Dynamics of protein interaction subnetworks

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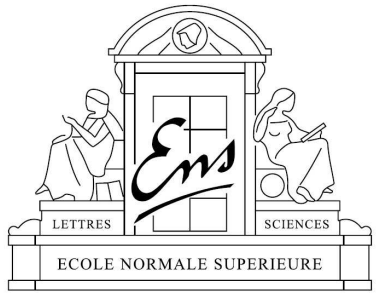
1. 2007 - 2010:
   Bachelor of Science in Physics

2. 2010 - 2012:
   Master of Science in Physics
   Theoretical Physics curriculum

Scientific experience

1. July-September 2011:
   CERN Summer Student Programme
   Project content:
   Monte Carlo event generators

2. February-June 2012:
   Exchange programme ENS Paris
   Master thesis:
   "Statistical models for coevolution in protein family profiles"



Biochemical networks in systems biology

Stochastic differential eqs. for protein concentrations

$$\frac{d\mathbf{x}(t)}{dt} = \underbrace{-\mathbf{K}(t)\mathbf{x}(t)}_{\text{Biochemical reactions}} + \underbrace{\xi(t)}_{\textbf{Random fluctuations}}$$

$\Downarrow$

Complex formation $\quad i + j \xrightarrow{k^{+}_{ij,l}} l$

Complex dissociation $\quad l \xrightarrow{k^{-}_{l,ij}} i + j$

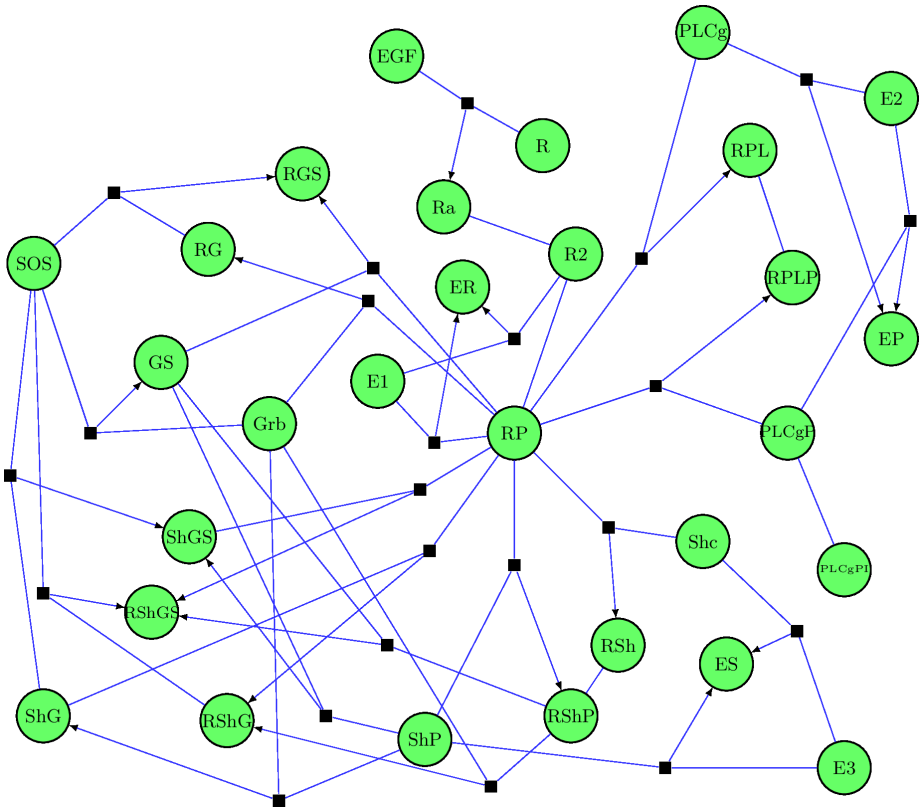
Conformational change $\quad i \xrightarrow{\lambda_{ij}} j$

$\Downarrow$

Temporally uncorrelated

Randomness from stochastic reactions of **finite** number of molecules (**intrinsic**)

Fundamental and practical limitations:

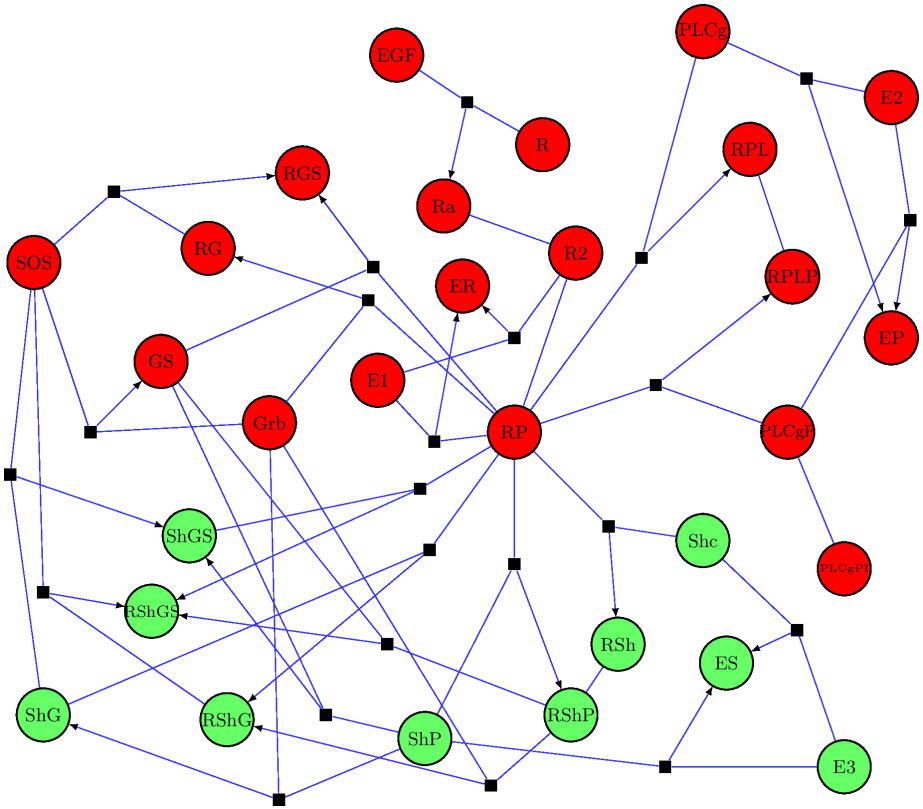


EGFR network from *Kholodenko et al. (1999)*

SIZE, COMPLEXITY, UNCERTAINTY

⇓

Statistical Physics for Model Reduction



Small subset of variables:

Subnetwork

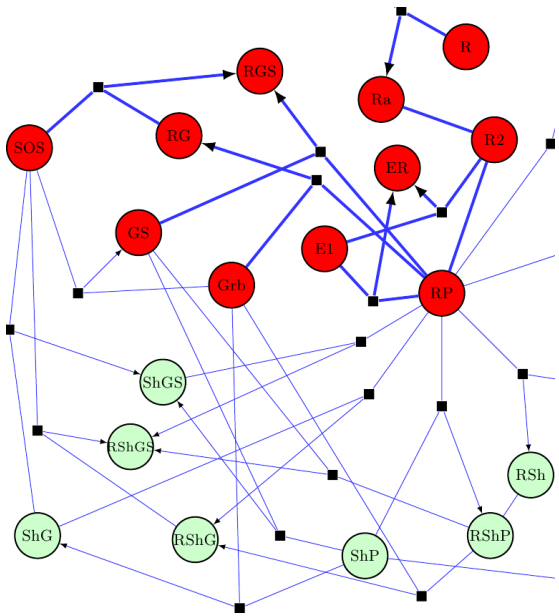
Embedded in a larger network:

Bulk

Description of subnetwork dynamics?

Subset of stochastic differential eqs.

$$\frac{d\mathbf{x}^S(t)}{dt} = -\mathbf{K}_{SS}(t)\mathbf{x}^S(t) + \int_0^t \underbrace{\mathbf{M}^T_{SS}(t,t')}_{\text{Memory function}}\ \mathbf{x}^S(t') + \underbrace{\chi^S(t)}_{\text{New random term}}$$



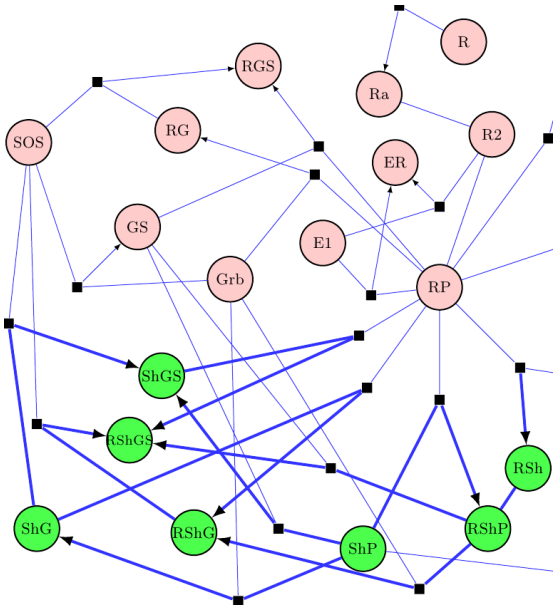
↓ Feedback

↓ Temporal correlation

Propagation through **Bulk**

Approximate linear dynamics +
Nonlinear corrections

Future directions



- **INFERENCE**
  Subnetwork → Bulk
  (UNKNOWN)

- **Statistics of memory + random term**

Theoretical Characterisation of Experimental Data

→ Intrinsic/Extrinsic randomness
→ Biological interpretation

Application target

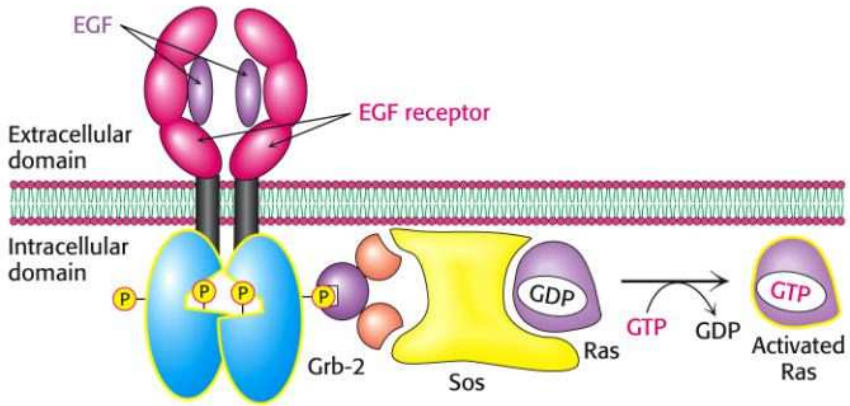
Intracellular Signalling pathways

$\Downarrow$

Epidermal Growth Factor Receptor (EGFR)

Protein-protein interactions
$\equiv$ Signal transduction

CELL DIFFERENTIATION



In collaboration with Randall Division of Cell and Molecular Biophysics, KCL

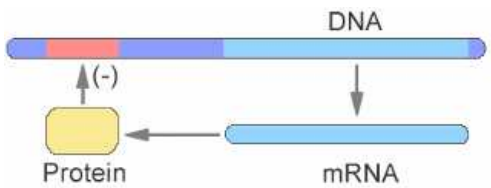
EGFR overexpression $\rightarrow$ oncogenic proliferation

$\Downarrow$

TARGETED CANCER THERAPIES

Need:

- **Elucidation of proteome dynamics**
  Tumour heterogeneity, differential response, resistance
- **Coupling to gene expression**



Genetic mutations +
dysregulated signalling pathways

Scientific training

King's College London

- **Master courses**
  e.g. Complex networks, Elements of statistical learning
- **Seminars and workshops**
  e.g. Statistical Mechanics of Glassy and Disordered Systems

External conferences

e.g. Statistical Physics and Information Processing in Biology
Paris, December 2012

Transferable skills training

- **Presentation skills**
  (Disordered Systems Group meetings)
- **Teaching experience** (Tutoring)
- **Research organisation, Academic writing**
  (Graduate School Training Programme)

Network-wide

NETADIS
Statistical Physics Approaches to Networks Across Disciplines

- **Netadis kick-off meeting** (Torino, February 2013)
- **Spring College on Physics of Complex Systems** (Trieste, May-June 2013)
- **Netadis 1^{st} Summer School** (Hillerod, September 2013)

Secondments

1. **TUB, Berlin**
   (June-August 2013)

Complementarity: Approximate inference methods
$\Rightarrow$ Parallel approach for subnetwork dynamics

2. **Rome/Torino**

Complementarity: Applications to cellular biochemical networks

Impact on future career

1. **Knowledge**
2. **Skills** (Scientific, transferable)
3. **Awareness**:
   Research in Academia,
   Applications

NETWORK

Opportunities, Contacts, Directions

$\Rightarrow$ **Engagement and personal effectiveness**

Thank you for your attention!