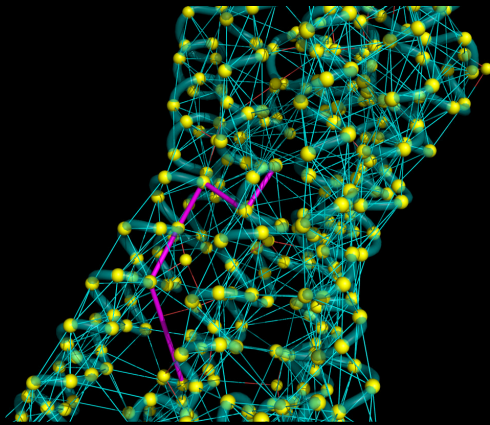
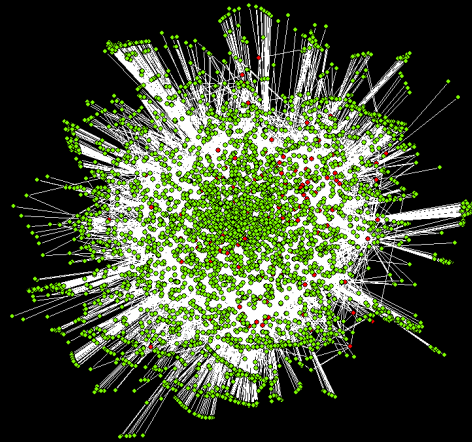


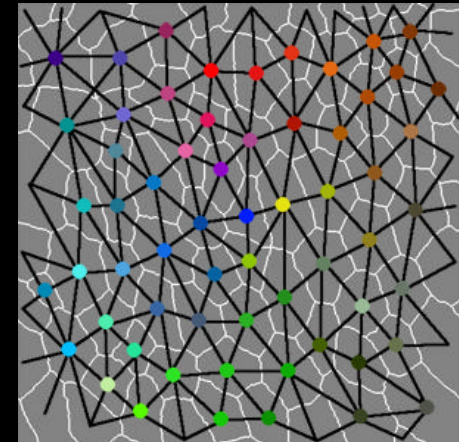
Uncovering organizing principles in biological systems by applying network theory at different scales



Atomic interaction network
 $\sim \text{\AA}$ (10^{-10} m)



Molecular interaction network
 $\sim \text{nm}$ (10^{-9} m)



Cellular interaction network
 $\sim \mu\text{m}$ (10^{-6} m)

CNN, Cambridge, 27 Sep 2011

M. Madan Babu

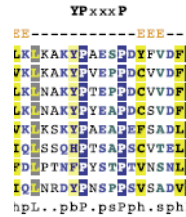
Senior Investigator

MRC Laboratory of Molecular Biology, Cambridge, UK

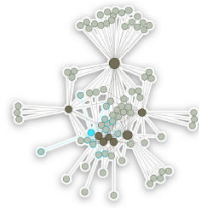
Regulatory Genomics and Systems Biology

Molecular Level

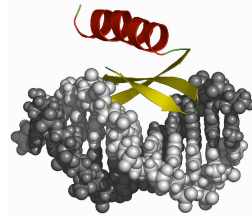
Discover new features of regulatory proteins



Molecular Cell (2008)



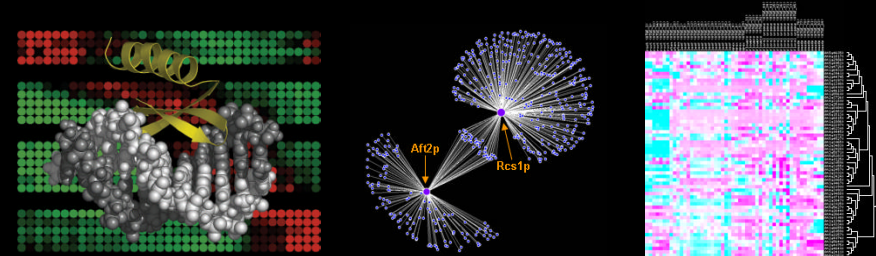
Cell Stem Cell (2010)



EMBO J (2011)

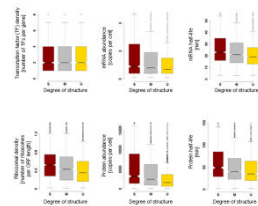
Molecules & regulation

- Defining features of regulatory proteins

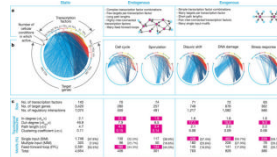


Systems Level

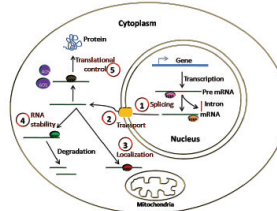
Principles of regulation for cellular homeostasis



Science (2008)



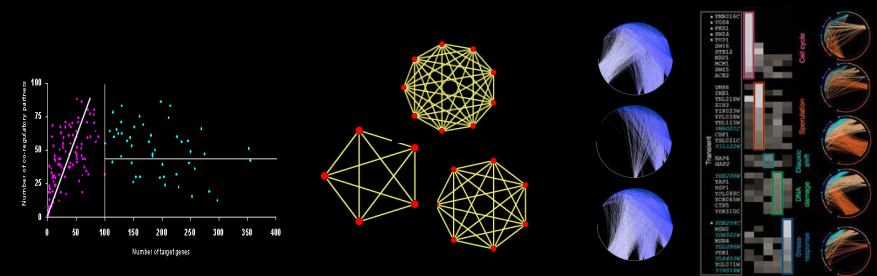
Nature (2004)



PNAS (2009)

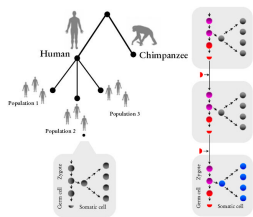
Systems & regulation

- Principles of regulation in cellular systems

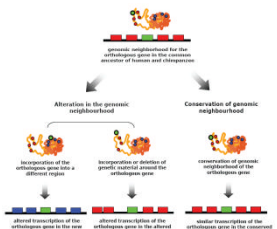


Genome Level

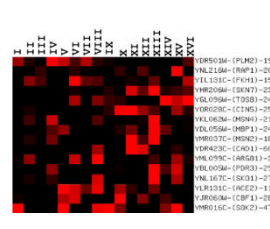
Regulation and genome evolution



PNAS (2010)



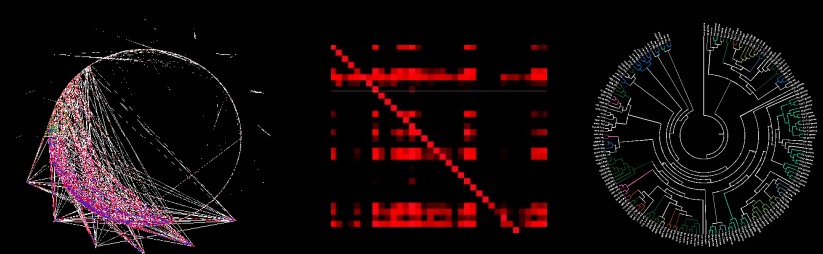
Genome research (2009)



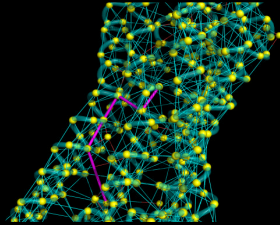
PNAS (2008)

Genomes & regulation

- Interplay between regulation and genome evolution

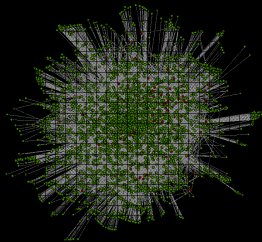


Outline



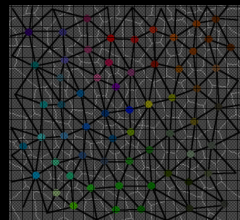
Atomic interaction network
 $\sim \text{\AA}$ (10^{-10} m)

Application of network approach to understand conformation changes in proteins



Molecular interaction network
 $\sim \text{nm}$ (10^{-9} m)

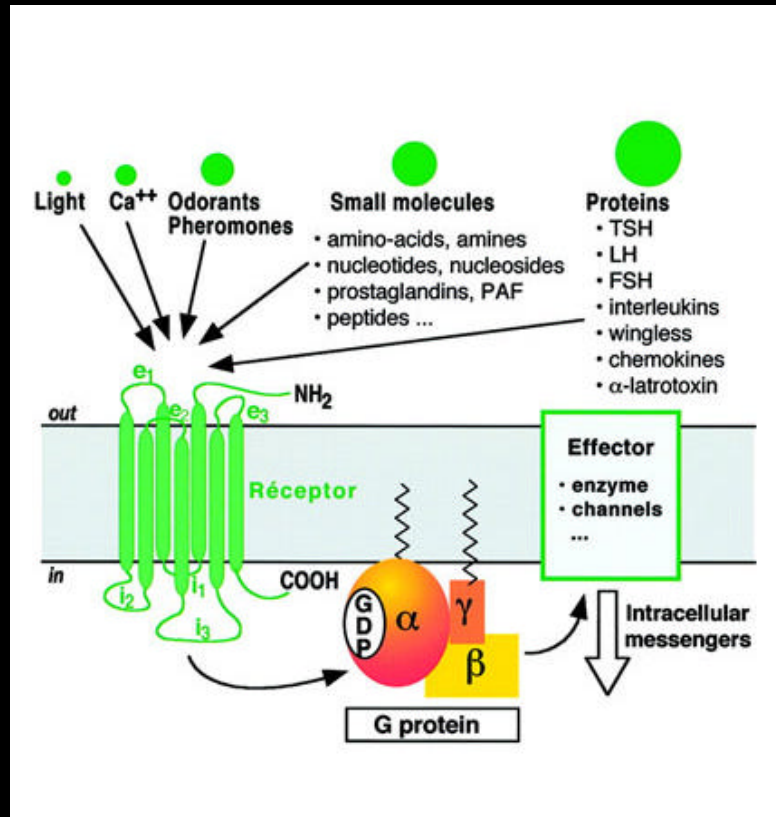
Application of network approach to understand the dynamics of molecular interaction networks



Cellular interaction network
 $\sim \mu\text{m}$ (10^{-6} m)

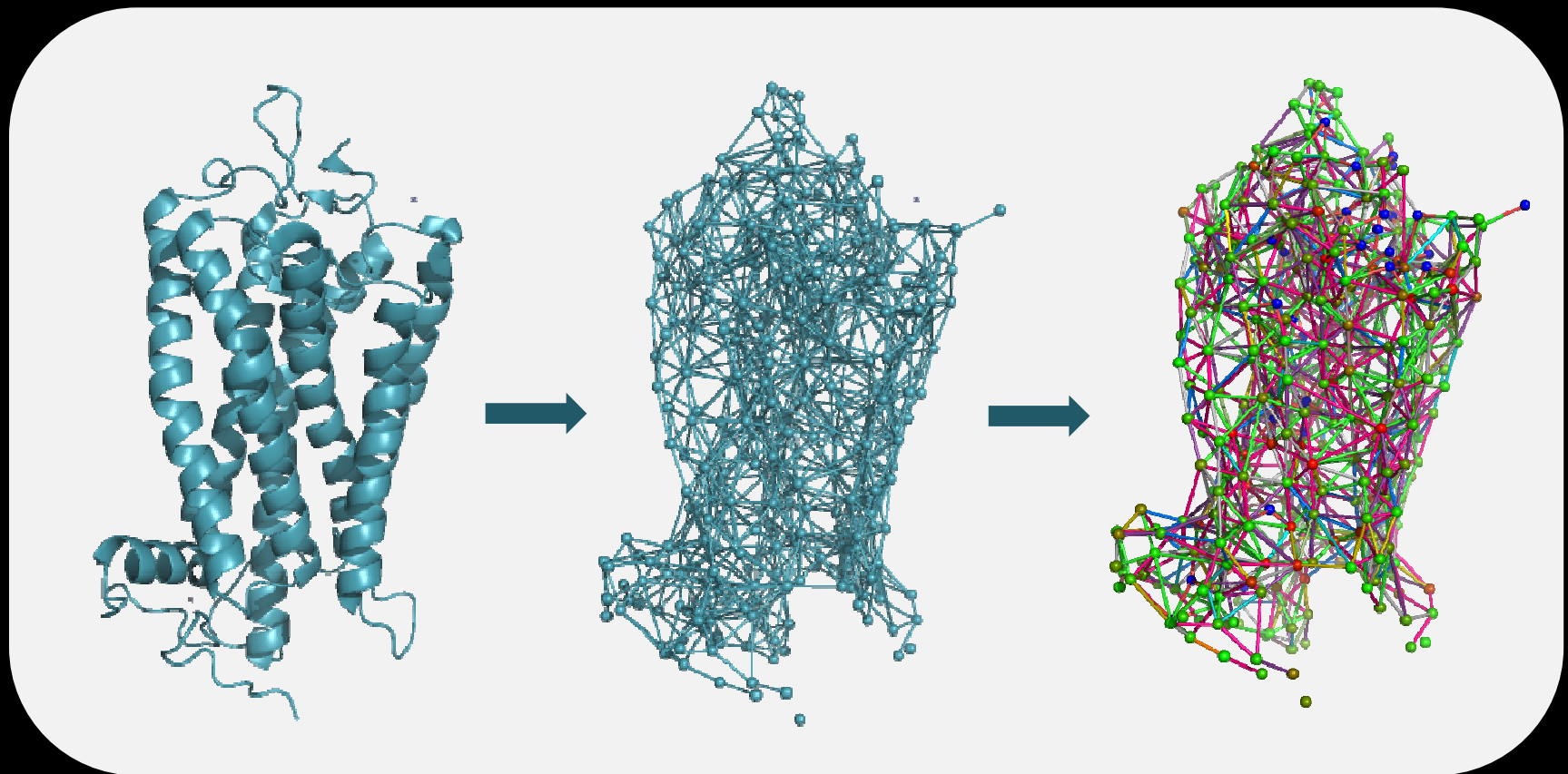
Application of network approach to understand patterns in cell-to-cell contacts during development

Conformational changes in proteins

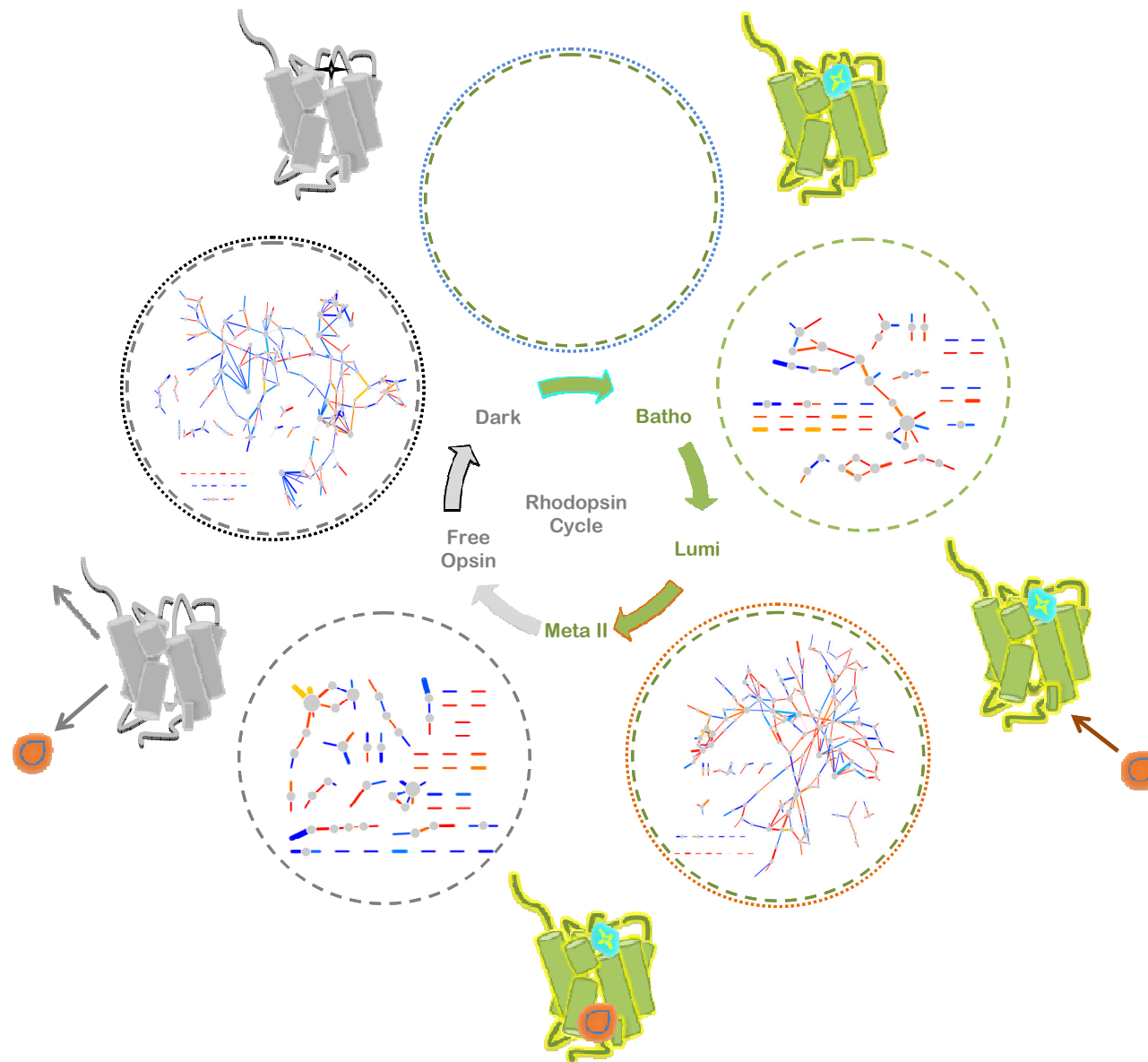


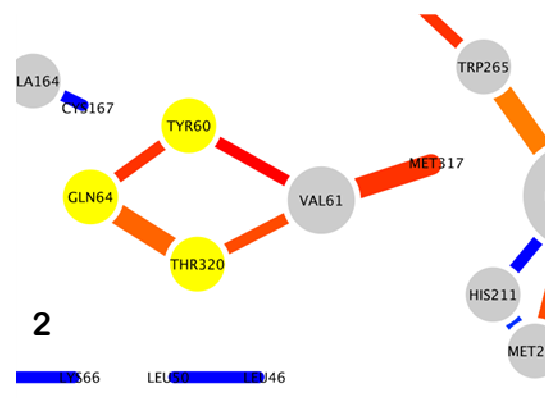
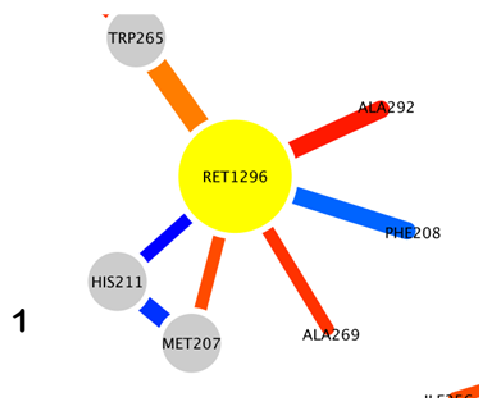
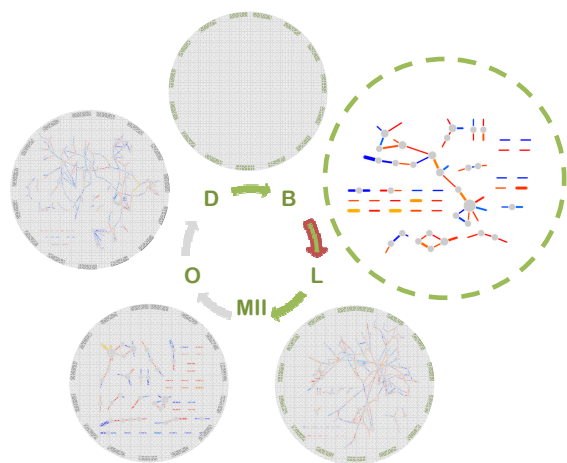
GPCR – an evolutionary success

To understand the conformational cycle in GPCR activation by investigating how the atomic interaction network changes in the different structures

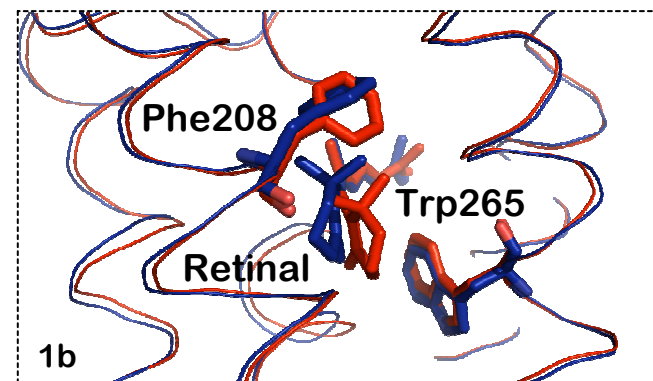
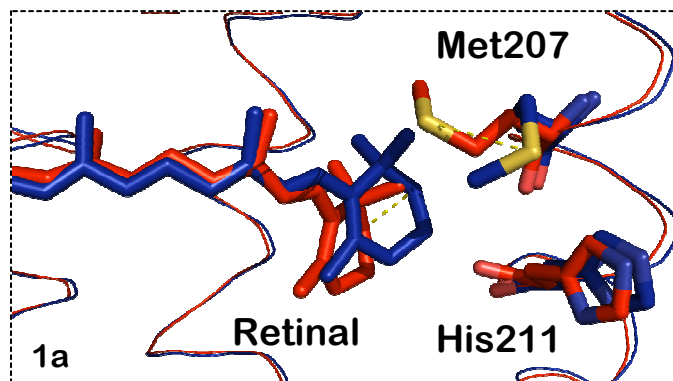
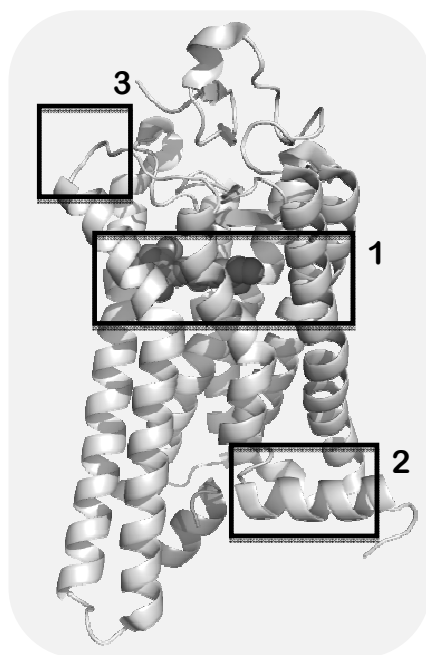


Network alignment and comparison

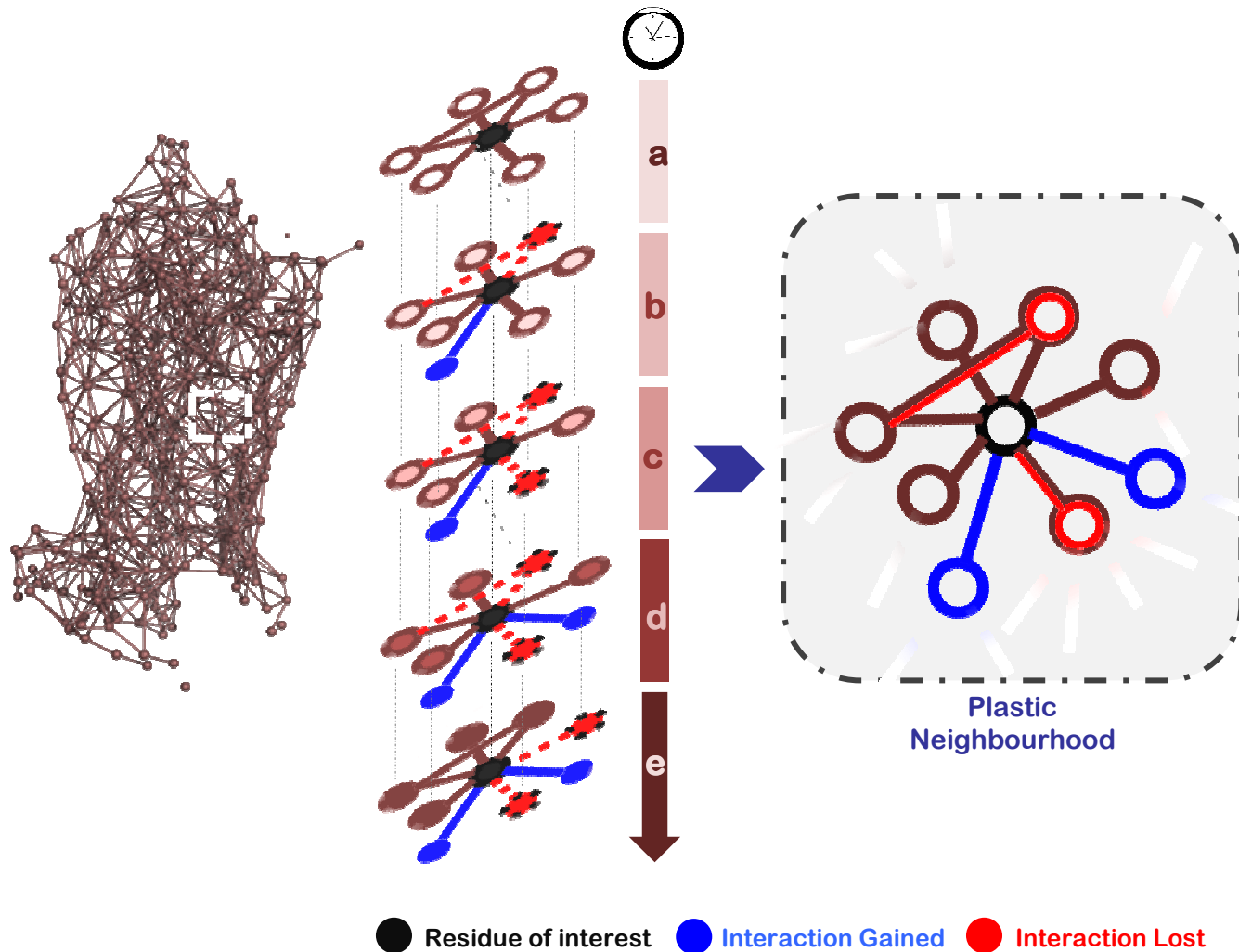




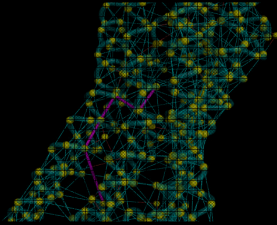
Removed: 44, Added: 24



Which are the key residues participating in the activation processes?

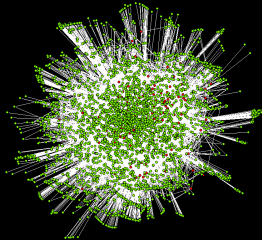


Outline



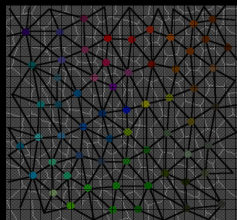
Atomic interaction network
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Cellular interaction network
 $\sim \mu\text{m}$ (10^{-6} m)

Application of network approach to understand patterns in cell-to-cell contacts during development

Molecular interaction networks in biology

Network

Nodes 

Links 

Protein Interaction

Proteins

Physical Interaction

Metabolic

Metabolites

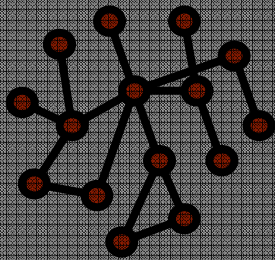
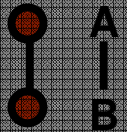
Enzymatic conversion

Transcriptional

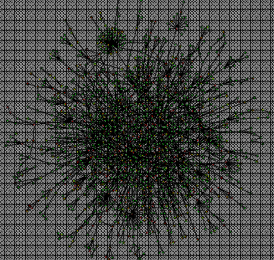
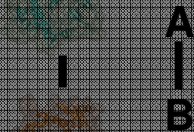
Transcription factor
Target genes

Transcriptional
Interaction

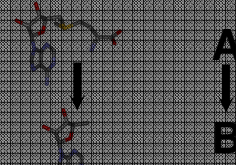
Interaction



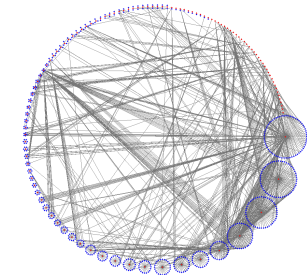
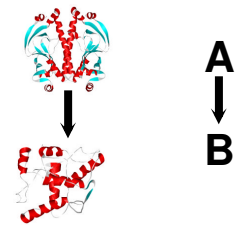
Protein-Protein



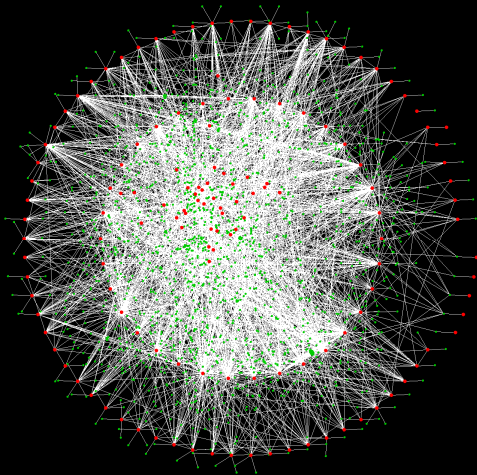
Protein-Metabolite



Protein-DNA



To understand the dynamics of the gene regulatory network in different time scales by investigating how network structure change in different time scales



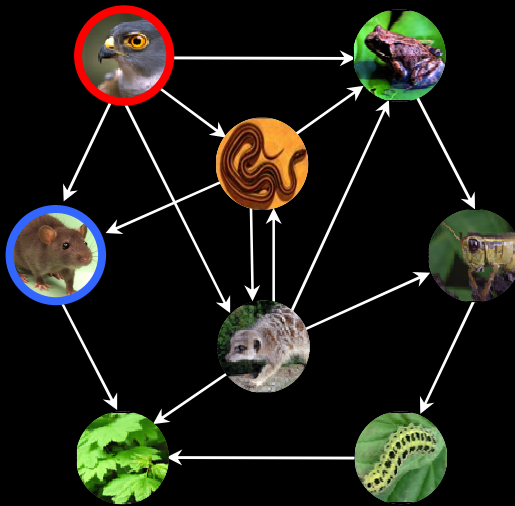
Transcriptional network

- Time scale of the evolution of species (\sim million years)
sequence information; *Nat Gen* 2004
- Time scale of the life of an organism (\sim hours or days)
expression information; *Nature* 2004
- Time scale of the life of molecules (\sim minutes)
Kinetic information; *Mol Sys Biol* 2009

Methods to infer hierarchical organization in networks

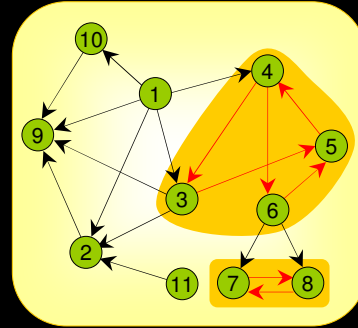
Food web network

predator \longrightarrow prey



Topological Sort: An approach to infer hierarchical organization in networks

1. Identify strongly connected components (SCCs)



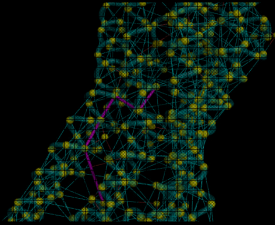
Classify Directed Acyclic Graph

Invert the layers

Remove nodes that are children of all nodes

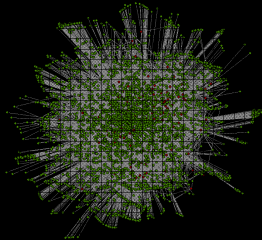
Remove nodes that are children of only one node

Outline



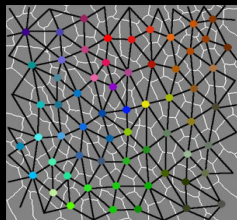
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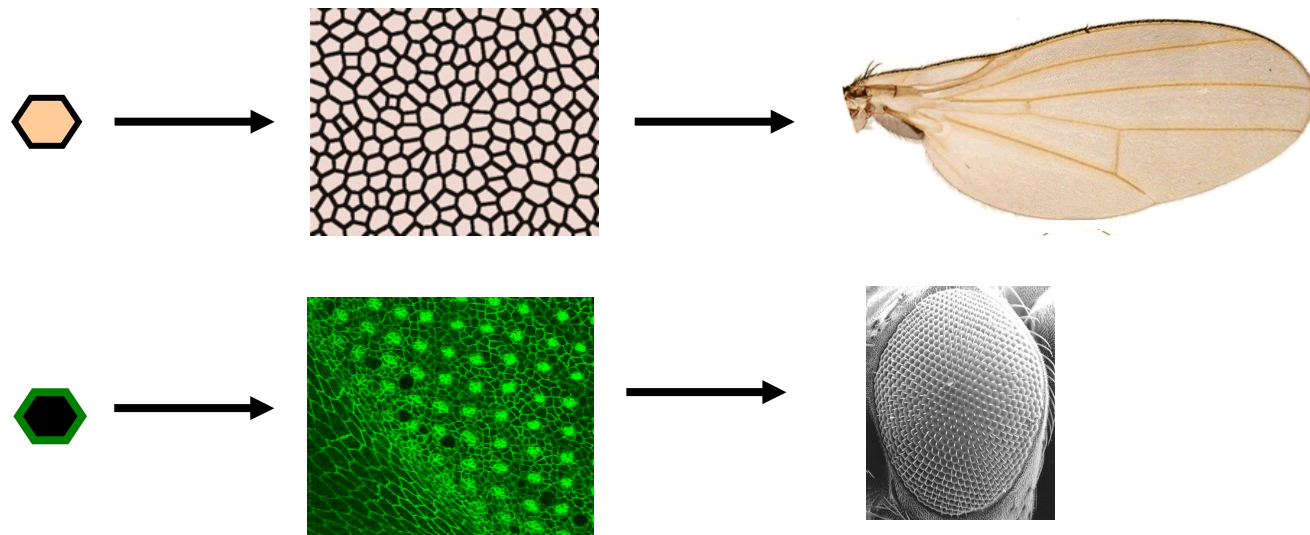
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Cellular interaction network
 $\sim \mu\text{m}$ (10^{-6} m)

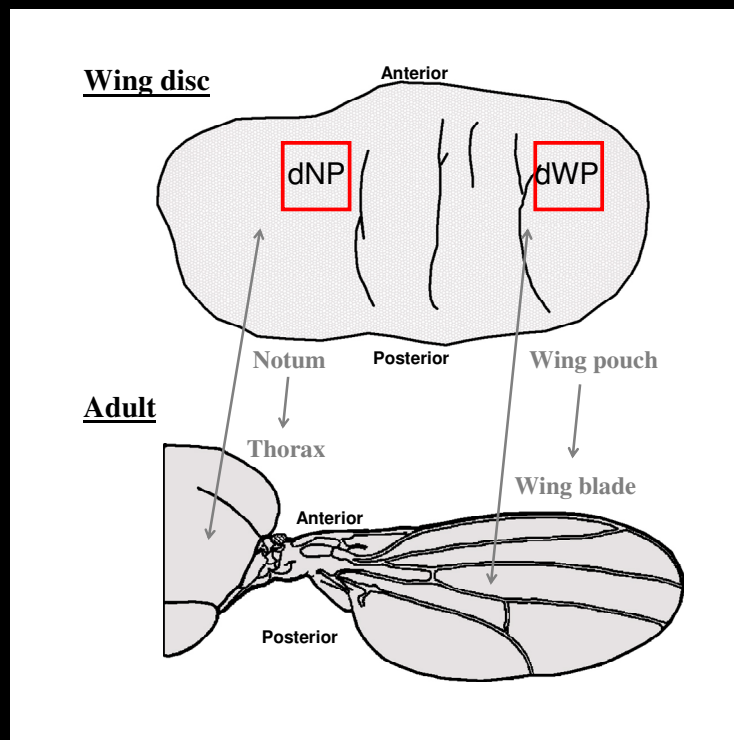
Application of network approach to understand patterns in cell-to-cell contacts during development

Patterns in the organisation of cells forming an epithelia

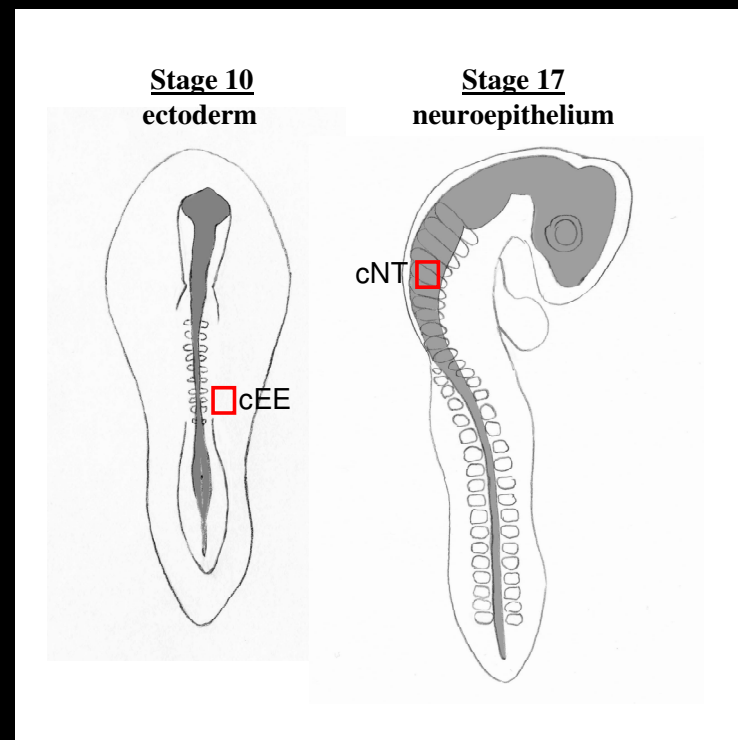


The emergence of differences in arrangement of cells is the first step towards establishment of many organs. Understanding this process is limited by the lack of systematic characterization of epithelial organisation.

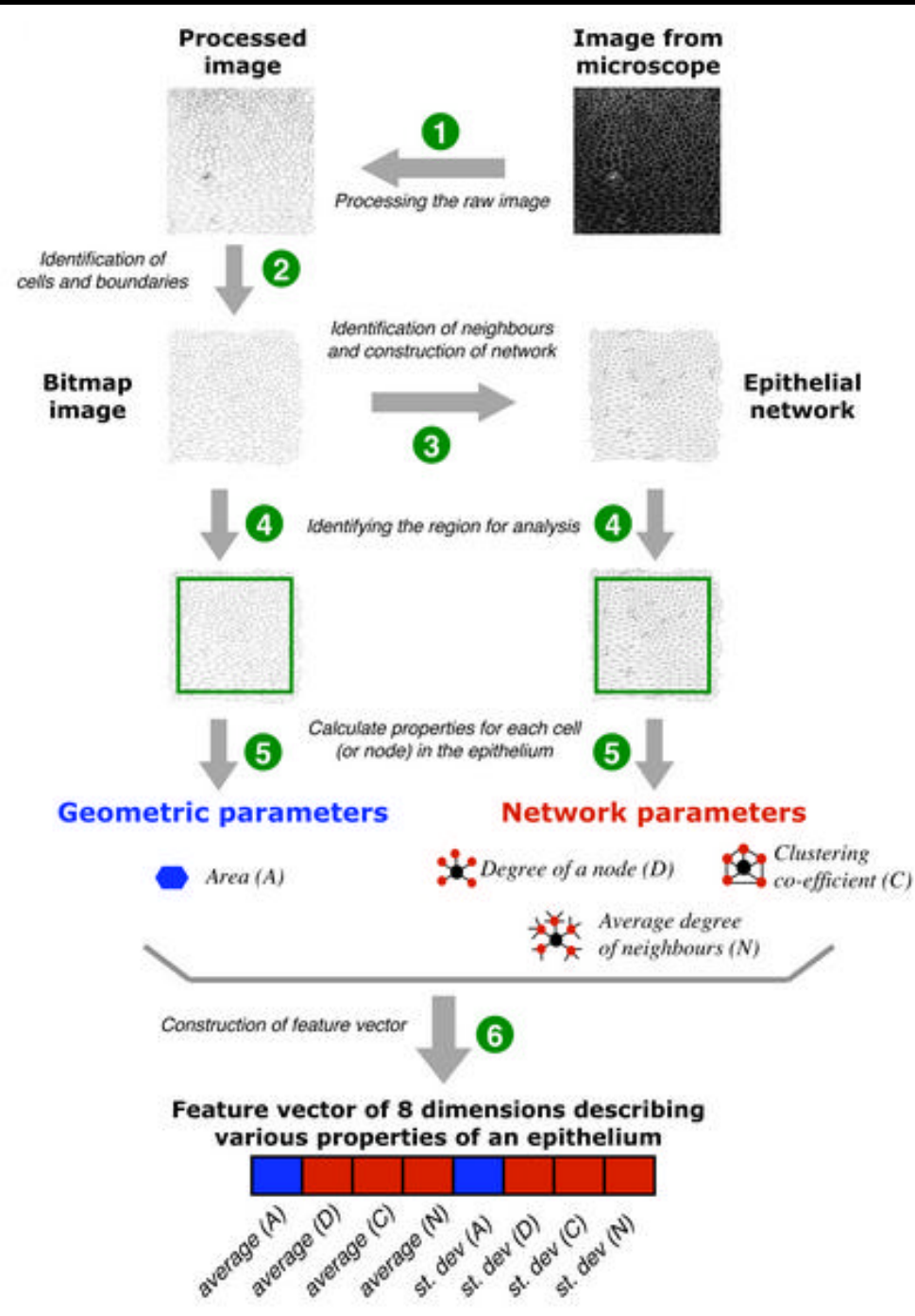
To understand organization of cells in epithelia of different types that are separated spatially, temporally and genetically perturbed by investigating topological patterns in the network of cellular contacts from different organisms



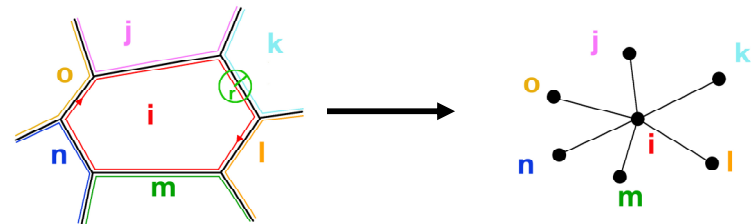
Drosophila

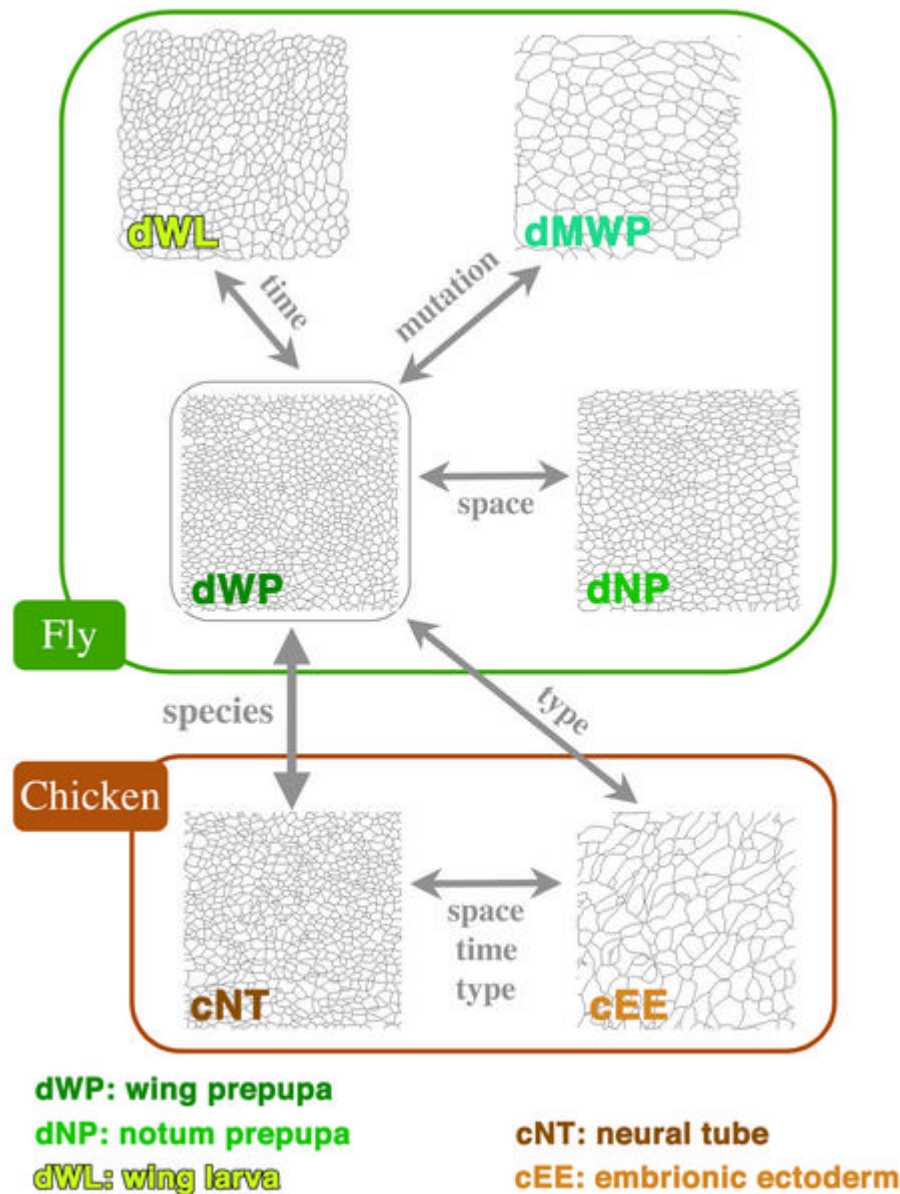


Chicken



Cell contact network

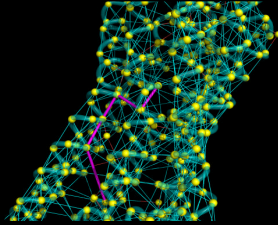




The features of individual cells, together with attributes of the cellular network produce a defining signature that distinguishes epithelia from different organs, species, developmental stages and genetic conditions.

The approach permits characterization, quantification and classification of normal and perturbed epithelia and establishes a framework for understanding molecular mechanisms that underpin the architecture of complex tissues.

Acknowledgements

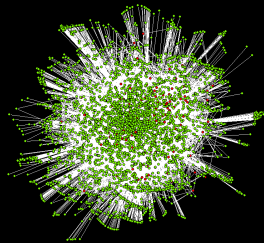


Atomic interaction network



A J Venkatakrishnan
Gebhard Schertler
Jorg Standfuss

*A J Venkatakrishnan et al,
unpublished*

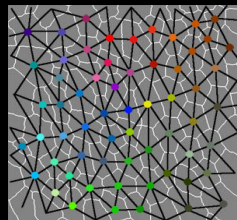


Molecular interaction network



Raja Jothi
Balaji Santhanam
Teresa Prytycka
Arthur Wuster
Joerg Gsponer
L Aravind

*Jothi et al,
Mol Sys Biol, 2009*



Cellular interaction network



Luisma Escudero
Luciano Costa
Anna Kicheva
James Briscoe
Matthew Freeman

*Escudero et al,
Nature Communications, in press*

Regulatory Genomics and Systems Biology Group

STRUCTURAL
STUDIES



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Regulatory Genomics & Systems Biology

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Post-doctoral Scientist
2010-2013



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Post-doctoral Scientist
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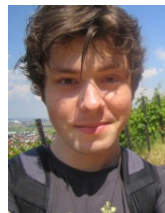
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2010-2013



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Masters Student
2010-2011



Katie Weber
Joint PhD Student
2007-2010



Benjamin Lang
PhD Student
2008-2011



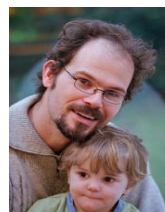
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PhD Student
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Guilhem Chalancon
Masters Student
2009-2011



Charles Ravarani
Masters Student
2010-2010



Sven Sewitz
Post-doc
2011

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Rekin's Janky, Post-doctoral Scientist, 2007-2010

Sarath Janga PhD Student, 2007-2010

Marie Schrynemackers, Masters Student, 2010

Subhajyoti De, Associate post-doc, 2008-2010

Joerg Gsponer, Associate post-doc, 2008-2009

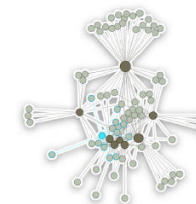
Nitish Mittal, Visiting PhD student, 2008-2009

Matthias Futschik, Visiting scientist, 2007

Henning Claussen, Visiting student, 2007

Pradeep Kota, Visiting student, 2007

...and members of the **Theoretical and Computational Biology group** at the LMB for helpful discussions



UNIVERSITY OF
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Philippe Wiener - Maurice Anspach



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