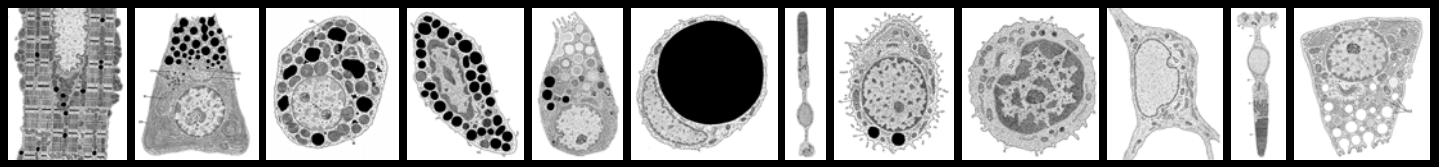
↑ x 1million ↓ 20 generations

Tissue

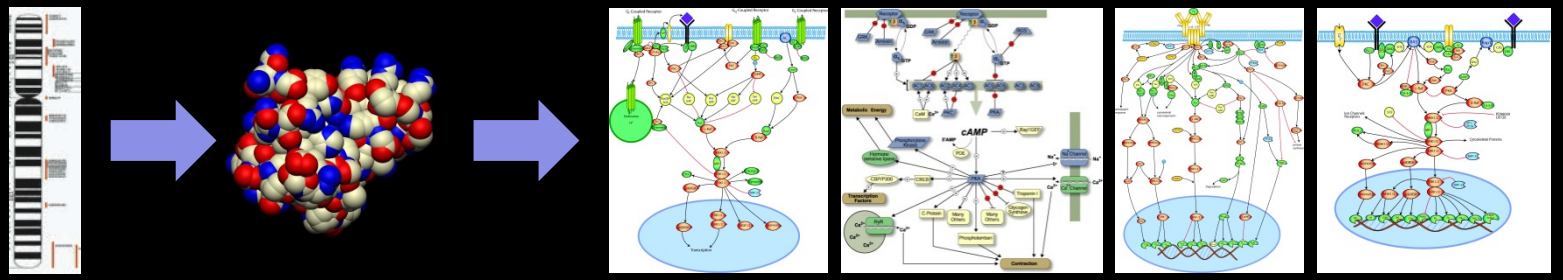
Cardiac sheets Acinus Osteon Lymph node Liver lobule Nephron



Cell



Network
Protein
Gene
Atom

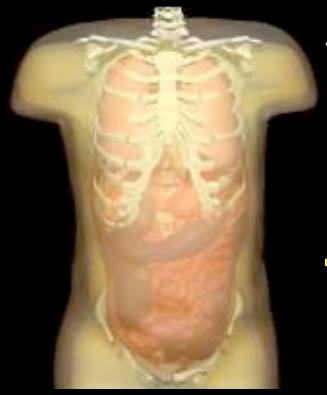


The heart physiome

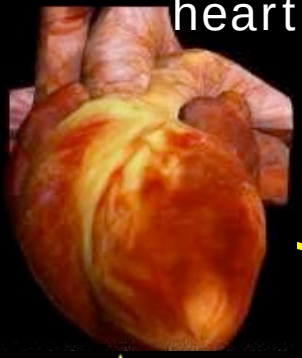
m
$=10^9$nm

nm

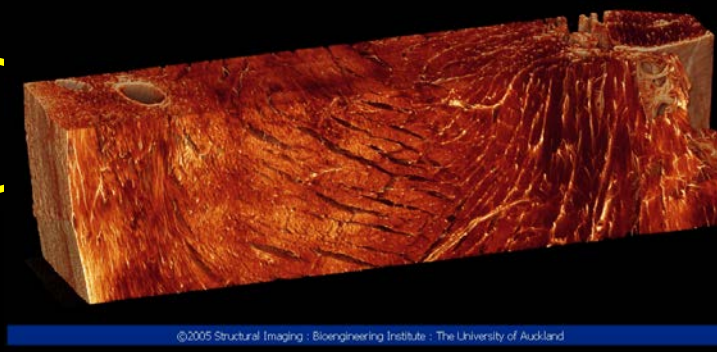
torso



heart

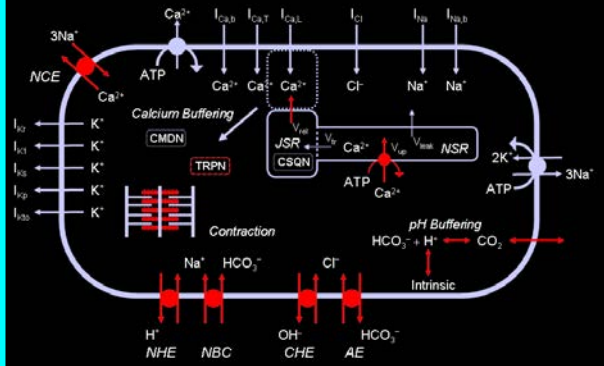


tissue

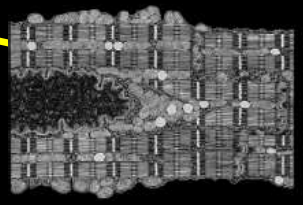


cell-cell
connections

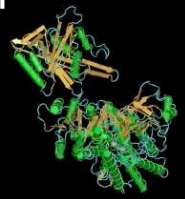
cellular processes



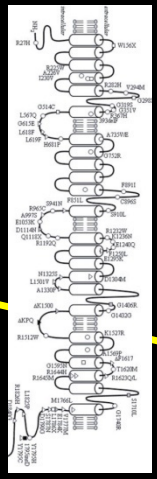
3D cell



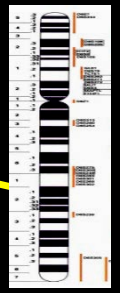
proteins



amino acid
sequence

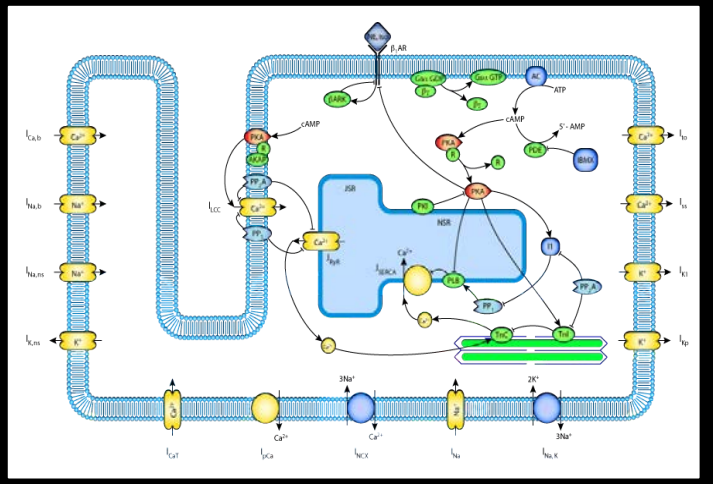


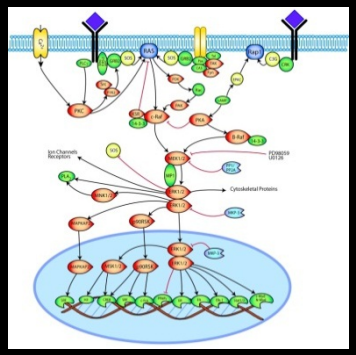
genomic
sequence

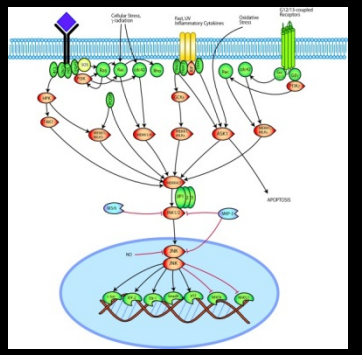


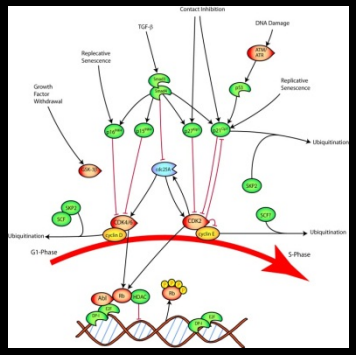
Signaling

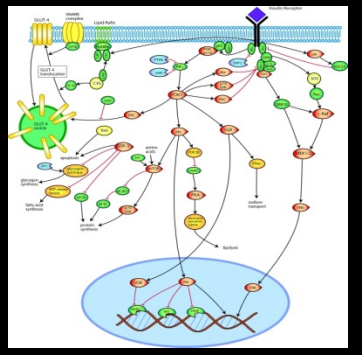
1. cAMP signalling
2. Calcium signalling - via
   - cADP-ribose signalling
   - NAADP signalling
   - Voltage operated channels (VOCs)
   - Receptor operated channels (ROCs)
   - IP_3-Ca^{2+} signalling (via PLC-PIP_2)
   - DAG-PKC signalling (via PLC-PIP_2)
   - PI4-5P_2 signalling
   - Inositol polyphosphate signalling
   - PI3-Kinase signalling
3. NO-cGMP signalling
4. Redox signalling
5. MAP-Kinase signalling
6. NF-kB signalling
7. Phospholipase D (PLD) signalling
8. Sphingomyelin signalling
9. JAK-STAT signalling
10. Smad signalling
11. Wnt signalling
12. Hedgehog signalling
13. Notch signalling
14. ER stress signalling
15. AMP signalling







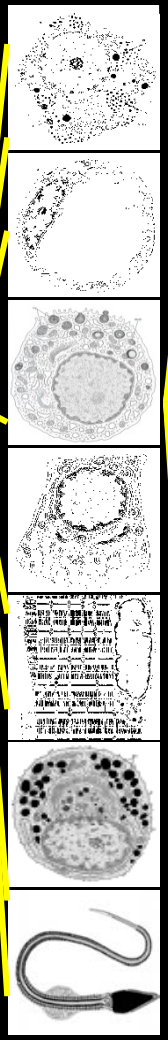




Infrastructure for linking Molecular Biology to Physiome

Physiome FieldML library

Cell type



Cell function

- Meiosis
- Sensing
- Mitosis
- Apoptosis
- Growth
- Motility
- Contraction
- Signalling
- Transport
- Adhesion
- ECM protein synthesis

Cell process

- Cell cycle
- Intracell. signalling
- Calcium transport
- Protein trafficking
- Protein degradation
- Electro-physiology
- Cellular metabolism
- Protein synthesis
- Protein regulation
- Gene regulation
- Gene transcription

CellML & SBML libraries

Model components annotated with ontologies

- Cell receptors
- Signalling modules
- Ion channels
- Metabolic modules
- Gene networks
- ...

Molecular Biology

- Genes
- miRNA
- mRNA
- ...
- Proteins
- Sequence
- Structure
- PTMs
- Binding motifs
- ...
- Lipids
- ...
- Carbo-hydrates
- ...

Scale Imaging Multi-scale Modelling

Organism

Organ system

Organ

Tissue

Cell

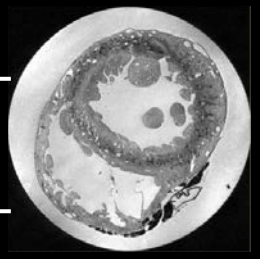
Network
Protein
Gene
Atom

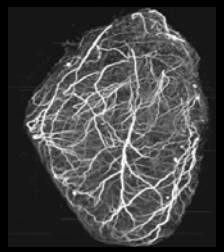
1m

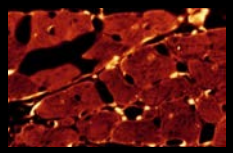
10^{-3}

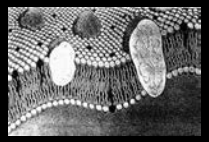
10^{-6}

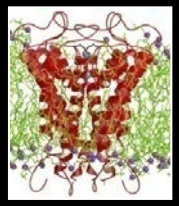
10^{-9}











Partial differential equations (PDEs)

Reaction-diffusion $\frac{\partial C}{\partial t} + \boldsymbol{u}.\nabla C = -\nabla.(-k\nabla C) + f_s$

Fluid flow $\frac{\partial \boldsymbol{u}}{\partial t} + \boldsymbol{u}.\nabla \boldsymbol{u} = -\frac{1}{\rho}\nabla p + \upsilon\nabla^2\boldsymbol{u}$

Finite elasticity $\tau^{ij}\big|_i = f^j \qquad \tau^{ij} = f(e_{ij})$

$e_{ij} = \frac{1}{2}\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} + \frac{\partial u_k}{\partial x_i}\cdot\frac{\partial u_k}{\partial x_j}\right)$

Electro-magnetic $\nabla.\boldsymbol{E} = \frac{\rho}{\epsilon} \qquad \nabla x\boldsymbol{E} = -\frac{\partial \boldsymbol{B}}{\partial t}$

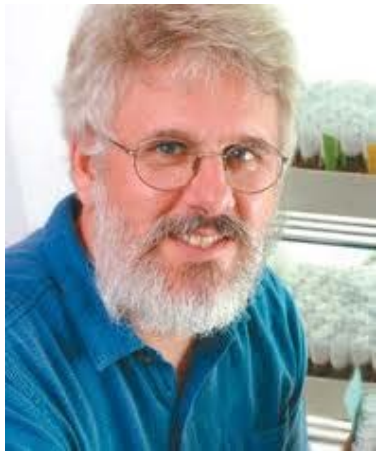
$\nabla.\boldsymbol{B} = 0 \qquad \nabla x\boldsymbol{B} = \mu\left(\boldsymbol{J} + \epsilon\frac{\partial \boldsymbol{E}}{\partial t}\right)$

Differential algebraic equations

Bayesian network description

Molecular dynamics/coarse graining

Poisson-Boltzmann ...



Phenomics: the next challenge

David Houle, Diddahally R. Govindaraju‡ and Stig Omholt§||*

Abstract | A key goal of biology is to understand phenotypic characteristics, such as health, disease and evolutionary fitness. Phenotypic variation is produced through a complex web of interactions between genotype and environment, and such a 'genotype–phenotype' map is inaccessible without the detailed phenotypic data that allow these interactions to be studied. Despite this need, our ability to characterize phenomes — the full set of phenotypes of an individual — lags behind our ability to characterize genomes. Phenomics should be recognized and pursued as an independent discipline to enable the development and adoption of high-throughput and high-dimensional phenotyping.

Pleiotropy
The ability of a single genetic change to affect more than one phenotype.

**Department of Biological Science, Florida State University, Tallahassee, Florida 32306-4295, USA.*
‡Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, 221 Longwood Avenue, Boston, Massachusetts 02115, USA.
§Centre for Integrative Genetics (CIGENE), Department of Animal and Aquacultural Sciences, Norwegian University of Life Sciences, N-1432 Ås, Norway.
||Centre for Ecological and Evolutionary Synthesis, University of Oslo, NO-0316 Oslo, Norway.
e-mails: dhoule@bio.fsu.edu; dgovindaraju@partners.org; stig.omholt@umb.no
doi:10.1038/nrg2897

When the debate over whether to fund a human genome project flowered in the late 1980s, one of the scientific arguments offered in opposition was that only a small part of the genome was really worth knowing — the 3–5% that was then estimated to lie in and close to protein-coding regions[1,2]. The alternative approach to a genome project was molecular genetics as usual: first identify a region of the genome that is of functional interest, then target it for sequencing. Calls to continue this traditional model for dealing with genotyping were rapidly swept aside, and the Human Genome Project was realized in a few years.

Over the past 15 years, many authors have proposed that phenomics — large-scale phenotyping — is the natural complement to genome sequencing as a route to rapid advances in biology[3–8]. The response to these propositions has mostly been silence, implying that 'phenotyping as usual'— measuring a limited set of phenotypes that seem the most relevant — is adequate. We disagree and argue that the case for phenomics is as compelling now as the case for genomics was 25 years ago and indeed shares many similarities with that case.

Phenomic-level data are necessary to understand which genomic variants affect phenotypes, to understand pleiotropy and to furnish the raw data that are needed to decipher the causes of complex phenomena, including health, crop yields, disease and evolutionary fitness. Our limited ability to understand many important biological phenomena suggests that we are not already measuring all important variables and that broadening the possibilities will pay rich dividends. Fundamentally, we can choose between focusing our efforts on what we already think is important or deciding that much of what we do not yet measure will prove useful and interesting. The question 'why not measure it all?' was fortunately affirmatively answered for genomes; it is now time to ask the same question for phenotypes.

The time is ripe to consider the value of phenomic-level efforts for several reasons. First, technologies for high-throughput phenotyping are becoming increasingly available. Second, conceptual, analytical and bioinformatics approaches that enable the use of very high-dimensional data are advancing rapidly. Third, dynamic models that link phenomena across levels — from genes to cells, to organs and through to the whole organism — are in reach. Finally, in most cases, phenotypic data continue to be the most powerful predictors of important biological outcomes, such as fitness, disease and mortality. Although analyses of genomic data have been successful at uncovering biological phenomena, they are — in most cases — supplementing rather than supplanting phenotypic information.

In this Review, we identify the scientific rationales for carrying out phenomics research and outline current approaches to obtaining phenomic data. We then describe some of the conceptual challenges to taking full advantage of phenomic-level data. Finally, we consider how to establish phenomics as an independent discipline.

What is phenomics?

The current usage of the word 'phenome' to refer to the phenotype as a whole is due to the evolutionary biologist Michael Soulé[9]. We now define phenomics as the acquisition of high-dimensional phenotypic data on an organism-wide scale. Although phenomics is defined in analogy to genomics, the analogy is misleading in one respect. We can come close to completely characterizing a genome but not a phenome, because the information content of phenomes dwarves those of genomes:

Unknown Cardiovascular state

?

Known state

measure-ments on patient

measure-ments on model

error

Cardiovascular model

$\dot{X} = f(x,u,\alpha,t)$

Adjust α (parameters) for minimum error

Avicenna Alliance
Association for Predictive Medicine

The Virtual Physiological Human will revolutionise the way health knowledge is produced, stored and managed as well as the way in which healthcare is currently delivered.

European Commission

Putting the James Black approach on steroids by use of multiscale physiological modelling

$$\left\{\begin{matrix}\alpha_{11}\\ \alpha_{12}\\ .....\\ \alpha_{1n}\end{matrix}\right\} = \overline{\alpha_1} \rightarrow M_1 \rightarrow \overline{P_1} = \left\{\begin{matrix}P_{11}\\ P_{12}\\ .....\\ P_{1m}\end{matrix}\right\}$$

↓

Multidimensional sensitivity analysis ($S(\overline{\alpha_1}, \overline{P_1})$)

↓

Identify putative drug targets (α_{1j}, α_{1k})

↓

Construct lower-level model M_2

$$\left\{\begin{matrix}\alpha_{21}\\ \alpha_{22}\\ .....\\ \alpha_{2z}\end{matrix}\right\} = \overline{\alpha_2} \rightarrow M_2 \rightarrow \overline{P_1} = \left\{\begin{matrix}P_{21} = \alpha_{1j}\\ P_{22} = \alpha_{1k}\\ .....\\ P_{2v}\end{matrix}\right\}$$

↓

Multidimensional sensitivity analysis ($S(\overline{\alpha_2}, \overline{P_2})$)

↓

Identify putative drug targets (α_{2i}, α_{2l})

↓

.....

↓

Drug design targeting parameters (α_{ji}, α_{jl})

Causally cohesive prediction of drug effect

Drug targeting becomes a merge between multiscale physiological modelling + nonlinear control engineering + deep phenotyping