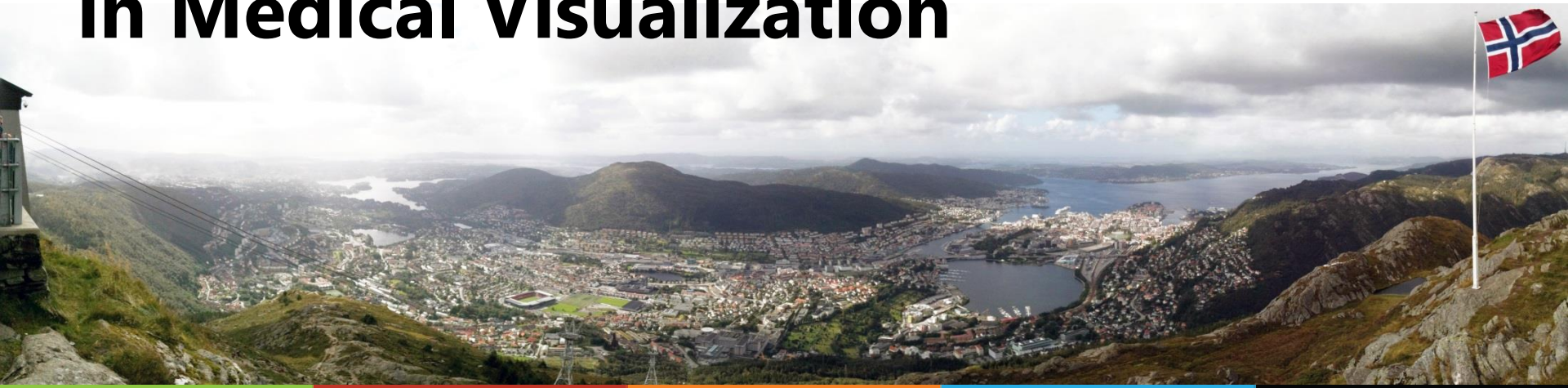# From Anatomy to Physiology in Medical Visualization

Helwig Hauser
University of Bergen

These 30 mins.

Motivation

Physiology

Capturing physiology
  – data
  – models

Selected examples
  – hemodynamics in aneurysms (Preim et al.)
  – tissue perfusion (Hauser et al.)
  – functional brain studies (Lundervold et al.)
  – protein–ligand binding (Byška et al.)

Challenges

Motivation

Medicine—it's about the *living* patient!

- – focus on the physiological (dys-)function

- – relates to anatomy, often, of course,
  but goes much further beyond

Visualization—substantial challenges!

- – time-dependent phenomena

- – multi-scale phenomena, both in space & time

- – heterogeneous data (and models)

- – multi-disciplinary

Physiology

Definition(s):

... the mechanical, physical, and biochemical functions of humans, their organs, and the cells...

... specific characteristics and mechanisms of the human body that make it a living being

... life processes

As compared to anatomy:

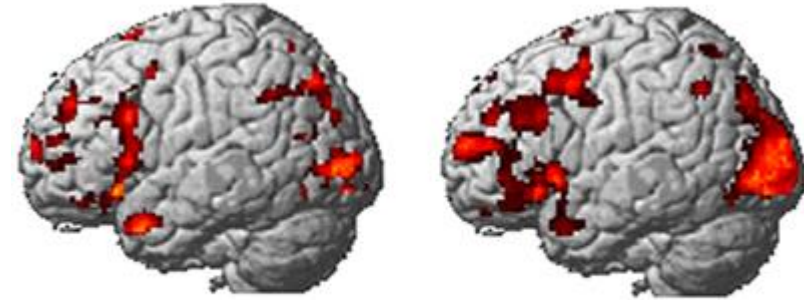... the shape and structure of living things

Medical Physiology

Guyton and Hall Textbook:
- Cell physiology
- Membrane, Nerve and Muscle physiology
- Metabolism and temperature regulation
- Heart physiology
- The circulation
- The body fluids and kidneys
- Blood Cells, Immunity, and Blood Clotting
- Respiration
- Aviation, Space and Deep-Sea-Diving physiology
- The Nervous System and Sensory physiology
- The Nervous System: The special senses
- Motor and Integrative neurophysiology
- Gastrointestinal physiology
- Endocrinology and Reproduction
- Sport physiology

Capturing Physiology

Data

– functional imaging like fMRI, PET, CEUS, ...

– numerical simulation as from blood flow simulation

...

Models

– physical models, e.g., kinematic models

– biochemical models, e.g., pathway models

...

HAPPY   SAD

[Kassam et al., 2013; PLOS one]

[Evans et al., 2015; ... stenosis prevention...]
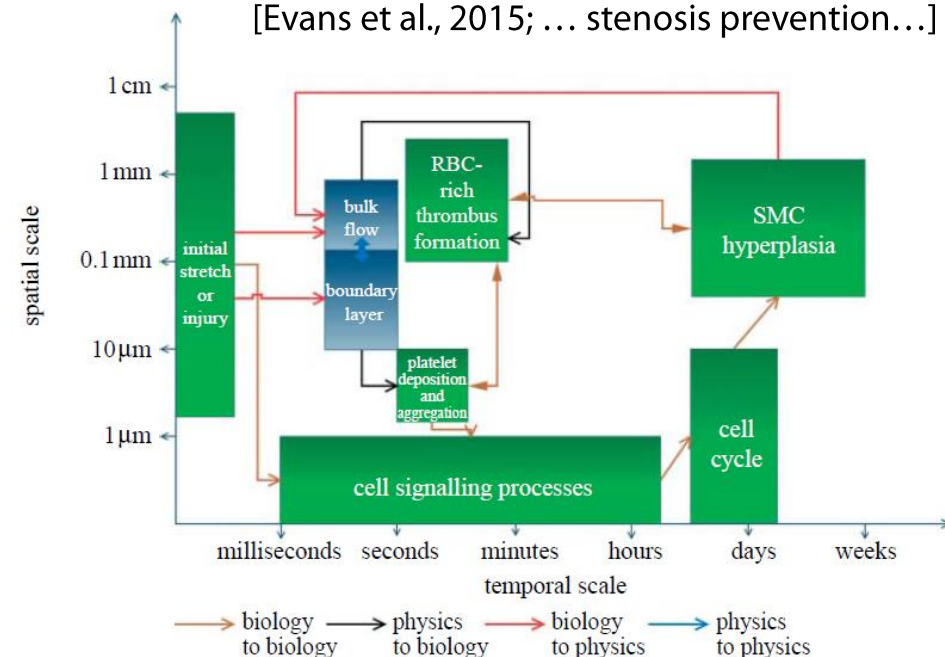
Data Acquisition—Functional Imaging

Cellular physiology	Nerve, muscle, membrane	Metabolism	Heart physiology	Blood circulation
Microscopy	Microscopy	Microscopy, PET, SPECT	Ultrasound, CT, MR, ECG, PET, SPECT	Ultrasound, MR, CFD
Micro circulation	Body fluids and kidneys	Blodd cells and immunity	Respiration	Gastro-intestinal
Ultrasound, MR, CT	MR	?	CT, MR, US	US, MR, CT
Brain	Endocrinology & reproduction	Sport physiology	Aviationn, space, deep-sea phys.	Kinematics
fMRI, EEG (PET/SPECT)	?	ECG, GPS, WattMeters, other sensors	?	Tracking sensors

[Mesoscope.org, Johnson et al.]
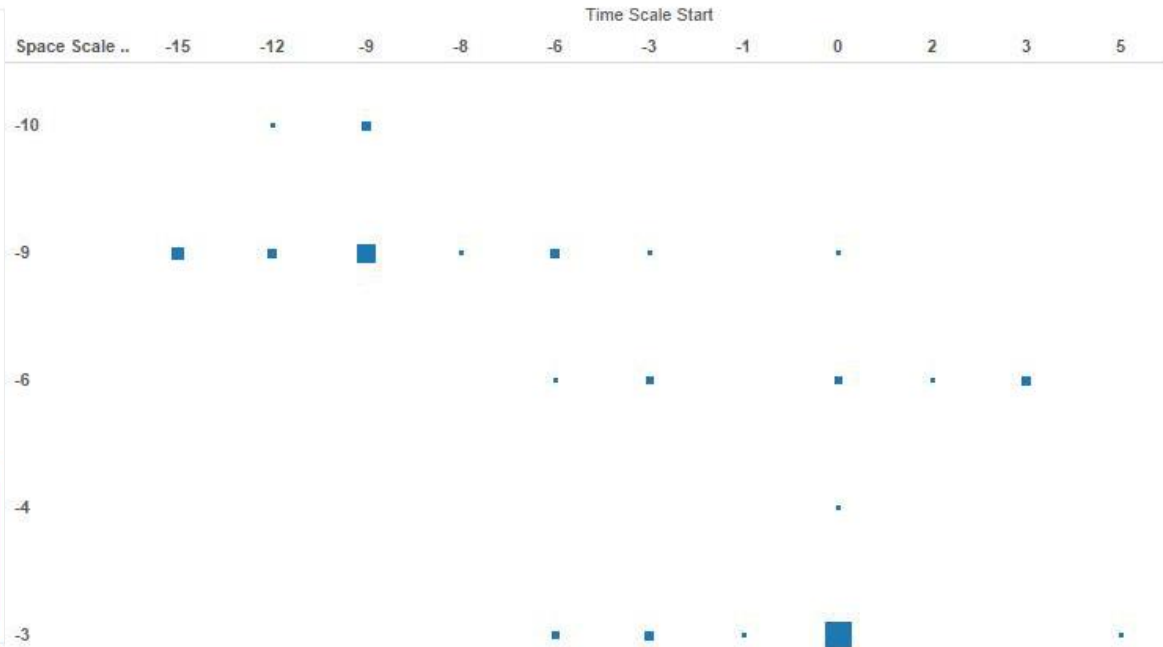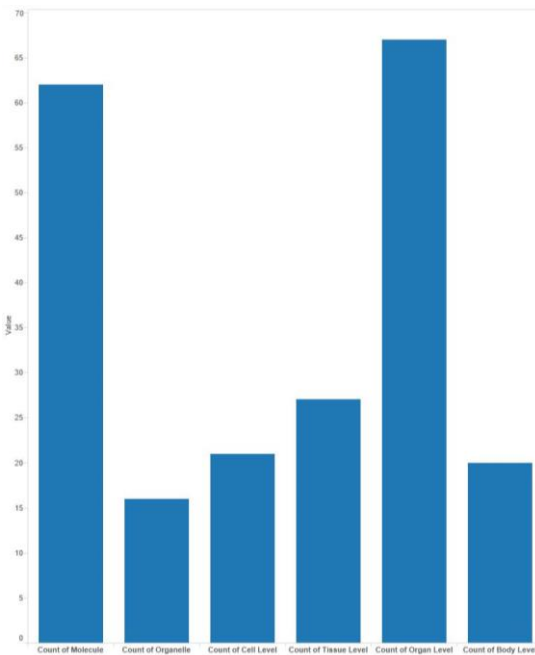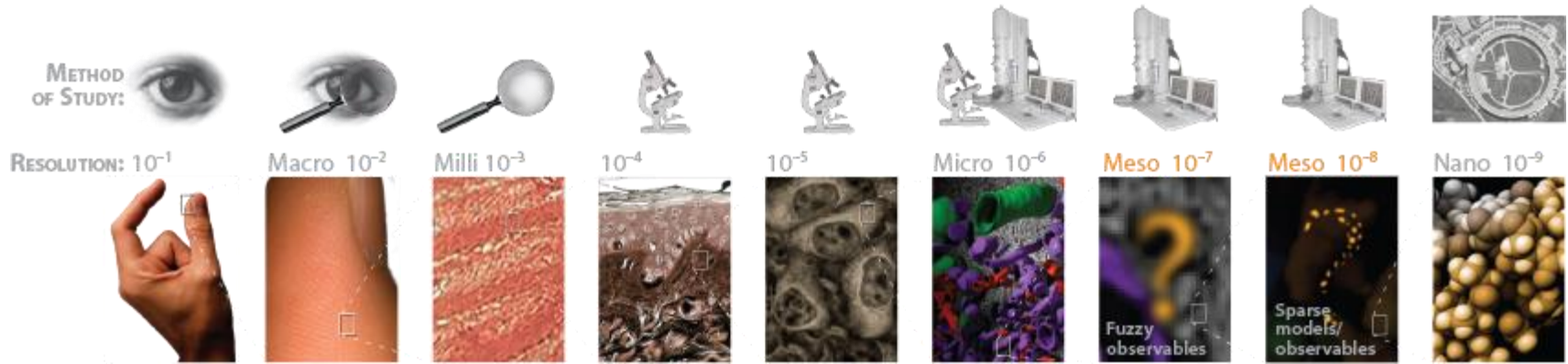
Multi-scale modeling of human phyisology

Atom 10^{-12}m	Protein 10^{-9}m ProteinML	Cell 10^{-6}m CellML	Tissue 10^{-3}m TissueML	Organ 10^{0}m AnatML	Organ system & organism PhysioML
Gene Networks	Pathway models	Stochastic models	ODEs	Continuum models (PDEs)	Systems models

10^{-6}s
molecular events
(ion channel gating)

10^{-3}s
diffusion
cell signalling

10^{0}s
motility

10^{3}s
mitosis

10^{6}s
protein
turnover

10^{9}s
human
lifetime

Hunter et al.., *2002*

Approaches vs. Scale

Winslow et al. Computational Medicine: Translating Models to Clinical Care
Science Translational Medicine (2012)
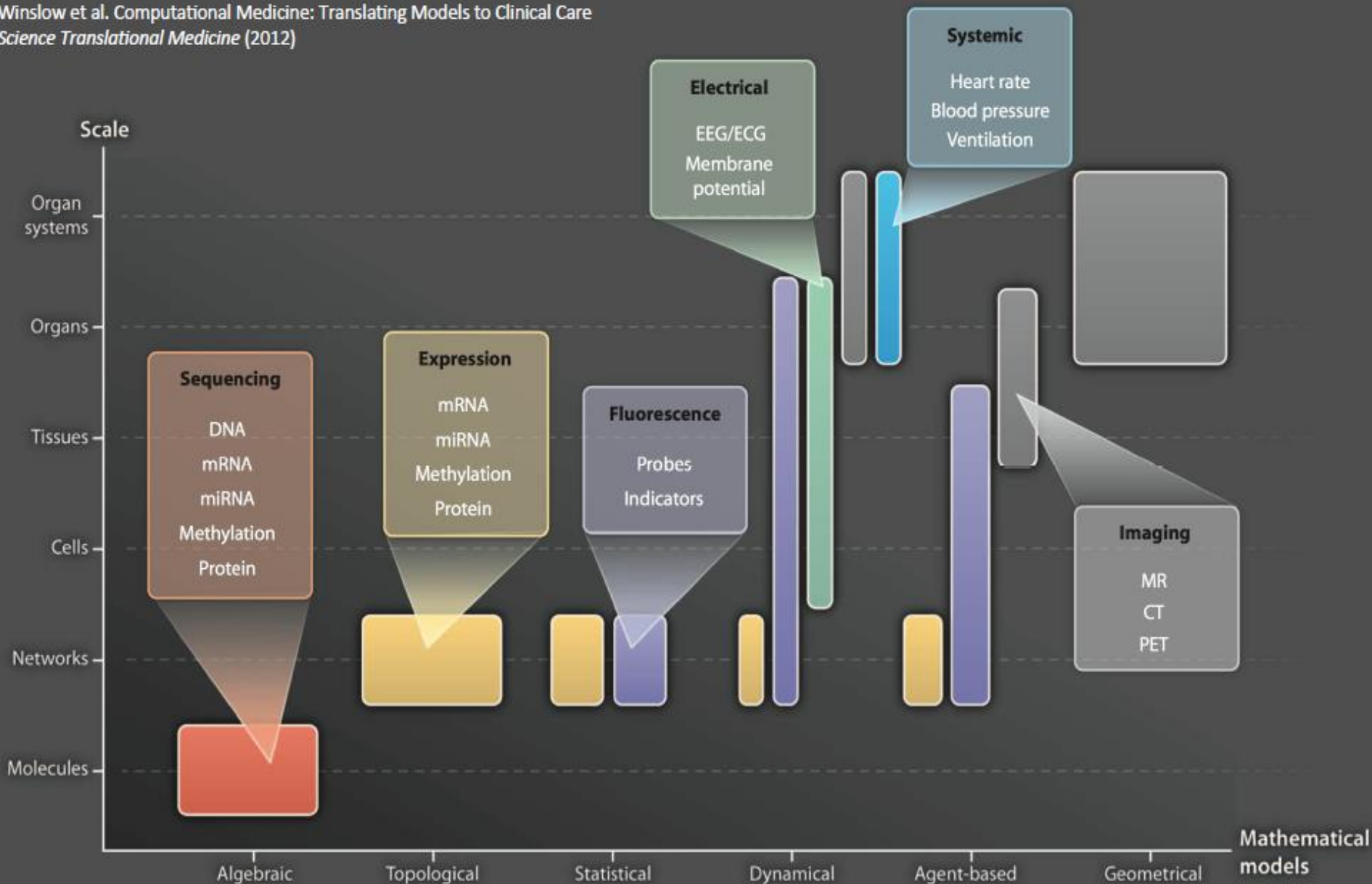
Imaging & visualization → mental model → model formalization → model definition → quantitative results
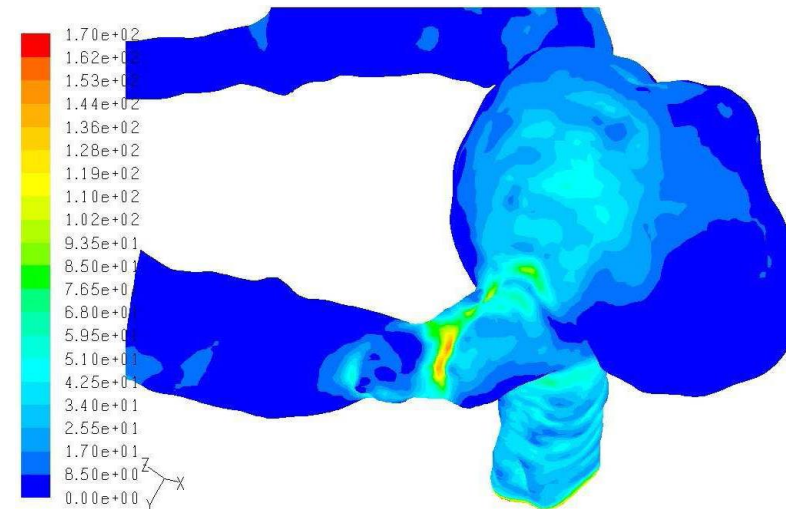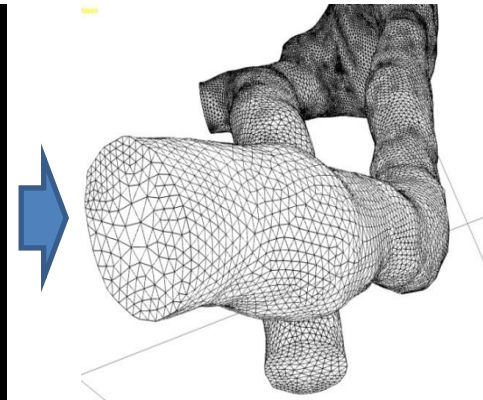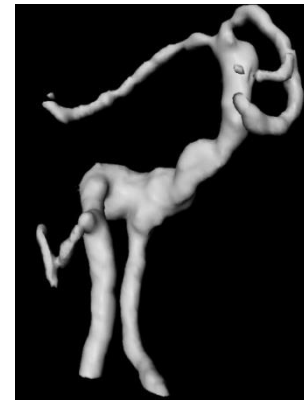

Image courtesy of Edda Klipp
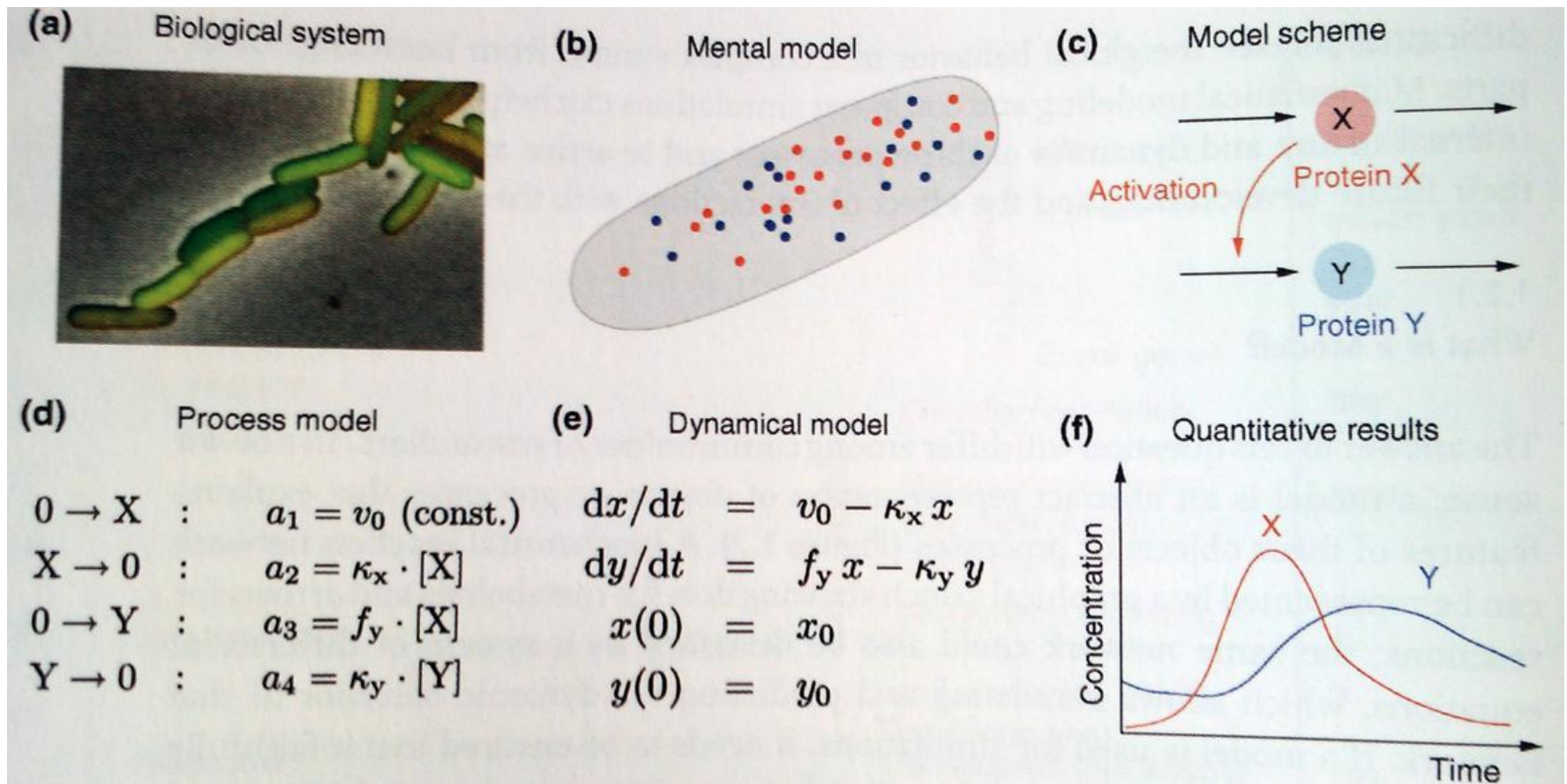
Hemodynamics important for rupture risk assessment

- – anatomical imaging
- – geometric vessel reconstruction
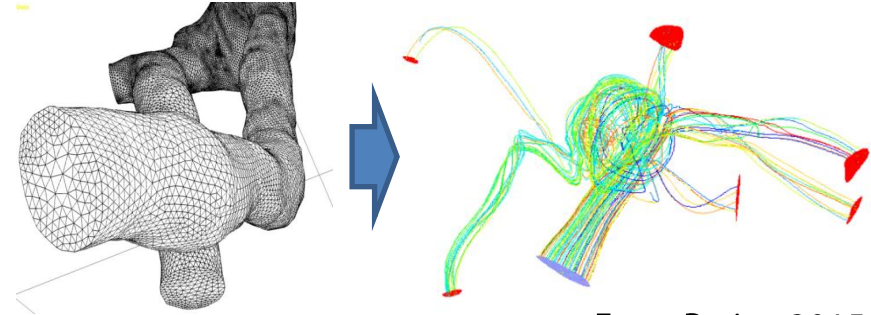- – gridding & numerical simulation
- – joint visualization
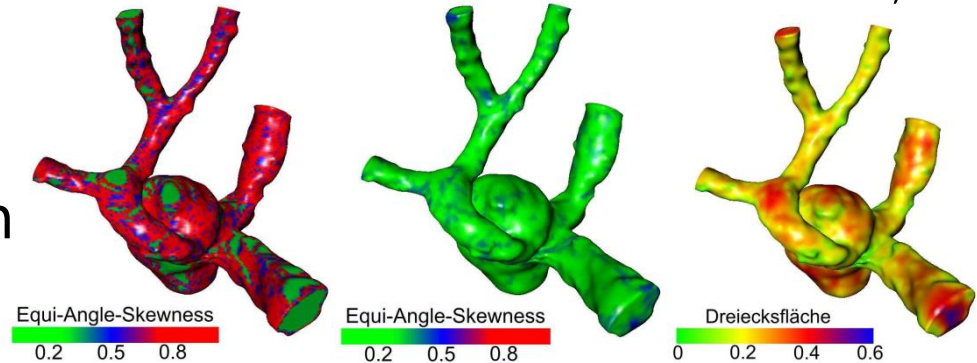
From Preim, 2015
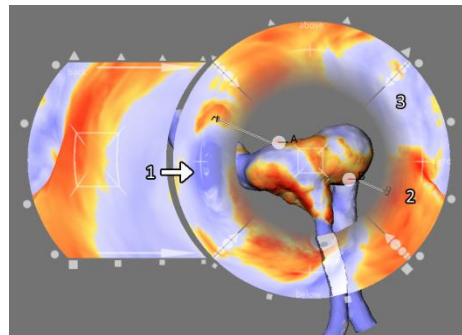
[SimVis 2008]

Challenges

Interdisciplinary solution

- computational fluid dynamics, incl. gridding

From Preim, 2015

- image processing, incl. surface reconstruction

Equi-Angle-Skewness
0.2 0.5 0.8

Equi-Angle-Skewness
0.2 0.5 0.8

Dreiecksfläche
0 0.2 0.4 0.6
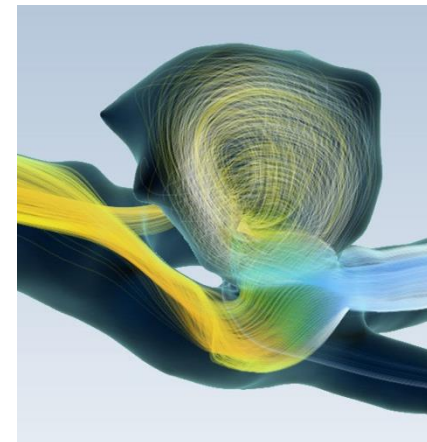
- mixed volume & flow visualization

[CARS 2009]   [EuroVis 2009]   [VCBM 2010]   [EuroVis 2011]

Example: Studying Tissue Perfusion

Data from perfusion imaging, *e.g.*, DCE-MRI[1] or CEUS[2]
[1] … dynamic contrast-enhanced magnetic resonance imaging; [2] … constrast-enhanced ultrasound

- **2D or 3D**, **time-dependent data**

Analysis via **time-intensity curves** (TICs)
- **either directly** (many curves)
- or via **derived perfusion params.**

Results:
- **general / detailed overview of perfusion** (ROI-independent)
- **fast perfusion-based segmentation**

Application(s):
- **ischemic stroke** (tissue at risk analysis) [4, 5], **heart infarct** (CHD) [5]
- **brain tumors** (gliomas) [1, 3], **abdominal lesions**, e.g., liver lesions [2], **breast tumors** (via mammography) [4, 5]

Reference(s):
1. Glaßer, Oeltze, Preim, Bjørnerud, Hauser, Preim: **Visual analysis of longitudinal brain tumor perfusion**. Proc. SPIE Medical Imaging, 2013, DOI:10.1117/12.2007878
2. Angelelli, Nylund, Gilja, Hauser: **Interactive Visual Analysis of Contrast-enhanced Ultrasound Data based on Small Neighborhood Statistics**. Computers & Graphics 35(2):218–226, 2011
3. Oeltze, Preim, Hauser, Rørvik, Lundervold: **Visual Analysis of Cerebral Perfusion Data – Four Interactive Approaches and a Comparison**. Proc. 6th Int'l Symp. on Image & Signal Processing & Analysis (ISPA 2009), pp. 582–589
4. Muigg, Kehrer, Oeltze, Piringer, Doleisch, Preim, Hauser: **A Four-level Focus+Context Approach to IVA of Temporal Features in Large Scientific Data**. Computer Graphics Forum 27(3):775-782, 2008 *(35* cited)*
5. Oeltze, Doleisch, Hauser, Muigg, Preim: **Interactive Visual Analysis of Perfusion Data**. IEEE Transactions on Visualization and Computer Graphics 13(6):1392–1399, 2007 *(29* cited)*
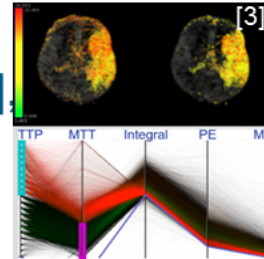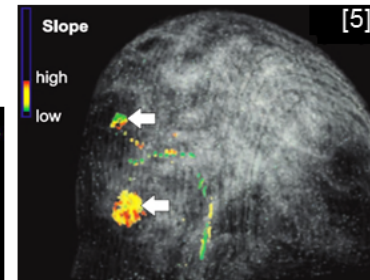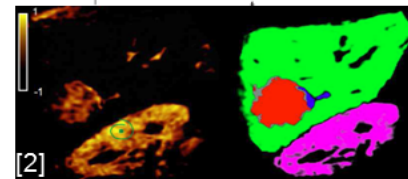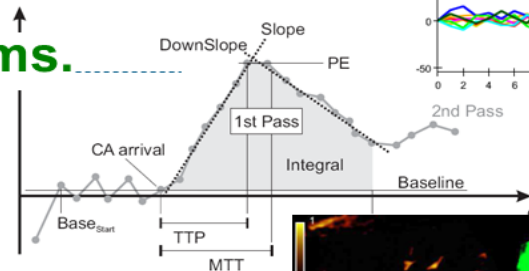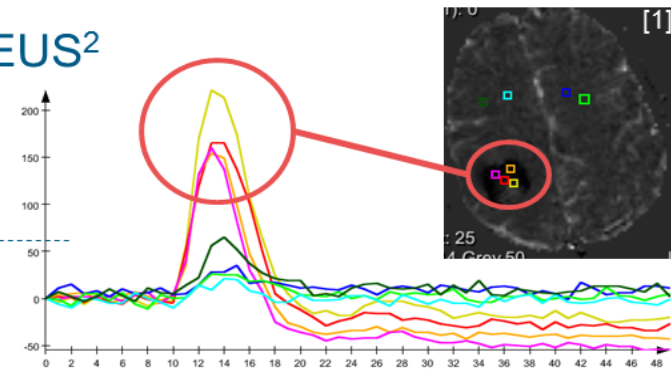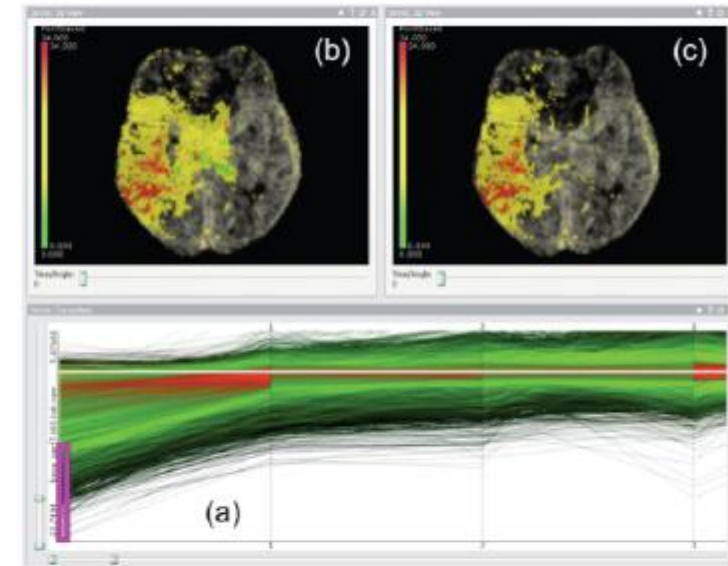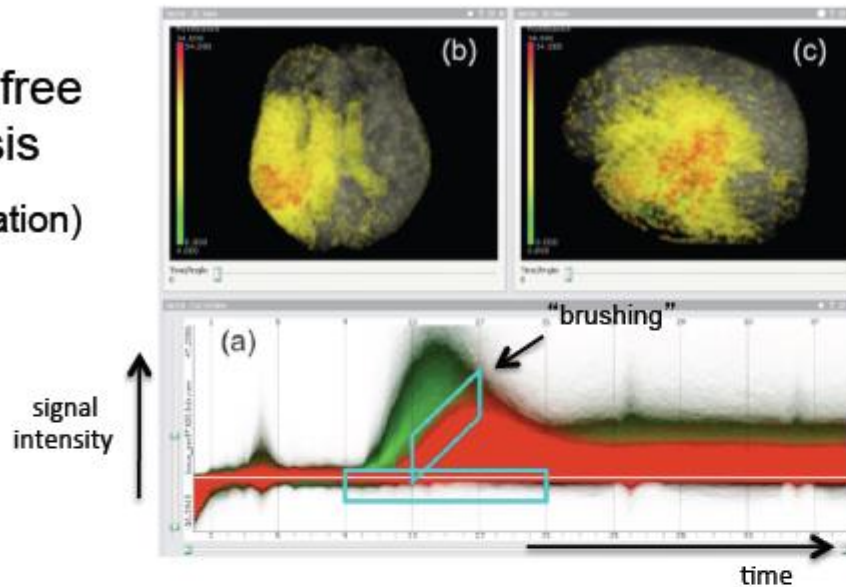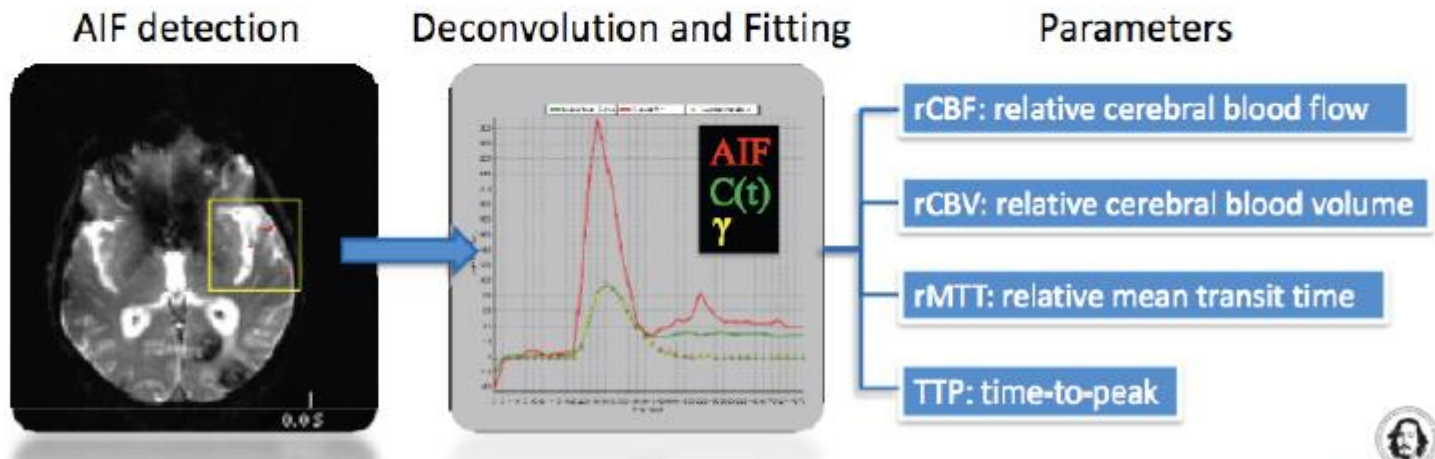
Cooperation:
- **Univ. of Magdeburg**
- **VRVis**

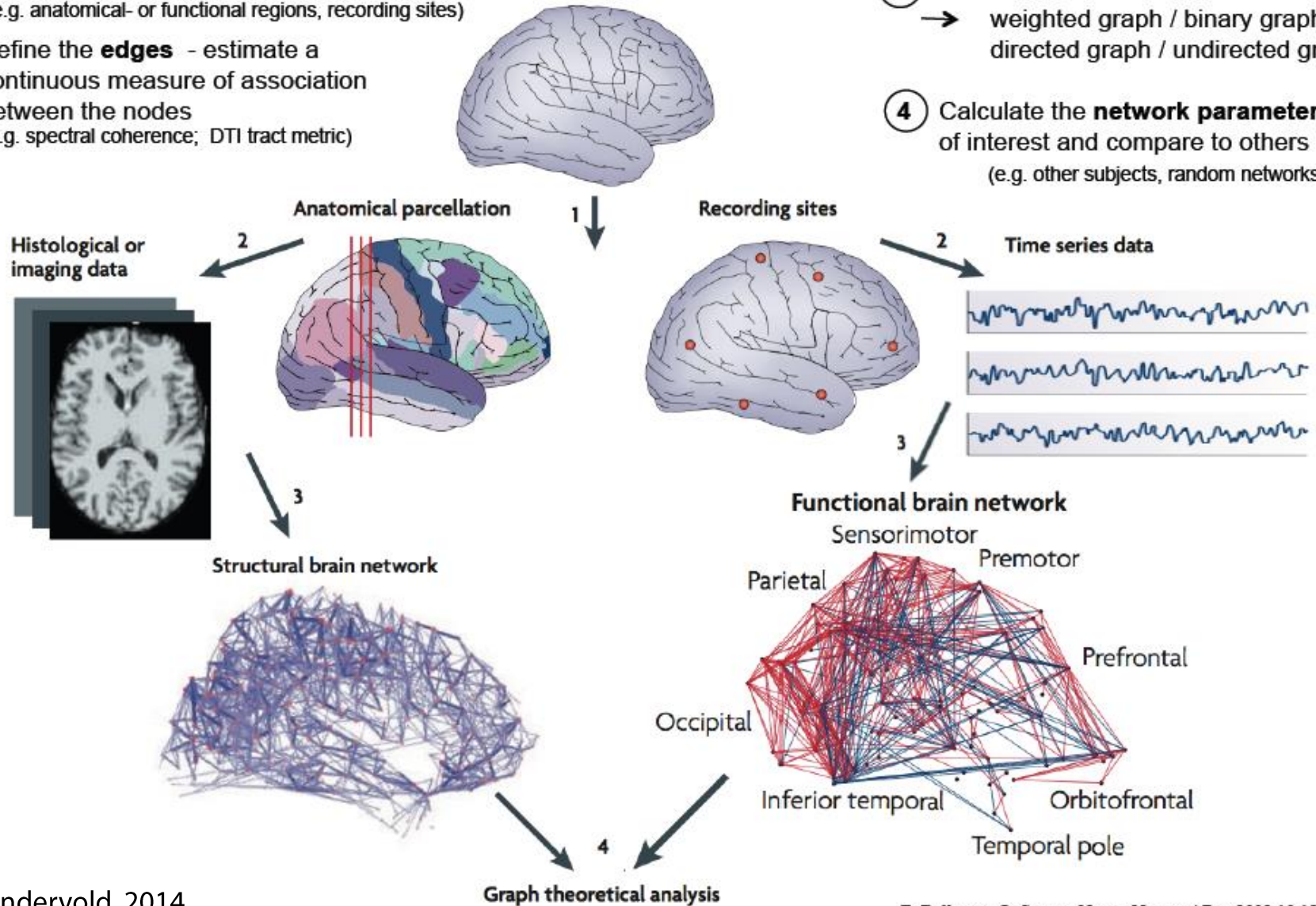# Quantitative Perfusion Analysis

Model-free analysis (visualization)

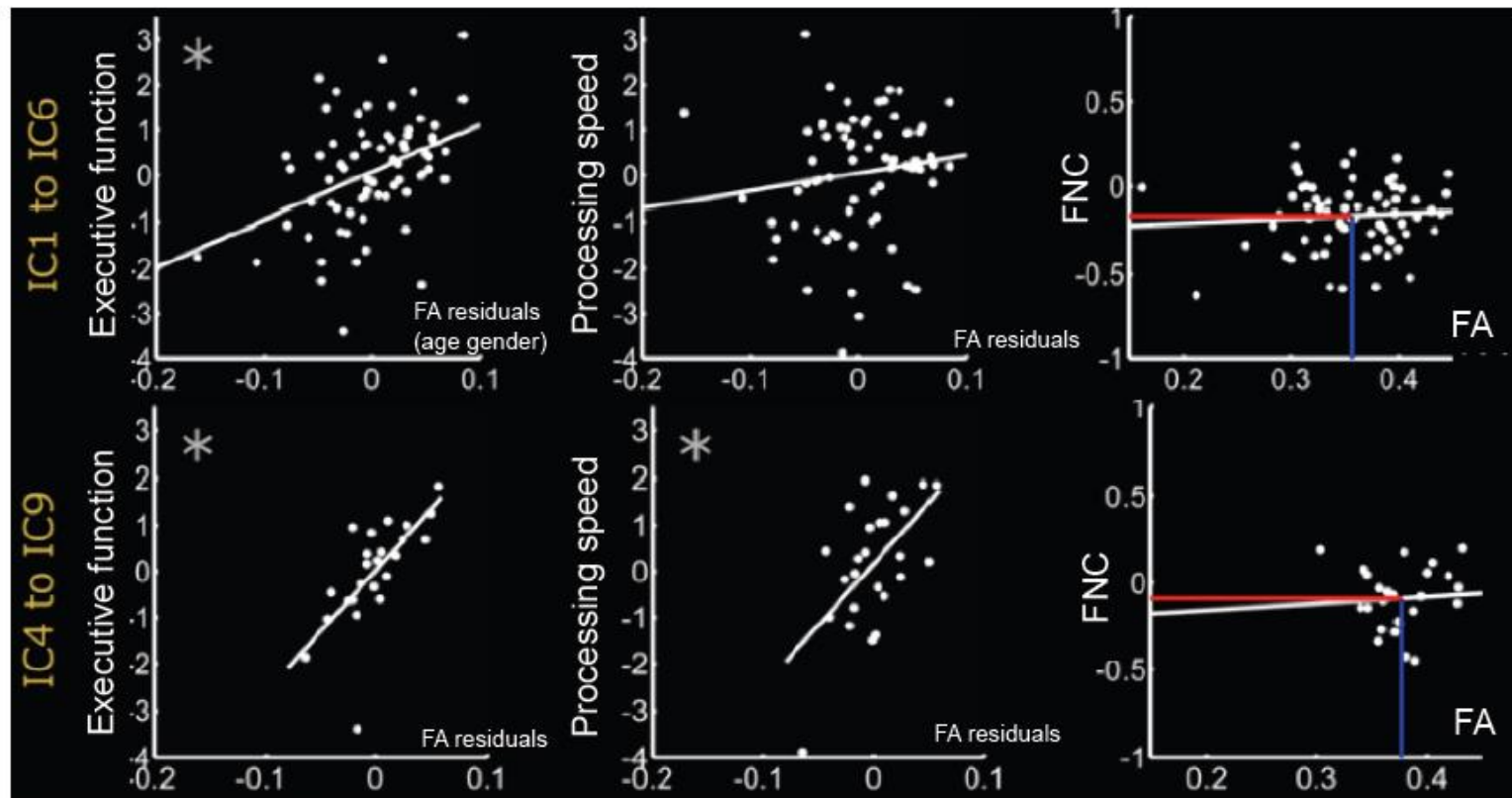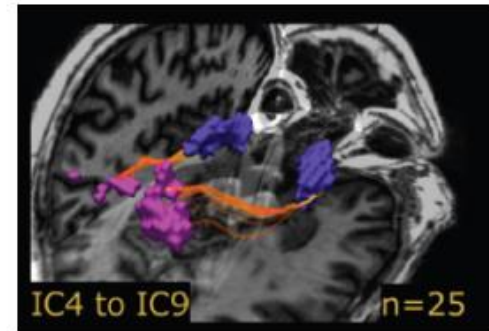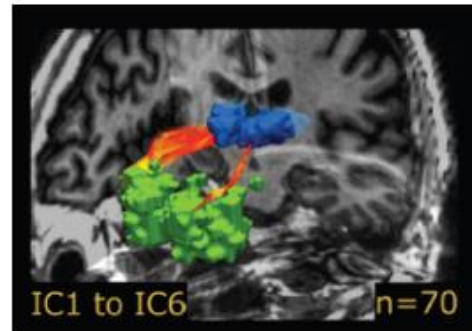Model-based analysis (parameter estimation)

AIF detection

Deconvolution and Fitting

Parameters

rCBF: relative cerebral blood flow

rCBV: relative cerebral blood volume

rMTT: relative mean transit time

TTP: time-to-peak

From Lundervold, 2014

S. Oeltze[1], H. Hauser[2], J. Rørvik[3], A. Lundervold[4], B. Preim[1]   ISPA 2009

Example: Functional Brain Studies

① Define the network **nodes**
(e.g. anatomical- or functional regions, recording sites)

② Define the **edges** - estimate a continuous measure of association between the nodes
(e.g. spectral coherence; DTI tract metric)

③ Generate the **adjacency matrix**
→ weighted graph / binary graph
directed graph / undirected graph

④ Calculate the **network parameters** of interest and compare to others
(e.g. other subjects, random networks)

Anatomical parcellation

Recording sites

Histological or imaging data

Time series data

Functional brain network

Structural brain network

Sensorimotor
Premotor
Parietal
Prefrontal
Occipital
Inferior temporal
Orbitofrontal
Temporal pole

Graph theoretical analysis

From Lundervold, 2014

E. Bullmore, O. Sporns. Nature Neurosci Rev 2009;10:186-198

Brain-behavior relationship

From Lundervold, 2014:
Cortico-strial connection and cognition

Ystad et al. *Neuroimage* 2010 Suppl. Fig 4

FA = Fractional anisotropy (DTI);   FNC = Functional network connectivity (rs-fMRI)
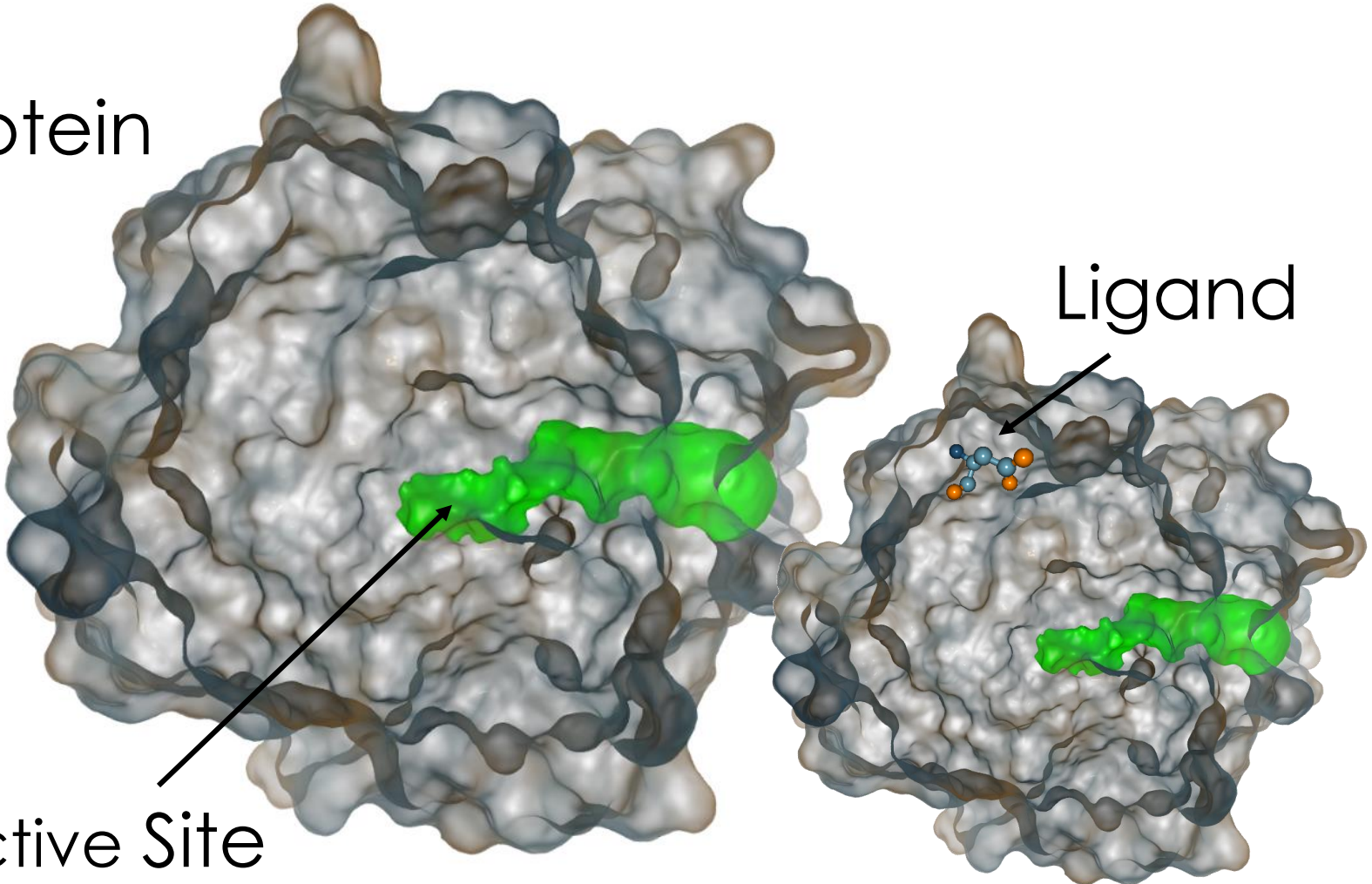
Example: Ligand Docking

Fri., first session! Jan Byška et al.

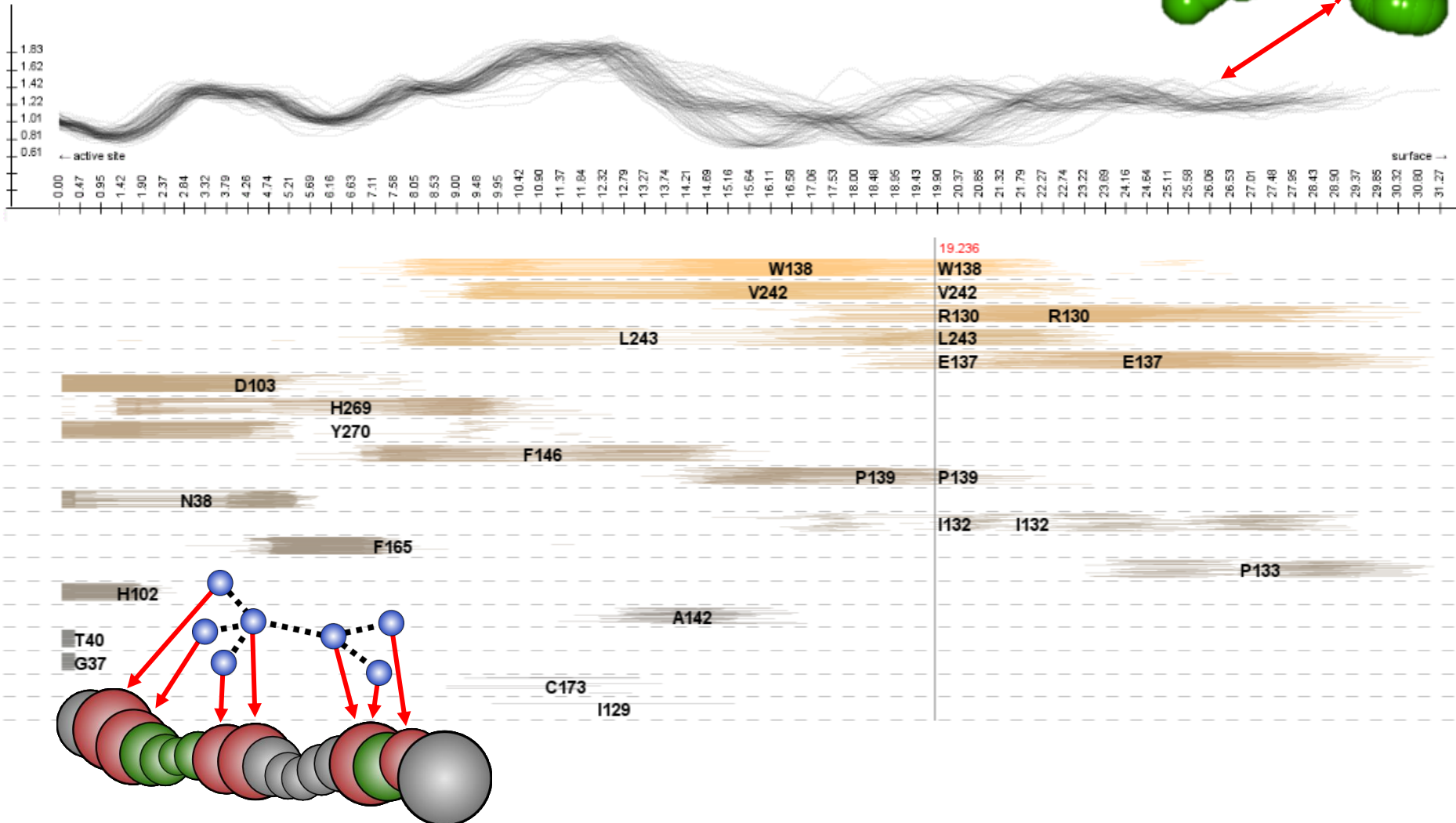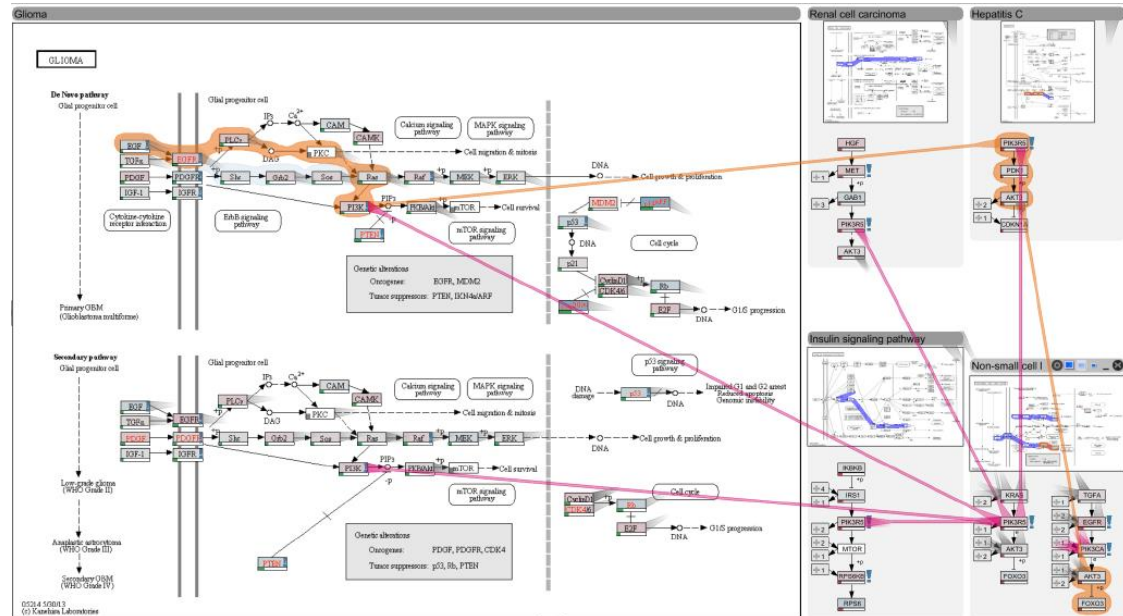Protein

Ligand

Active Site

Tunnel study over time → targeted mutations
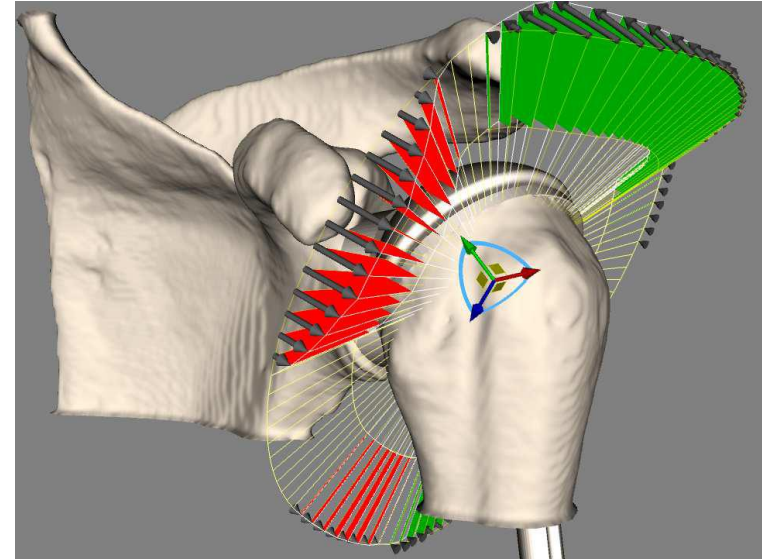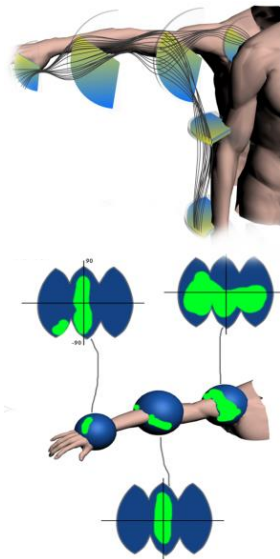
Further examples
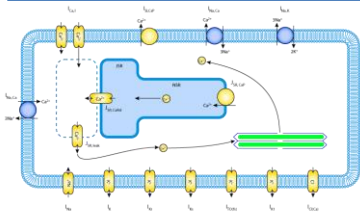
Pathways
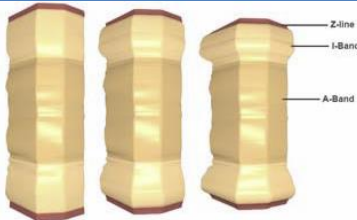
– Lex et al., 2013–

Kinematics

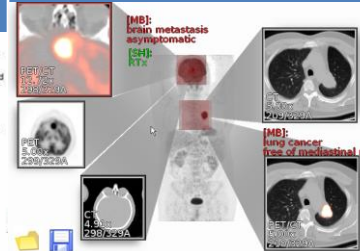– Krekel et al., 2006–

Large Field of Research Opportunities
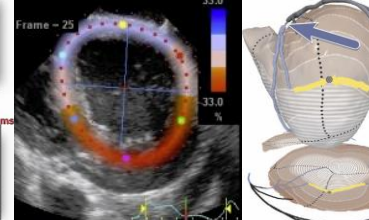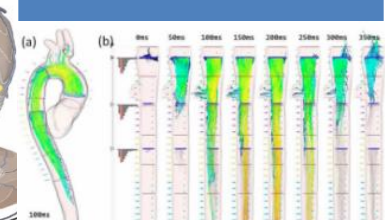

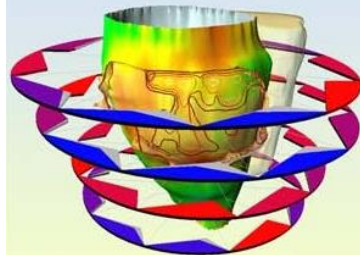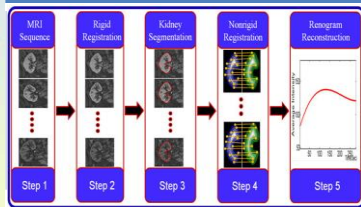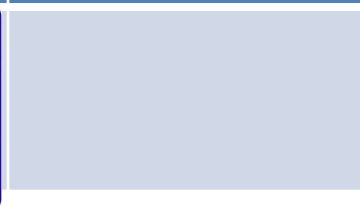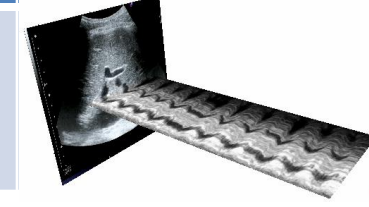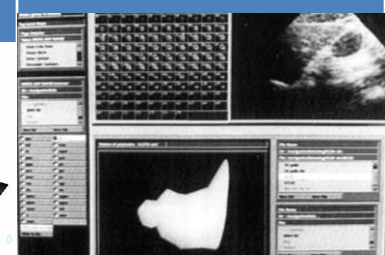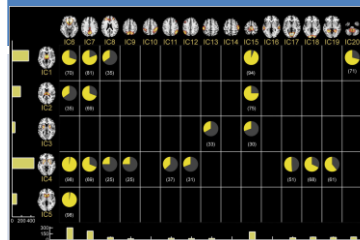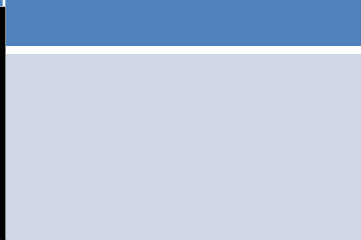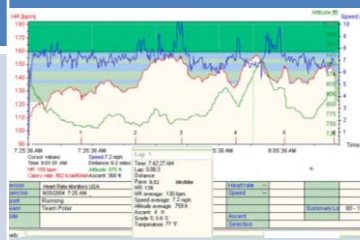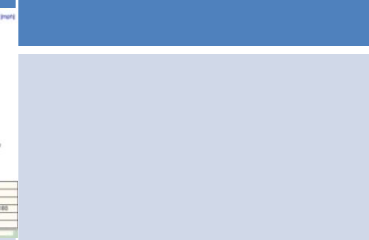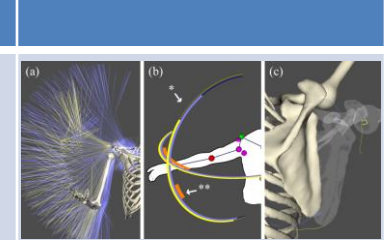| Cellular physiology | Nerve, muscle, membrane | Metabolism | Heart physiology | Blood circulation |
| Micro circulation | Body fluids and kidneys | Blodd cells and immunity | Respiration | Gastro-intestinal |
| Brain | Endocrinology & reproduction | Sport physiology | Aviationn, space, deep-sea phys. | Kinematics |

Challenges

Multi-scale visualization

- – both in space and time
- – truly many scales

Long time sequences

- – for ex., MD (molecular dynamics)

Model-based visualization

- – integration of data and models
- – bridging missing information

Systematic approach

- – complementing reductionism

Reductionist approach:

Components
biology

HT analytical chemistry:
genomics,
transcriptomics,
proteomics

20th-Century biology

Integrative approach:

Systems
biology / Systems
medicine

Integrative analysis:
bioinformatics,
mathematical models,
computer (*in silico*)
simulation

21st-Century biology

B. O. Palsson, Systems biology: Properties of reconstructed networks, Cambridge University Press, 2006.

from Lundervold, 2014

VCBM = Eurographics Workshop on Visual Computing for Biology and Medicine

- 2016 in Bergen, Norway

- collocated with MedViz 2016, a >100 participants interdiscipl. meeting of medicine & techn.

- important dates:
  - June, 2016: full paper deadline
  - Sept. 7–9, 2016: workshop

Acknowledgements

You!

Paolo Angelelli (physiology visualization),
Atle Bjørnerud (brain perfusion),
Jan Byška et al. (ligand binding),
Helmut Doleisch et al. (SimVis),
Sylvia Glasser (brain perfusion),
Erlend Hodneland (kidney perfusion),
Ivan Kolesár (illustrating physiology),
Arvid Lundervold (computational medicine),
Kim Nylund et al. (CEUS),
Steffen Oeltze-Jafra (perfusion),
Bernhard Preim (MedViz),
et al.