From multiscale modelling to digital twins

Life Sciences at FIAS
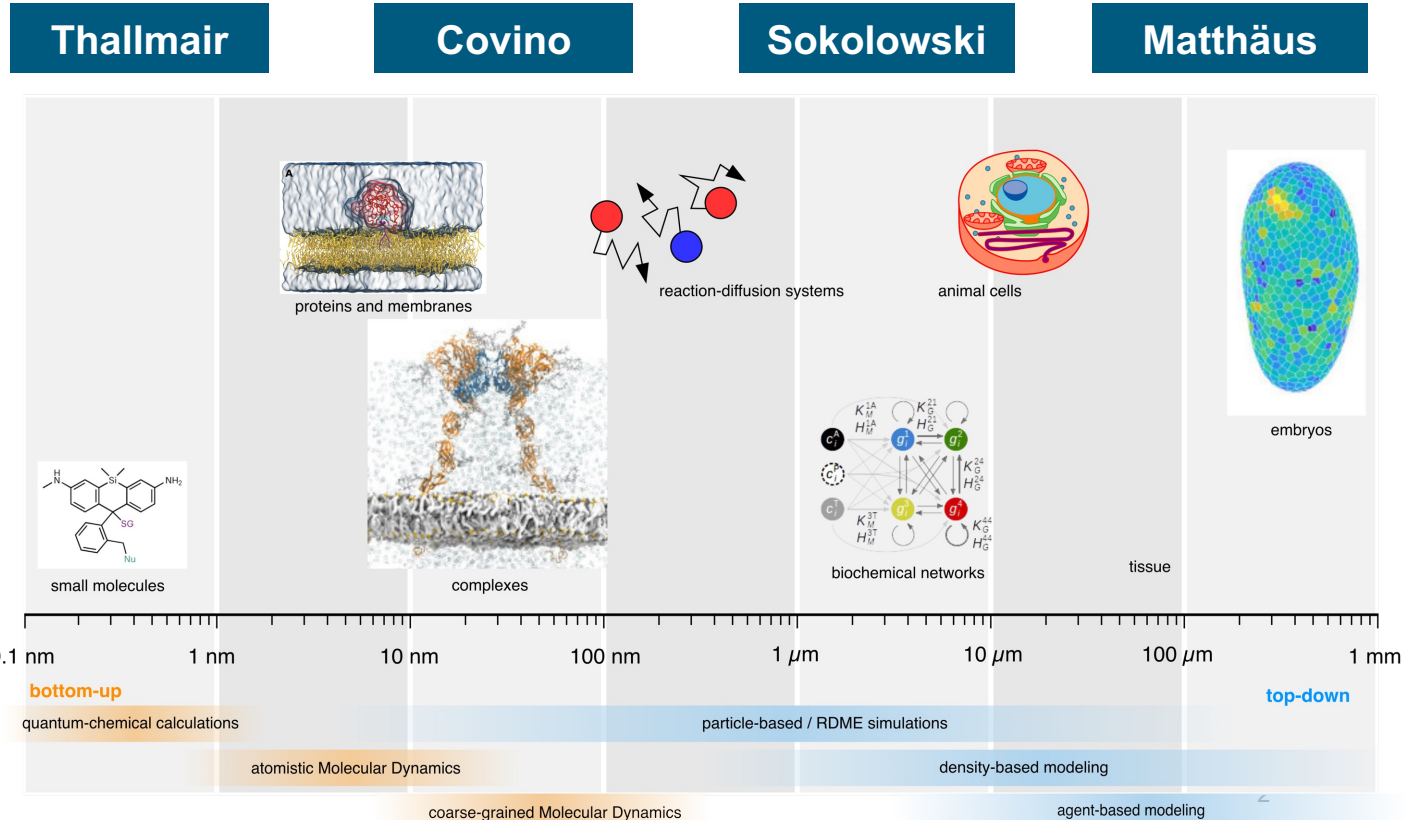
Multi-scale modelling and simulations of biological systems

CMMS

Multi-scale modelling

Integration of theory and experiments

High-performance computing

Thallmair

Covino

Sokolowski

Matthäus

proteins and membranes

reaction-diffusion systems

animal cells

embryos

small molecules

complexes

biochemical networks

tissue

0.1 nm   1 nm   10 nm   100 nm   1 μm   10 μm   100 μm   1 mm

bottom-up

top-down

quantum-chemical calculations

particle-based / RDME simulations

atomistic Molecular Dynamics

density-based modeling

coarse-grained Molecular Dynamics

agent-based modeling

FIAS Frankfurt Institute for Advanced Studies

Thallmair: Controlling and inhibiting protein function
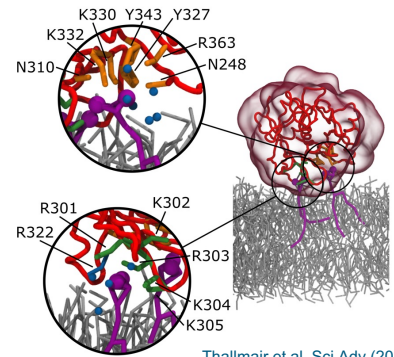
Development of chemical probes

Development and characterization of a glutathione-sensing platform for live-cell imaging
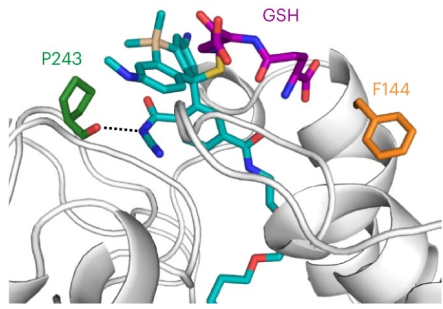
Emmert et al. Nat Chem (2023)

Protein-Lipid interactions

Membrane binding mechanism for decoding of spatio-temporal phospholipid signals in cells

Thallmair et al. Sci Adv (2022)

Coarse-grained force-field development

Reparameterization of the Martini force field for general purpose coarse-grained molecular dynamics
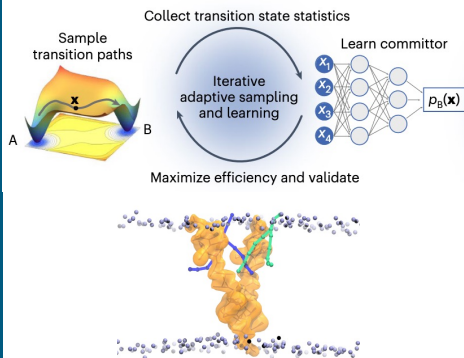

Souza et al Nat Meth (2021)

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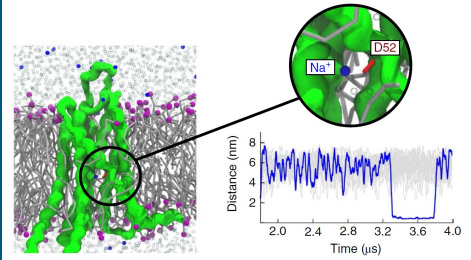
Covino: AI for biomolecular simulation and analysis
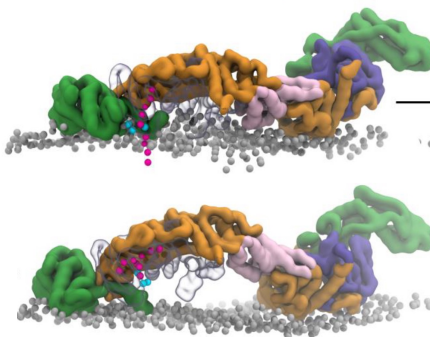

Physics-based simulators and AI

Integration of AI and MD to enhance simulations of structural reorganization

Jung et al. Nat Comp Sci (2023) Lazzeri et al. JCTC (2023)

High-Performance Simulation
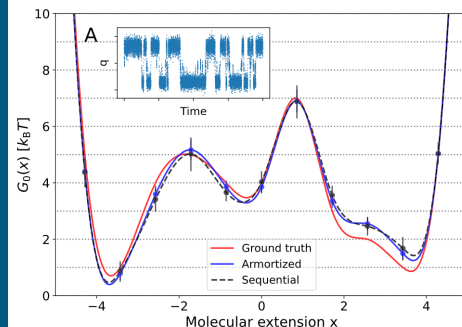
Atomistic and coarse-grained MD of molecular mechanisms in proteins and membranes

Nishimura et al. Sci Adv (2023)

AI & Bayesian inference of exp.

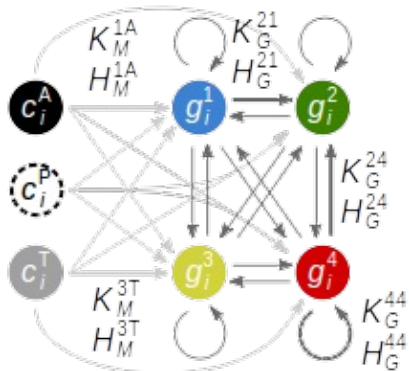Extracting mechanistic models from spectroscopy and microscopy experiments

Dingeldein et al. Mach Learn Sci Tech. (2023)

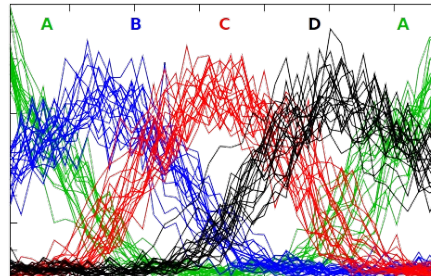# Sokolowski: Noise-control in cells and tissues

Biophysics Theory

- Statistical physics
- Information theory
- Biochemical networks

Sokolowski, Gregor, Bialek, Tkačik (2023)
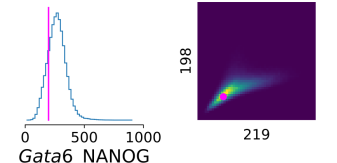
High-Performance Simulation

- Spatial-stochastic models
- Event-driven algorithms
- Tissue development

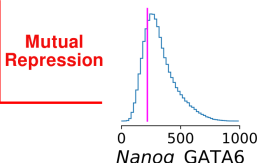Majka, Becker, ten Wolde, Zagorski, Sokolowski (2023)

Optimization, Inference & AI

- Simulation-based inference (SBI)
- Stoch. optimization
- Rare-event sampling

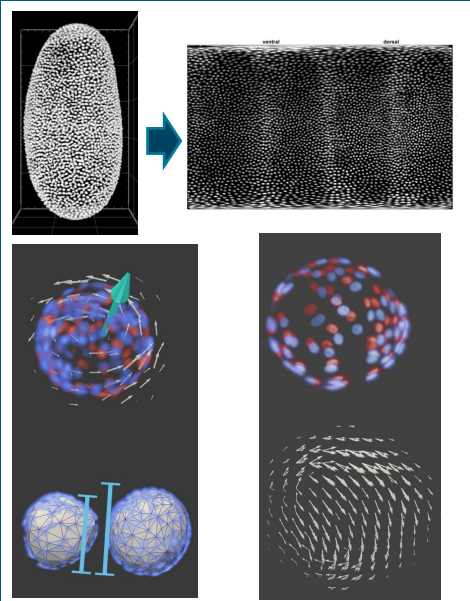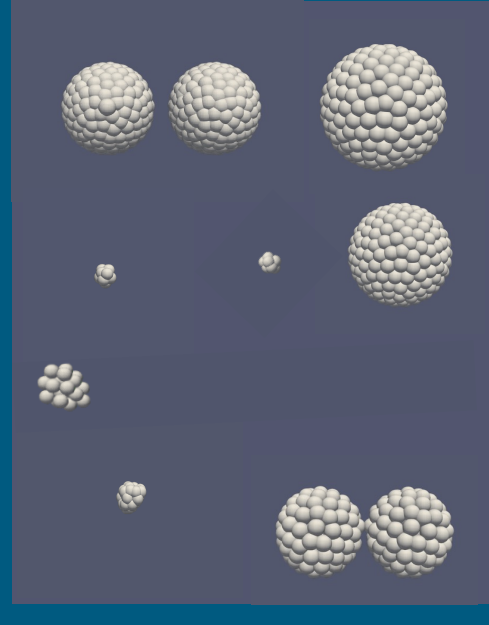Stoch. mouse embryo model inferred via SBI

Mutual Repression

*Gata*6_NANOG

*Nanog*_GATA6

Ramírez-Sierra & Sokolowski (2024)

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Matthäus: Modeling of multi-cellular systems

Analysis of 3D-time-lapse microscopy

Agent based modelling

Force inference

Fluorescently marked cell nuclei

Restricted Voronoi diagram

Segmentation and cell shape reconstruction

n

Mean cell tension [au]

Inference of mechanical stress
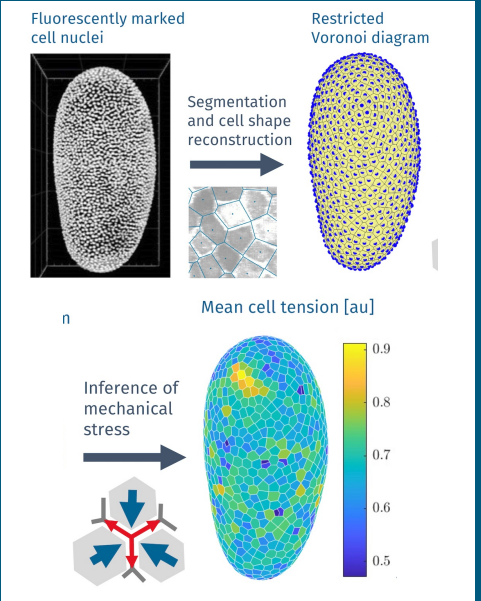
A community of passionate scientists

High scientific productivity (last 3 years):
- Publications: 37
- Preprints: 11

High-impact and international visibility:
- Sci Adv, Nature Methods, Neuron

Enthusiastic and dedicated community of early career researchers

Research consortia

Cluster of Excellence "SCALE"

SFB "Membrane-Associated Protein Assemblies, Machineries and Supercomplexes"

IMPRS "Cellular Biophysics"

SFB "Molecular principles of Light-control in complex environments" (evaluation)

SFB "Acute and chronic liver failure" (preproposal)

LOEWE Schwerpunkt "Lipid Space" (preproposal)

Deep integration in the Frankfurt landscape

Next generation multi-scale modelling: the digital twin

Quantitative in silico cell biology experiments
- Verifiable predictions
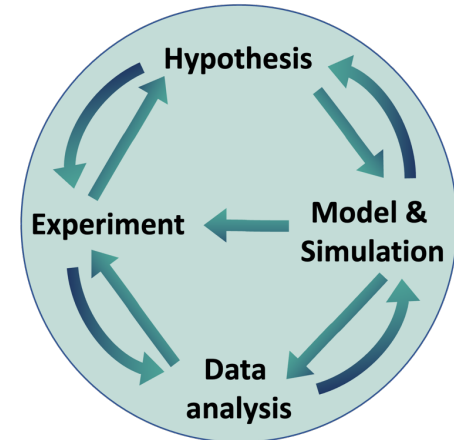- Design of in vitro and in situ experiments

Strategy: developing **Digital Twins**
- Bridging multi-scale descriptions
- Simulation intelligence: AI, HPC, and physics-based modelling
- Doctoral research school for methodological development

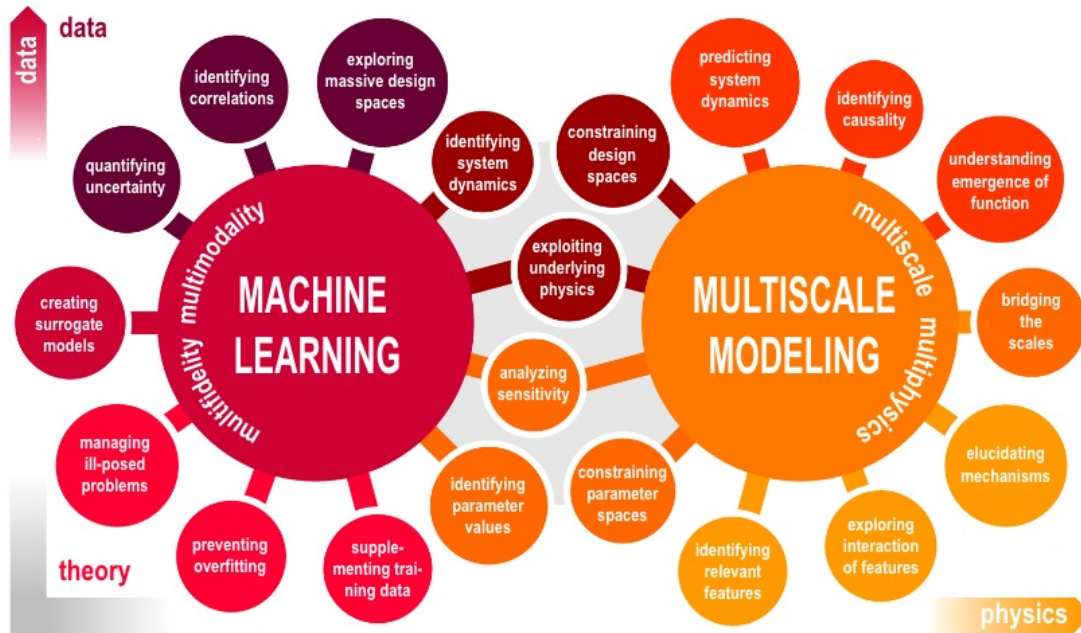**Full scientific and strategic support to the Cluster of Excellence SCALE**

**Flagship project:
DT of Subcellular Compartments**

Primed for the next phase of digital biology

Aber et al. Nature Digital Medicine (2019)

Digital Twin

Integration of pipelines, datasets, visualization techniques, physics-based simulations, and AI4science.

FIAS is **uniquely** equipped to tackle the methodological challenges that will lead us to developing **quantitative in silico biology**

FIAS Frankfurt Institute for Advanced Studies