UNIVERSITÀ DEGLI STUDI DI PADOVA

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

Population models for complex non-linear phenomena in biology: from mitochondrial dynamics to brain networks

Chiara Favaretto

Advisor: Prof. Angelo Cenedese

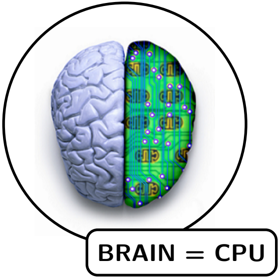
Padova - February, 22nd, 2018

Motivation

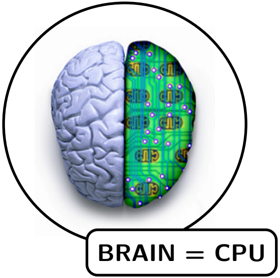
Motivation

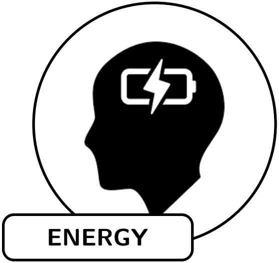

VENERATION
BENEVOLENCE
HOPE
FIRMNESS
SUBLIMITY
MIRTHFULNESS
REFLECTIVES
CAUSALITY
IDEALITY
ACQUISITIVENESS
DESTRUCTIVENESS
TIME
LOCALITY
EVENTUALITY


VENERATION
BENEVOLENCE
SUBLIMITY
ACQUISITIVENESS
FIRMNESS


BRAIN = CPU

Motivation





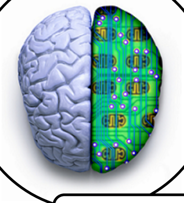
Motivation

COMPLEXITY

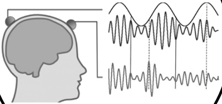
BRAIN = CPU

ENERGY

COMPLEXITY



BRAIN = CPU



OSCILLATIONS

ENERGY

What if something goes wrong?

Alzheimer

What if something goes wrong?

Alzheimer

Stroke

What if something goes wrong?

Alzheimer

Stroke

What if something goes wrong?

Parkinson's Disease

Alzheimer

Stroke

What if something goes wrong?

Parkinson's Disease

... and many others ...

State of the Art:

State of the Art:

- we still don't know how to treat them

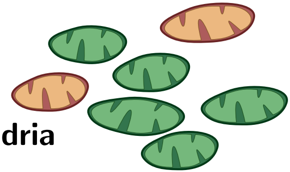
State of the Art:

- we still don't know how to treat them
- we still don't know how to predict them

State of the Art:

- we still don't know how to treat them
- we still don't know how to predict them
- they are related to energy-impairment

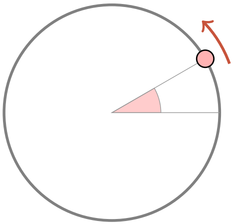
mitochondria



State of the Art:

- we still don't know how to treat them
- we still don't know how to predict them
- they are related to energy-impairment
- they are related to wrong oscillatory patterns

phase models



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Our Aim

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Our Aim

To make use of Systems Theory to analyze and characterize some aspects on the complex relationship

BRAIN $\longleftrightarrow$ ENERGY

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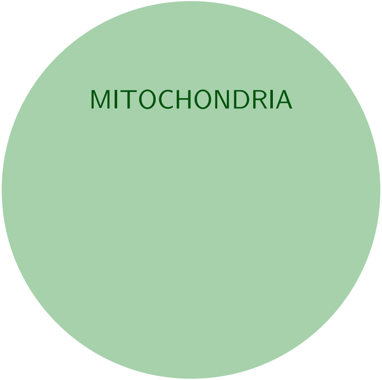
Our Aim

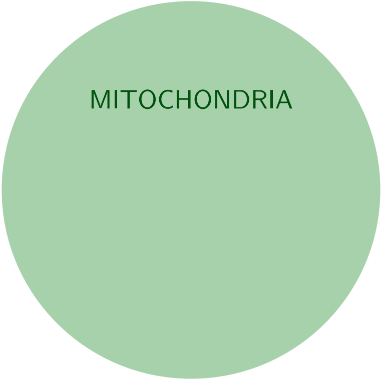
To make use of Systems Theory to analyze and characterize some aspects on the complex relationship

BRAIN $\longleftrightarrow$ ENERGY

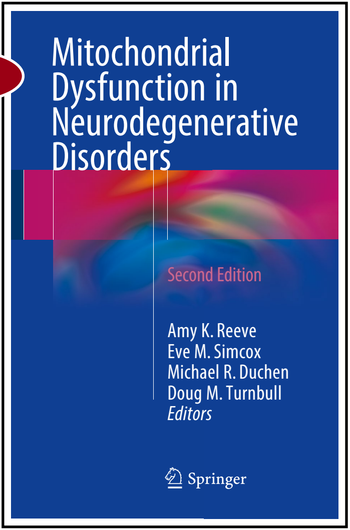
oscillations

Outline: how did we handle this goal?

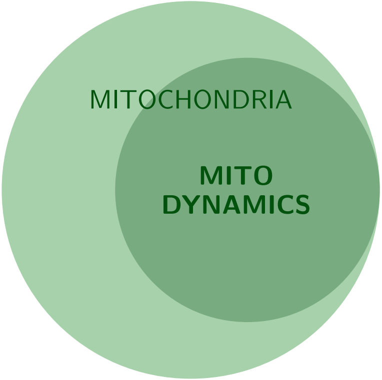



MITOCHONDRIA

2016


Mitochondrial Dysfunction in Neurodegenerative Disorders
Second Edition
Amy K. Reeve
Eve M. Simcox
Michael R. Duchen
Doug M. Turnbull
Editors
Springer

Outline: how did we handle this goal?



Outline: how did we handle this goal?

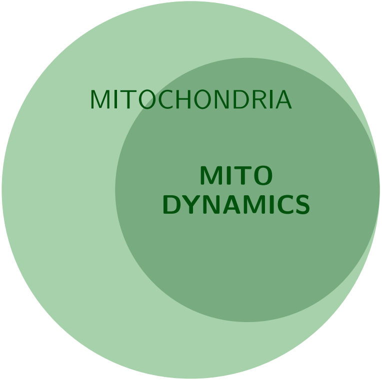
2013

Review

Cell

Mitochondrial dynamics in neurodegeneration

Kie Itoh[1], Ken Nakamura[2,3], Miho Iijima[1], and Hiromi Sesaki[1]



Outline: how did we handle this goal?

Review

Mitochondrial dynamic
neurodegeneration

Kie Itoh[1], Ken Nakamura[2,3], Miho Iijima[1], and Hir

2015

REVIEWS

Disturbed mitochondrial dynamics and neurodegenerative disorders

Florence Burté, Valerio Carelli, Patrick F. Chinnery and Patrick Yu-Wai-Man

frontiers in Aging Neuroscience

REVIEW
published: 10 June 2015
doi: 10.3389/fnagi.2015.00101

Implications of mitochondrial dynamics on neurodegeneration and on hypothalamic dysfunction

Antonio Zorzano[1,2,3*] and Marc Claret[3,4*]

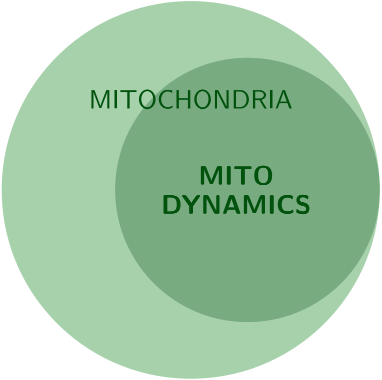
AIMS Molecular Science DOI: 10.3934/molsci.2015.2.161

Received date 17 March 2015, Accepted date 4 May 2015, Published date 7 May 2015

Review

Mitochondrial dynamics in neurodegeneration: from cell death to energetic states

Mireille Khacho and Ruth S. Slack *



© 2017. Published by The Company of Biologists Ltd | Journal of Cell Science (2017) 130, 671-681 doi:10.1242/jcs.171017

The Company of Biologists

COMMENTARY

Mitochondrial dynamics in neuronal injury, development and plasticity

Kyle H. Flippo and Stefan Strack*

REVIEWS

...ial dynamics

Kie Itoh[1], Ken Nakamura[2,3], Miho Iijima[1], and Hiromi Sesaki[1]

2017

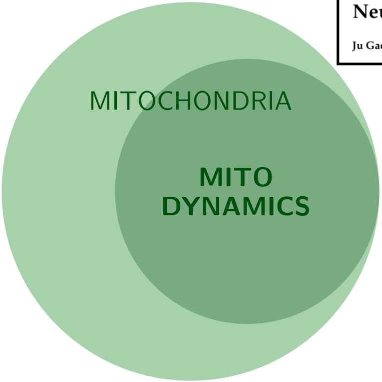
antioxidants

MDPI

Review

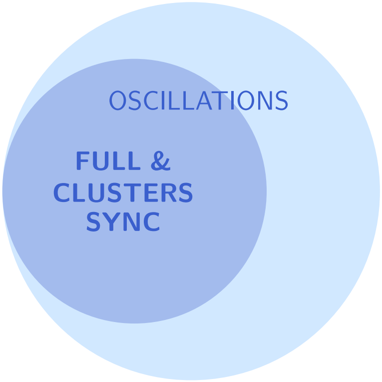
Abnormalities of Mitochondrial Dynamics in Neurodegenerative Diseases

Ju Gao [1], Luwen Wang [1], Jingyi Liu [1], Fei Xie [1], Bo Su [2] and Xinglong Wang [1,*]




OSCILLATIONS

Outline: how did we handle this goal?



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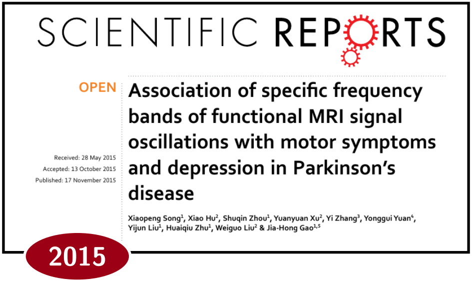

SCIENTIFIC REPORTS

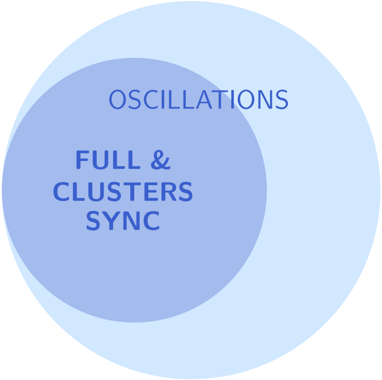
OPEN

Association of specific frequency bands of functional MRI signal oscillations with motor symptoms and depression in Parkinson's disease

Received: 28 May 2015
Accepted: 13 October 2015
Published: 17 November 2015

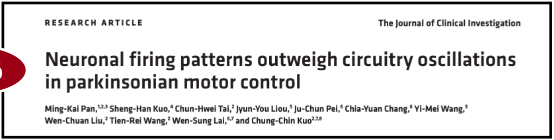
Xiaopeng Song[1], Xiao Hu[2], Shuqin Zhou[1], Yuanyuan Xu[2], Yi Zhang[3], Yonggui Yuan[4], Yijun Liu[1], Huaiqiu Zhu[1], Weiguo Liu[2] & Jia-Hong Gao[1,5]

2015



Outline: how did we handle this goal?

2016


RESEARCH ARTICLE

The Journal of Clinical Investigation

Neuronal firing patterns outweigh circuitry oscillations in parkinsonian motor control

Ming-Kai Pan,[1,2,3] Sheng-Han Kuo,[4] Chun-Hwei Tai,[2] Jyun-You Liou,[5] Ju-Chun Pei,[6] Chia-Yuan Chang,[6] Yi-Mei Wang,[3] Wen-Chuan Liu,[2] Tien-Rei Wang,[2] Wen-Sung Lai,[6,7] and Chung-Chin Kuo[2,7,8]

SCIENTIFIC REPORTS

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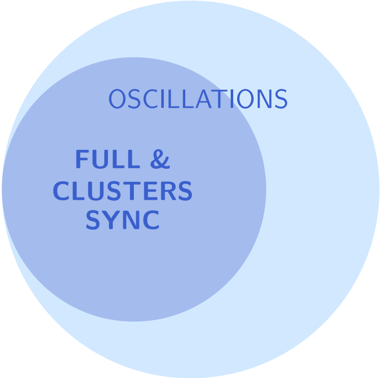

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RESEARCH ARTICLE — The Journal of Clinical Investigation

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Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

2017

Alzheimer's disease disrupts alpha and beta-band resting-state oscillatory network connectivity

Loes Koelewijn [a,*], Aline Bompas [a], Andrea Tales [b], Matthew J. Brookes [c], Suresh D. Muthukumaraswamy [d], Antony Bayer [e], Krish D. Singh [a]

SCIENTIFIC REPORTS

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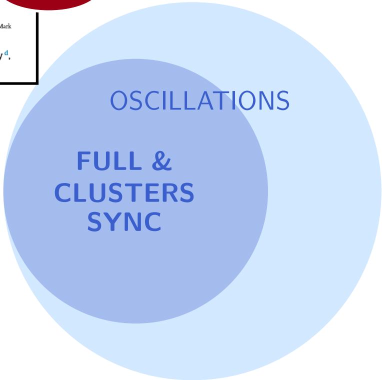
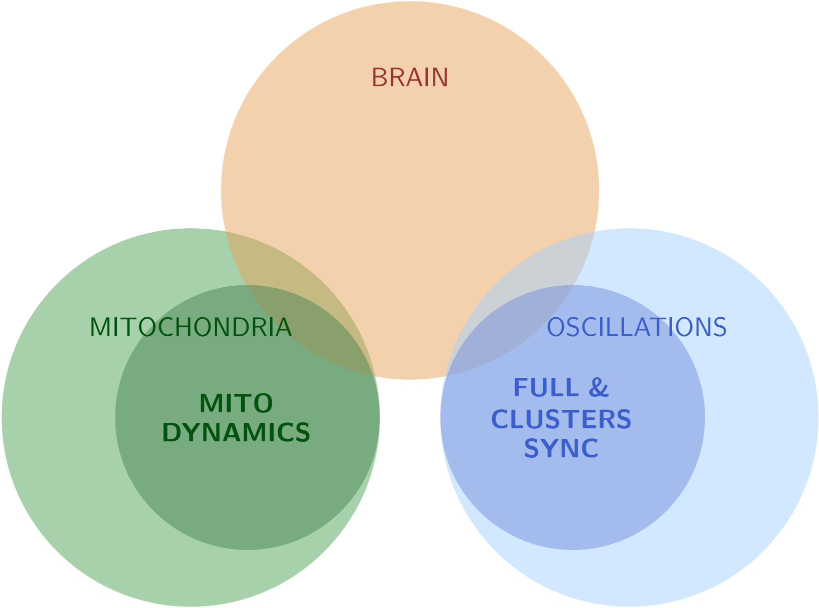
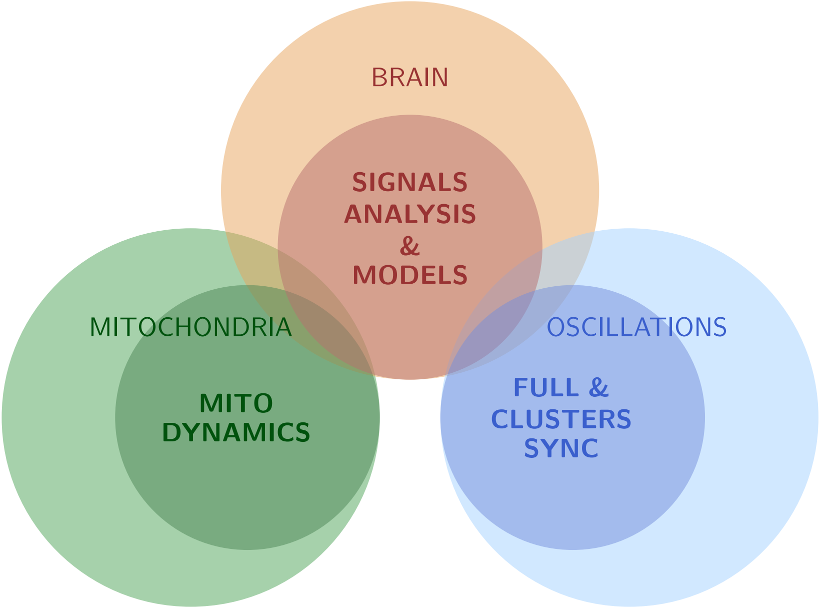
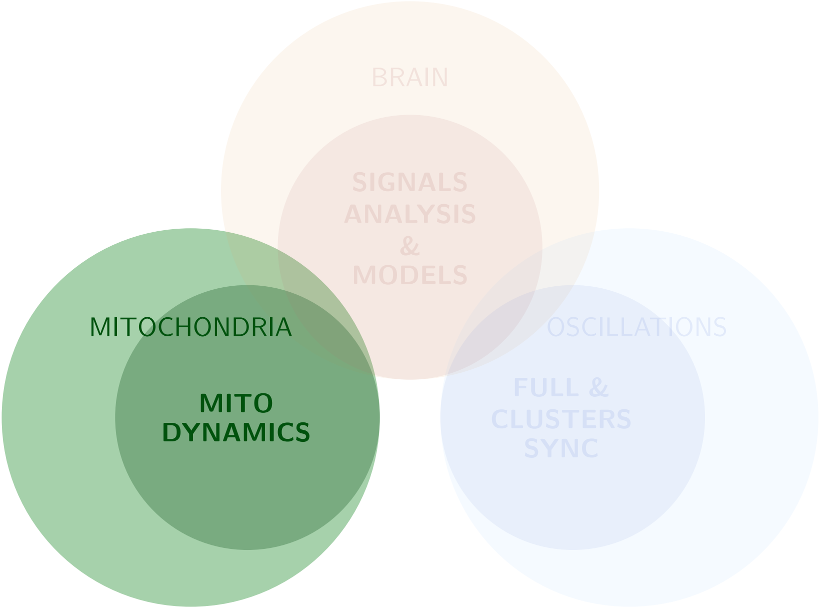



BRAIN
MITOCHONDRIA
OSCILLATIONS
MITO
DYNAMICS
FULL &
CLUSTERS
SYNC

Outline: how did we handle this goal?

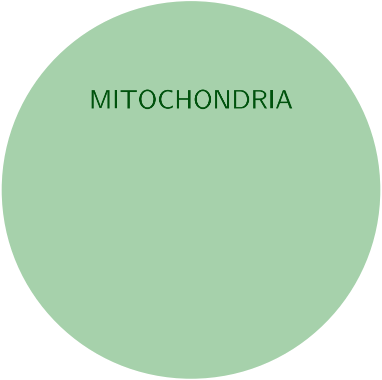


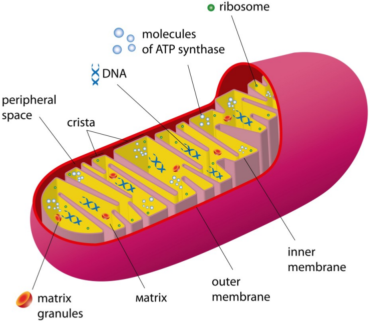
Mitochondria & Mitochondrial Dynamics



Mitochondria & Mitochondrial Dynamics

- double membrane-bound organelles found in all eukaryotic organisms
- possess their own genome (mitochondrial DNA)

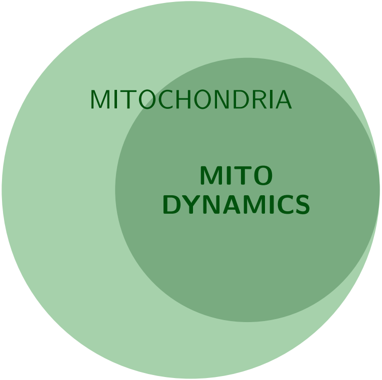


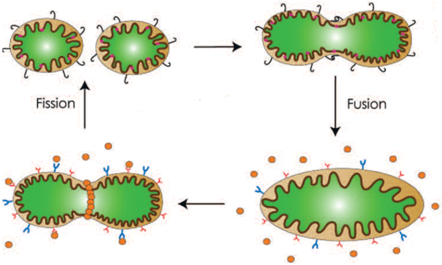


Mitochondrion

- involved in several tasks
- generate most of the cells supply of ATP (= energy)

Mitochondria & Mitochondrial Dynamics





ACNR 2014;V14(1):6-8

- constant changes in shape, size, number and location
- affected by mitochondrial morphology
- controlled mainly by the processes of fission and fusion

Models of Mitochondrial Dynamics in the Literature

- M. T. Figge et al. *PLoS Comput Biol*, 2012
- A. K. and T. B. L. Kirkwood. *PNAS*, 2011
- P. K. Mouli et al. *Biophysical Journal*, 2009
- P. K. Patel et al. *PLoS Comput Biol*, 2013
- V. M. Sukhorukov et al. *PLoS Comput Biol*, 2012
- Z. Y. Tam et al. *PLoS ONE*, 2013
- Z. Y. Tam et al. *PLoS Comput Biol*, 2013
- G. Dalmasso et al. *PLoS ONE*, 2017

Drawbacks of the proposed models

- M. T. F
- A. K. a
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- P. K. Patel et al. *PLoS Comput Biol*, 2013
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Drawbacks of the proposed models

- not analytically analyzable
- hard to understand by biologists
- need artificial constraints to avoid instability

Models of Mitochondrial Dynamics in the Literature

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V. M. Sukhorukov et al. *PLoS Comput Biol*, 2012

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G. Dalmasso et al. *PLoS ONE*, 2017

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Our Contribution

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A. K. a

P. K. M

P. K. Patel et al. *PLoS Comput Biol* 2013

V. M. S

Z. Y. T

Z. Y. T

G. Dalm

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New mathematical model:

- analytically analyzable
- easy to understand by biologists
- complete and self-controlled

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P. K. M
P. K. Patel et al. PLoS Comput Biol 2013
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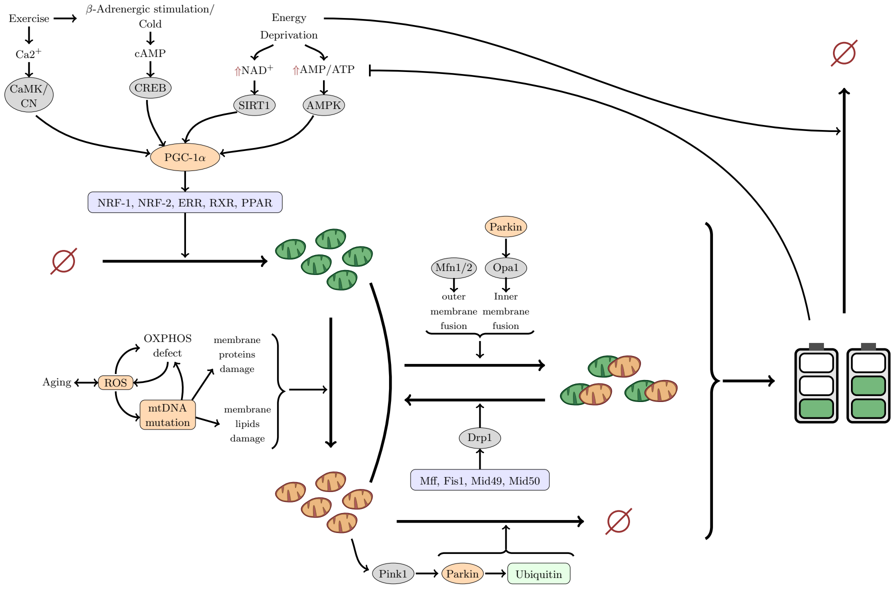
Mitochondrial Dynamics: the Model



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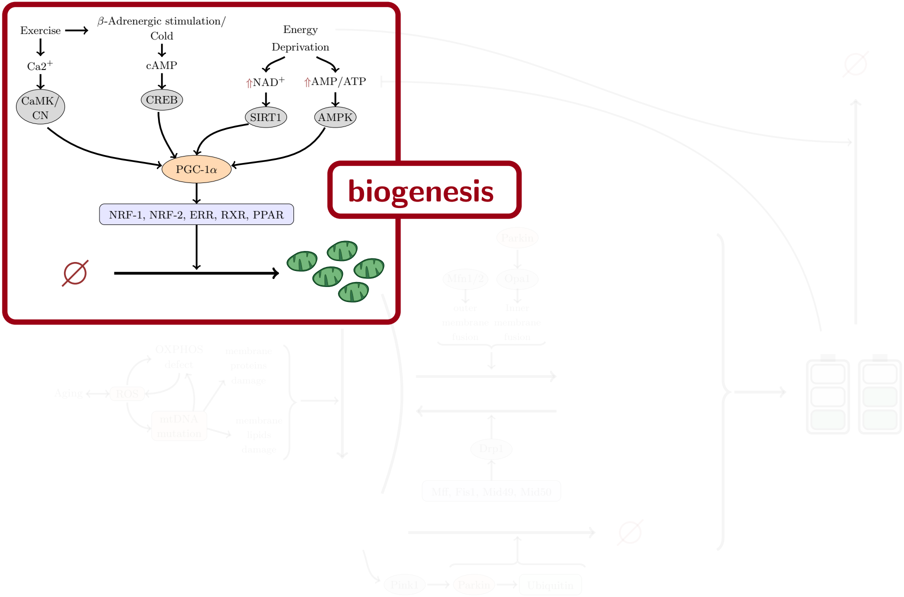

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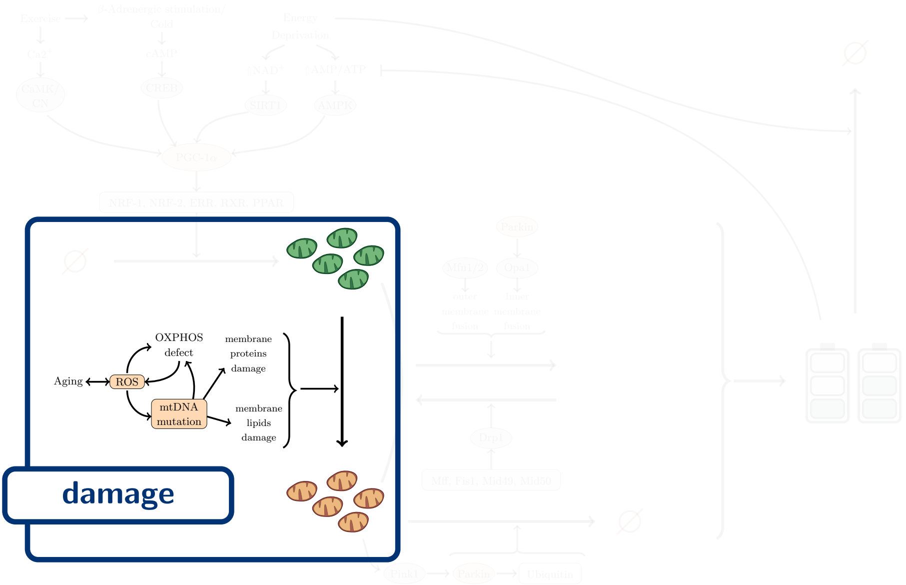
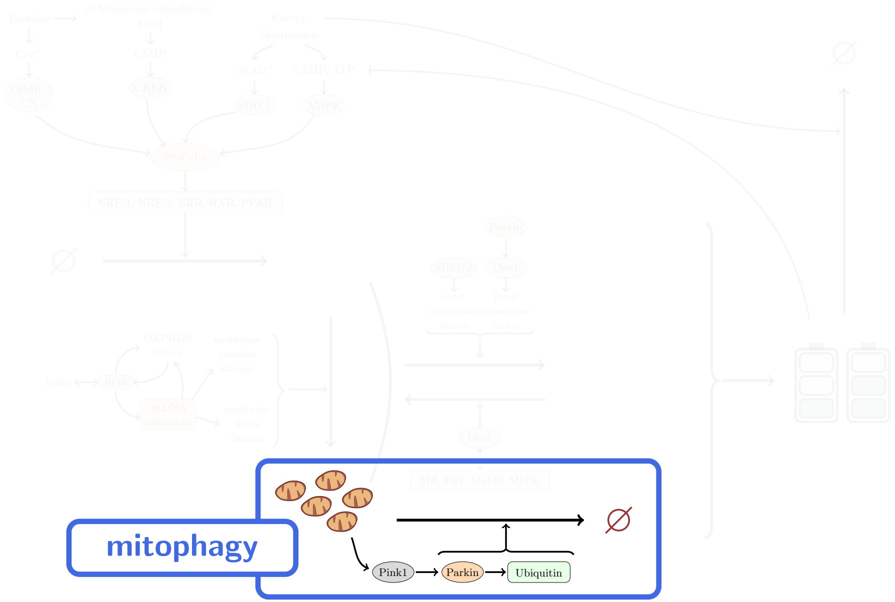
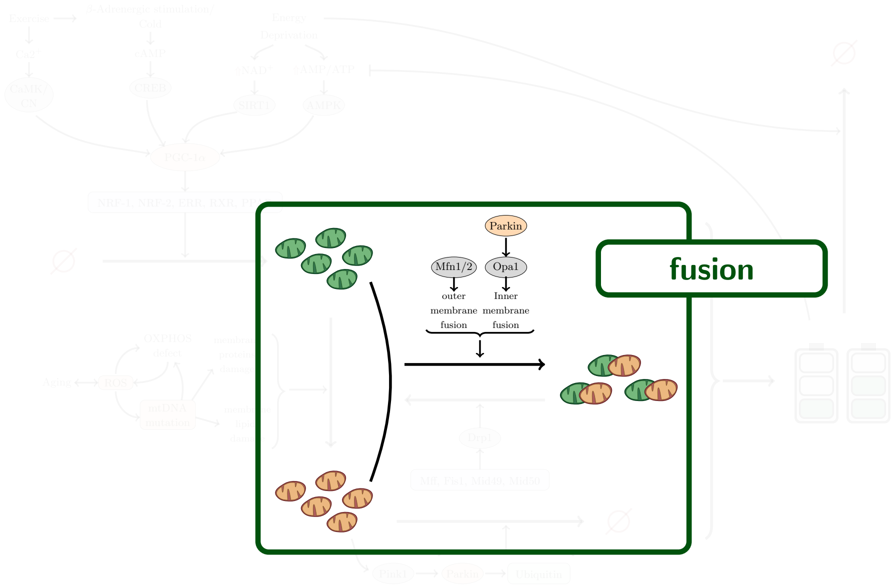




mitophagy
Pink1
Parkin
Ubiquitin

Mitochondrial Dynamics: the Model



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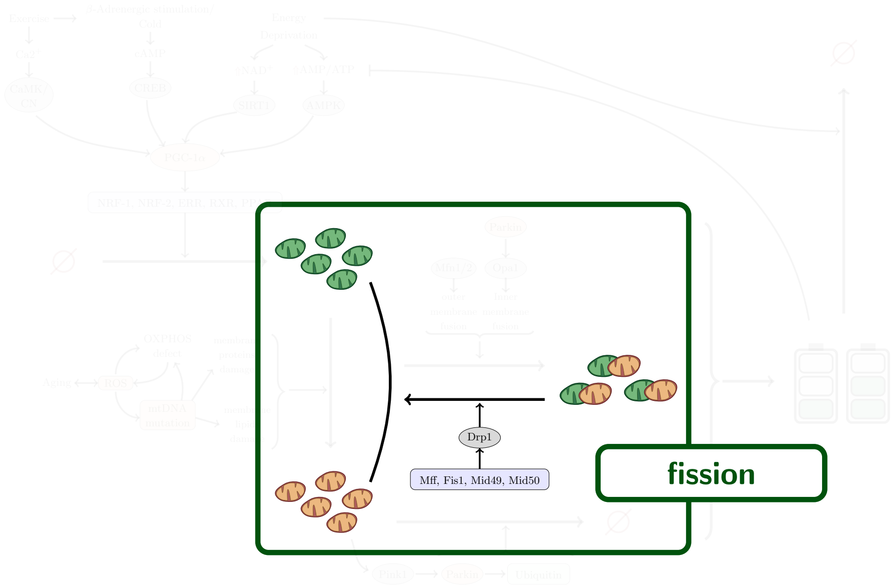

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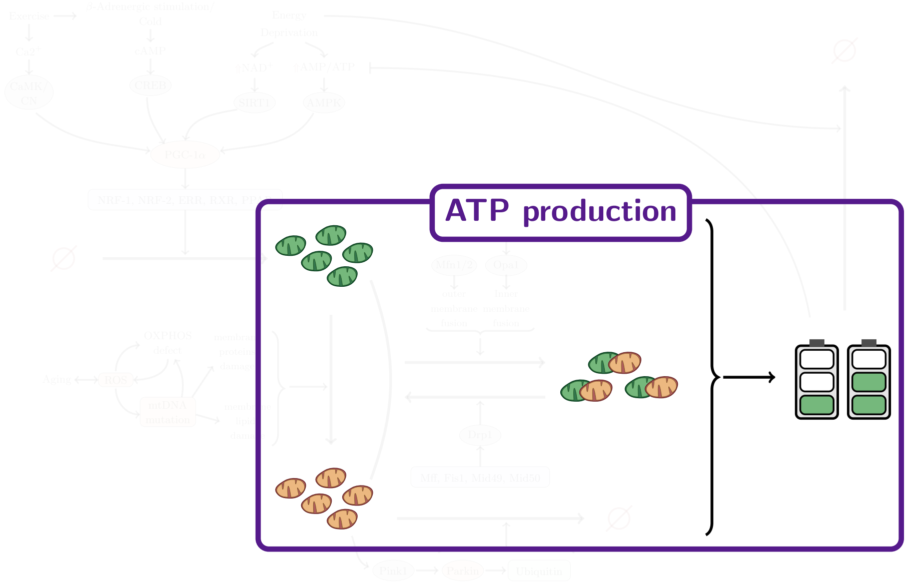

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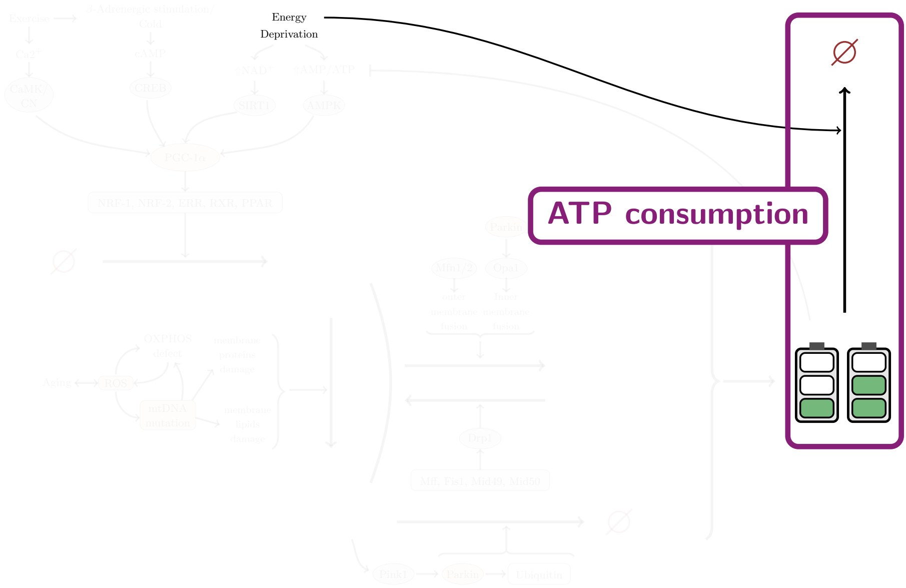

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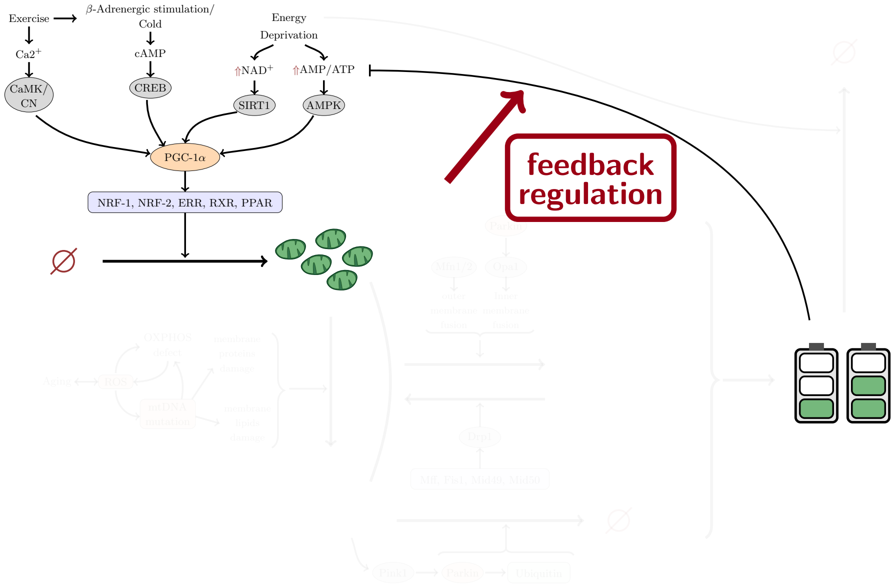

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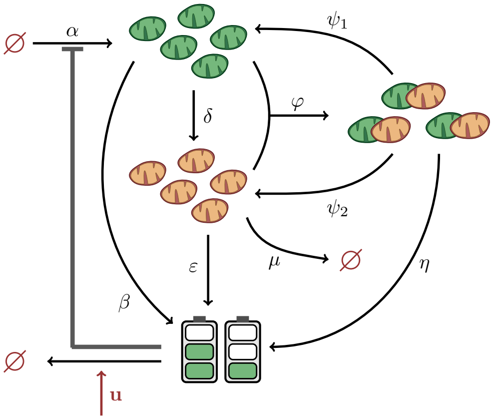


α: biogenesis

δ: damage

μ: mitophagy

φ: fusion

ψ_1, ψ_2: fission

β, η, ε: atp production

$\mathbf{u}$: energy stress

Differential equations

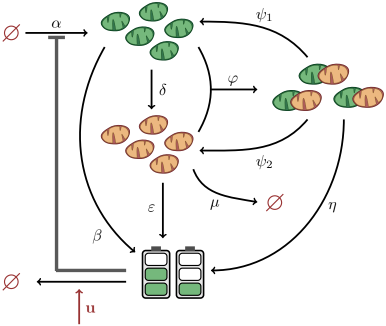
$$\dot{\mathbf{x}}_\mathbf{h} = \underbrace{\left(\alpha_0 + \frac{\alpha_1}{K + x_{\mathrm{ATP}}^n}\right) x_\mathrm{h}}_{\text{biogenesis}} + \underbrace{\psi_1 x_\mathrm{f}}_{\text{fission}} - \underbrace{\delta x_\mathrm{h}}_{\text{damage}} - \underbrace{\varphi x_\mathrm{h} x_\mathrm{d}}_{\text{fusion}}$$

$$\dot{\mathbf{x}}_\mathbf{d} = \underbrace{\delta x_\mathrm{h}}_{\text{damage}} + \underbrace{\psi_2 x_\mathrm{f}}_{\text{fission}} - \underbrace{\varphi x_\mathrm{h} x_\mathrm{d}}_{\text{fusion}} - \underbrace{\mu x_\mathrm{d}}_{\text{mitophagy}}$$

$$\dot{\mathbf{x}}_\mathbf{f} = \underbrace{\varphi x_\mathrm{h} x_\mathrm{d}}_{\text{fusion}} - \underbrace{(\psi_1 + \psi_2) x_\mathrm{f}}_{\text{fission}}$$

$$\dot{\mathbf{x}}_{\mathrm{ATP}} = \underbrace{\beta x_\mathrm{h} + \varepsilon x_\mathrm{d} + \eta x_\mathrm{f}}_{\text{atp production}} - \underbrace{\mathbf{u} \cdot x_{\mathrm{ATP}}}_{\text{atp use}}$$

x_h: healthy
x_d: damaged
x_f: fused
$\mathbf{u}$: input



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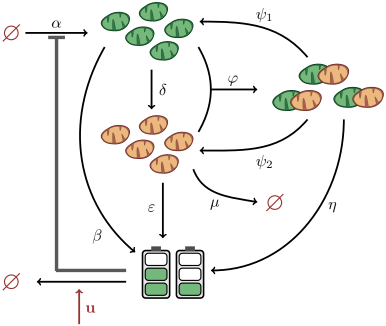
$$\dot{\mathbf{x}}_{\mathbf{f}} = \underbrace{\varphi x_{\mathrm{h}} x_{\mathrm{d}}}_{\text{fusion}} - \underbrace{(\psi_1 + \psi_2) x_{\mathrm{f}}}_{\text{fission}}$$

$$\dot{\mathbf{x}}_{\mathrm{ATP}} = \underbrace{\beta x_{\mathrm{h}} + \varepsilon x_{\mathrm{d}} + \eta x_{\mathrm{f}}}_{\text{atp production}} - \underbrace{\mathbf{u} \cdot x_{\mathrm{ATP}}}_{\text{atp use}}$$

x_{h}: healthy
x_{d}: damaged
x_{f}: fused
$\mathbf{u}$: input



Main issue:
nonlinearities $\longrightarrow$ complex stability analysis

Differential equations

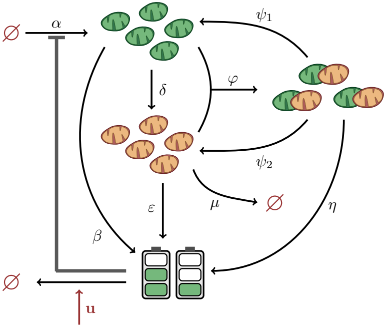
$$\dot{\mathbf{x}}_{\mathbf{h}} = \underbrace{\left(\alpha_0 + \frac{\alpha_1}{K + x_{\mathrm{ATP}}^n}\right) x_{\mathrm{h}}}_{\text{biogenesis}} + \underbrace{\psi_1 x_{\mathrm{f}}}_{\text{fission}} - \underbrace{\delta x_{\mathrm{h}}}_{\text{damage}} - \underbrace{\varphi x_{\mathrm{h}} x_{\mathrm{d}}}_{\text{fusion}}$$

$$\dot{\mathbf{x}}_{\mathbf{d}} = \underbrace{\delta x_{\mathrm{h}}}_{\text{damage}} + \underbrace{\psi_2 x_{\mathrm{f}}}_{\text{fission}} - \underbrace{\varphi x_{\mathrm{h}} x_{\mathrm{d}}}_{\text{fusion}} - \underbrace{\mu x_{\mathrm{d}}}_{\text{mitophagy}}$$

$$\dot{\mathbf{x}}_{\mathbf{f}} = \underbrace{\varphi x_{\mathrm{h}} x_{\mathrm{d}}}_{\text{fusion}} - \underbrace{(\psi_1 + \psi_2) x_{\mathrm{f}}}_{\text{fission}}$$

$$\dot{\mathbf{x}}_{\mathrm{ATP}} = \underbrace{\beta x_{\mathrm{h}} + \varepsilon x_{\mathrm{d}} + \eta x_{\mathrm{f}}}_{\text{atp production}} - \underbrace{\mathbf{u} \cdot x_{\mathrm{ATP}}}_{\text{atp use}}$$

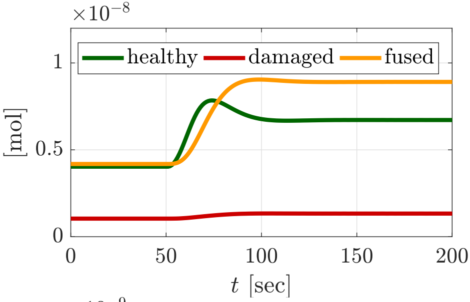
x_{h}: healthy
x_{d}: damaged
x_{f}: fused
$\mathbf{u}$: input

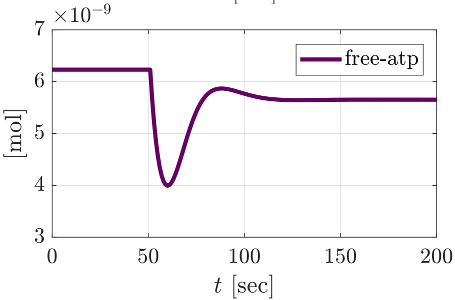


Main advantages:

1. atp-dependence
2. opportunity to test several hypotheses

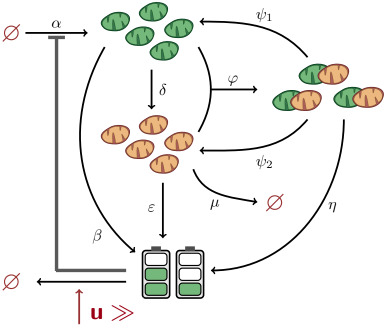
ATP feedback advantage





t = 50 sec: energy stress increases

atp-feedback ⟶ system reactivity



Equilibrium analysis

Equilibrium point

$$\bar{x}_{\mathrm{d}} = \frac{\psi_1 + \psi_2}{\psi_2 \varphi} \left(\frac{\alpha_1 - k\delta - \delta \bar{x}_{\mathrm{ATP}}}{k + \bar{x}_{\mathrm{ATP}}} \right) \qquad \bar{x}_{\mathrm{h}} = \frac{(\psi_1 + \psi_2)\mu}{\delta(\psi_1 + \psi_2) - \psi_1 \varphi \bar{x}_{\mathrm{d}}} \cdot \bar{x}_{\mathrm{d}}$$

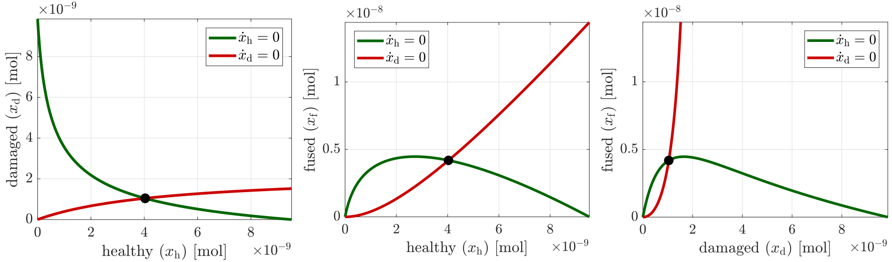
$$\bar{x}_{\mathrm{f}} = \frac{\varphi}{\psi_1 + \psi_2} \cdot \bar{x}_{\mathrm{h}} \bar{x}_{\mathrm{d}} \qquad \bar{x}_{\mathrm{ATP}} = \text{solution of 3rd-deg poly}$$

Equilibrium point

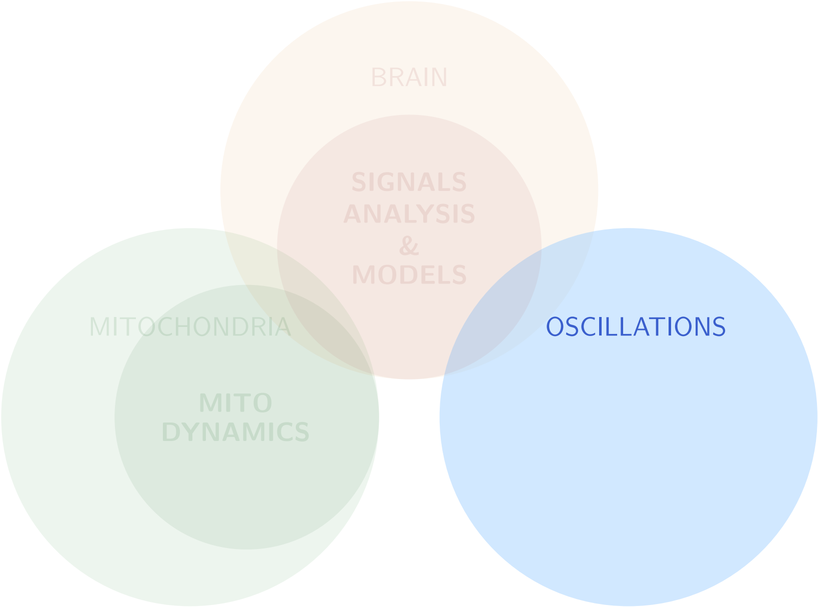
$$\bar{x}_\mathrm{d} = \frac{\psi_1 + \psi_2}{\psi_2 \varphi} \left(\frac{\alpha_1 - k\delta - \delta \bar{x}_\mathrm{ATP}}{k + \bar{x}_\mathrm{ATP}} \right) \qquad \bar{x}_\mathrm{h} = \frac{(\psi_1 + \psi_2)\mu}{\delta(\psi_1 + \psi_2) - \psi_1 \varphi \bar{x}_\mathrm{d}} \cdot \bar{x}_\mathrm{d}$$

$$\bar{x}_\mathrm{f} = \frac{\varphi}{\psi_1 + \psi_2} \cdot \bar{x}_\mathrm{h} \bar{x}_\mathrm{d} \qquad \bar{x}_\mathrm{ATP} = \text{solution of 3rd-deg poly}$$

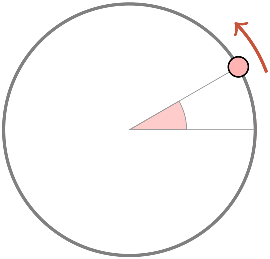
Nullclines analysis

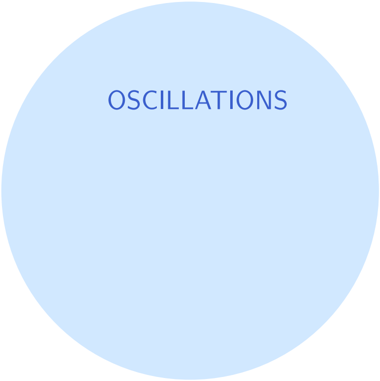


Synchronization: the Kuramoto Model



Oscillator: generator of signals characterized by a periodic pattern $\longrightarrow$ **PHASE**

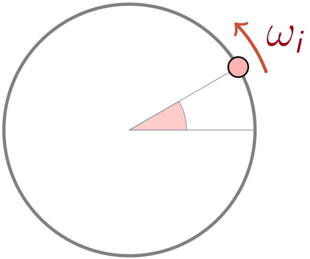




Oscillator: generator of signals characterized by a periodic pattern $\longrightarrow$ **PHASE**

Kuramoto Model

$$\dot{\theta}_i = \boxed{\omega_i} + \sum_{j=1}^{n} a_{ij} \sin(\theta_j - \theta_i)$$

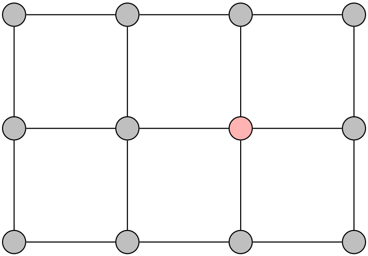


ω_i: natural frequency

Oscillator: generator of signals characterized by a periodic pattern $\longrightarrow$ **PHASE**

Kuramoto Model

$$\dot{\theta}_i = \omega_i + \sum_{j=1}^{n} a_{ij} \sin(\theta_j - \theta_i)$$



$\mathcal{G} = (\mathcal{V}, \mathcal{E})$: graph

$\mathcal{V} = \{1, \ldots, n\}$: set of nodes

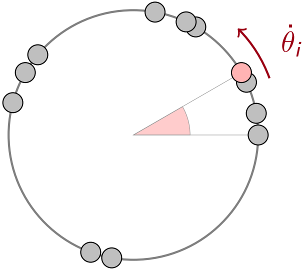
$\mathcal{E} \subseteq \mathcal{V} \times \mathcal{V}$: set of edges

$\mathbf{A} = [a_{ij}]$: weighted adjacency matrix

Oscillator: generator of signals characterized by a periodic pattern $\longrightarrow$ **PHASE**

Kuramoto Model

$$\dot{\theta}_i = \omega_i + \underbrace{\sum_{j=1}^{n} a_{ij} \sin(\theta_j - \theta_i)}_{\text{coupling}}$$

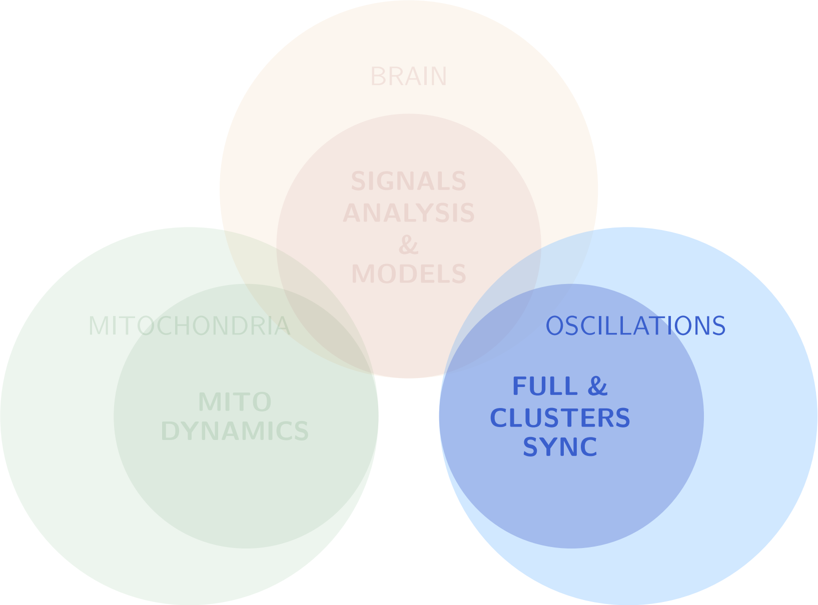


ω_i: isolated dynamics

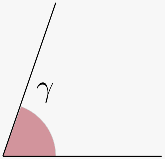
$[a_{ij}]$: adjacency matrix

$\sin(\theta_j - \theta_i)$: coupling function

Synchronization: the Kuramoto Model



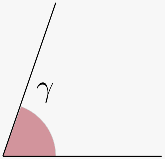
Synchronization overview



Synchronization overview

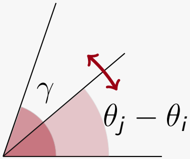
Phase cohesiveness

$$|\theta_j(t) - \theta_i(t)| \leq \gamma \qquad \forall i, j, t$$



Phase cohesiveness

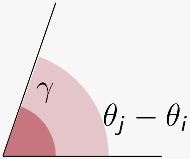
$$|\theta_j(t) - \theta_i(t)| \leq \gamma \qquad \forall i, j, t$$



Synchronization overview

Phase cohesiveness $|\theta_j(t) - \theta_i(t)| \leq \gamma \qquad \forall i, j, t$

Phase locking $|\theta_j(t) - \theta_i(t)| \equiv \gamma \qquad \forall i, j, t$



Synchronization overview

Phase cohesiveness	$\lvert\theta_j(t)-\theta_i(t)\rvert \le \gamma$	$\forall i,j,t$
Phase locking	$\lvert\theta_j(t)-\theta_i(t)\rvert \equiv \gamma$	$\forall i,j,t$
Phase synchronization	$\lvert\theta_j(t)-\theta_i(t)\rvert \equiv 0$	$\forall i,j,t$

$$\theta_j - \theta_i = 0$$

Synchronization overview

Phase locking	$|\theta_j(t) - \theta_i(t)| \equiv \gamma$	$\forall i, j, t$
Phase synchronization	$|\theta_j(t) - \theta_i(t)| \equiv 0$	$\forall i, j, t$
Frequency synchronization	$\left|\dot\theta_j(t) - \dot\theta_i(t)\right| \equiv 0$	$\forall i, j, t$

Synchronization overview

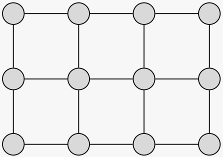
Full network synchronization

Phase cohesiveness

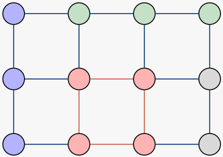
Phase locking

Phase synchronization

Frequency synchronization



Synchronization overview

	Full network synchronization	Clusters synchronization
Phase cohesiveness		
Phase locking		
Phase synchronization		
Frequency synchronization		

Synchronization overview

	Full network synchronization	**Clustered synchronization**
Phase cohesiveness		
Phase locking		
Phase synchronization		
Frequency synchronization		

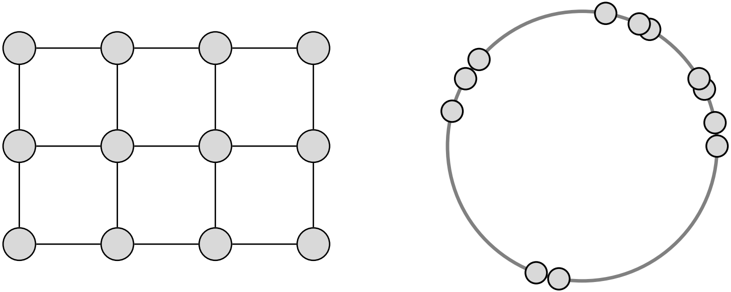
Synchronization overview

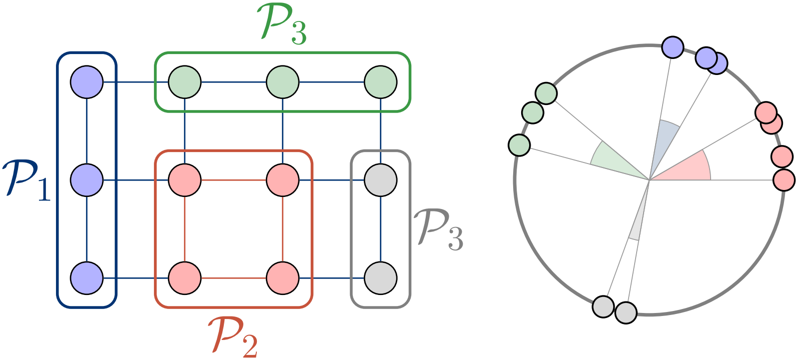
	Full network synchronization	Clustered synchronization
Phase cohesiveness	✓	✓
Phase locking		✓
Phase synchronization		✓
Frequency synchronization		✓

Synchronization overview

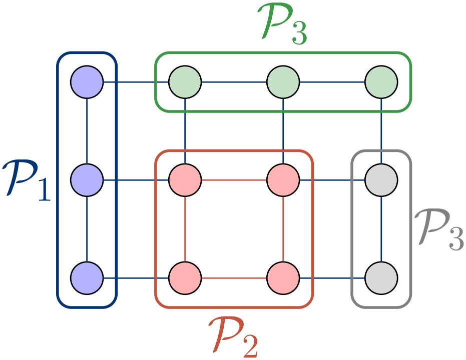
	Full network synchronization	**Clustered synchronization**
Phase cohesiveness	✓	✓
Phase locking		✓
Phase synchronization		✓
Frequency synchronization		✓

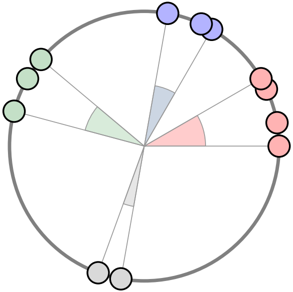
Clusters synchronization



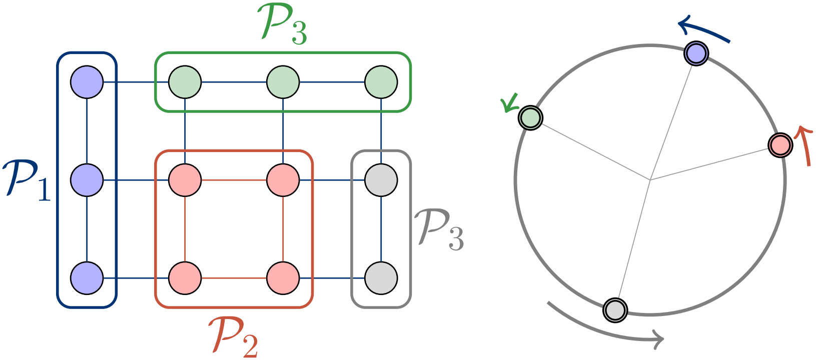


$$\mathcal{P} = \{\mathcal{P}_1, \ldots, \mathcal{P}_4\}: \qquad \bigcup_k \mathcal{P}_k = \mathcal{V} \quad \mathcal{P}_i \bigcap \mathcal{P}_j = \varnothing$$





Phase & Frequency synchronizable $\mathcal{P}$



Phase & Frequency synchronizable $\mathcal{P}$

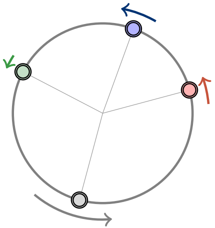
$$\exists\, \boldsymbol{\theta}(0): \quad \begin{cases} \theta_i(t) = \theta_j(t) \\ \dot{\theta}_i(t) = \dot{\theta}_j(t) \end{cases} \quad \forall i, j \in \mathcal{P}_k \text{ and } \forall k$$

Clusters synchronization: our contribution

Analysis	**Necessary** and **sufficient** conditions for clusters invariance

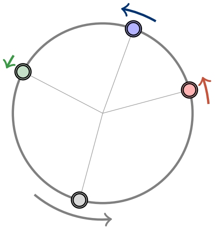
Analysis

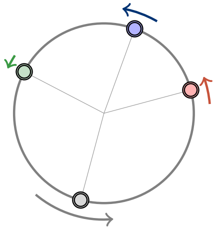
Necessary and **sufficient** conditions
for clusters invariance



$t = 0$

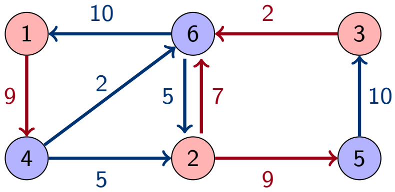
Analysis	**Necessary** and **sufficient** conditions for clusters invariance





Analysis

Necessary and **sufficient** conditions
for clusters invariance



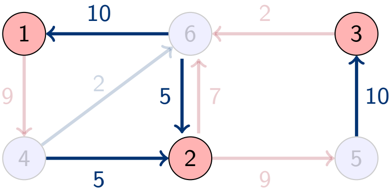
$$\sum_{k \in \mathcal{P}_\ell} a_{ik} - a_{jk} = 0 \quad \forall i, j \in \mathcal{P}_z \quad \forall \ell \neq z$$

Generalized Equitable Partition
(**GEP**)

$$\mathcal{P}_1 = \{1, 2, 3\} \rightarrow \omega_1$$
$$\mathcal{P}_2 = \{4, 5, 6\} \rightarrow \omega_2$$

Analysis

Necessary and **sufficient** conditions
for clusters invariance



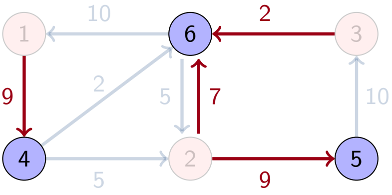
$$\sum_{k\in\mathcal{P}_2} a_{ik} - a_{jk} = 0 \qquad \forall i,j \in \mathcal{P}_1$$

Generalized Equitable Partition
(**GEP**)

$$\mathcal{P}_1 = \{1,2,3\} \rightarrow \omega_1$$
$$\mathcal{P}_2 = \{4,5,6\} \rightarrow \omega_2$$

Analysis

Necessary and **sufficient** conditions for clusters invariance

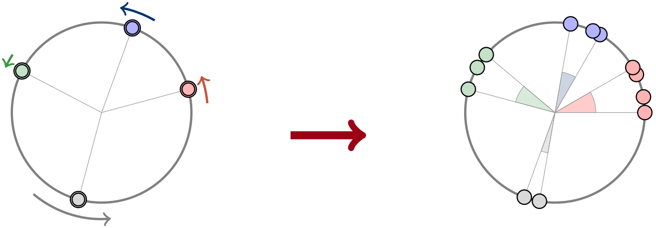


$$\sum_{k \in \mathcal{P}_1} a_{ik} - a_{jk} = 0 \qquad \forall i, j \in \mathcal{P}_2$$

Generalized Equitable Partition (**GEP**)

$$\mathcal{P}_1 = \{1, 2, 3\} \rightarrow \omega_1$$
$$\mathcal{P}_2 = \{4, 5, 6\} \rightarrow \omega_2$$

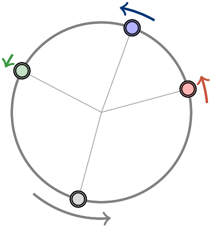
Analysis	**Necessary** and **sufficient** conditions for clusters invariance
Control	How to **modify** the adjacency matrix to impose clusters invariance with structural constraints



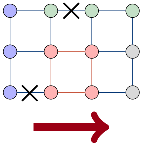
$t = 0$ $\longrightarrow$ $t > 0$

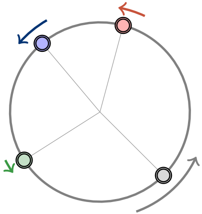
Clusters synchronization: our contribution

Analysis	**Necessary** and **sufficient** conditions for clusters invariance
Control	How to **modify** the adjacency matrix to impose clusters invariance with structural constraints



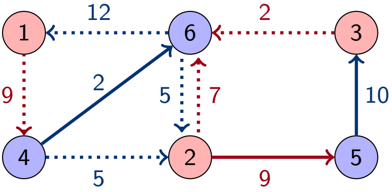
$t = 0$

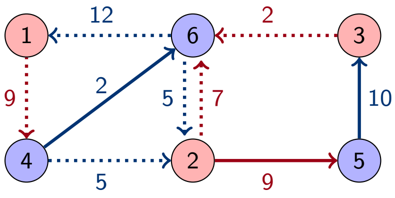




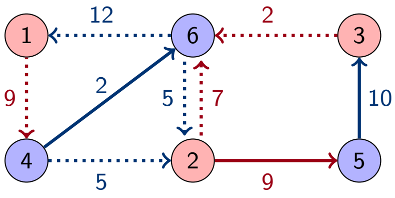
$t > 0$

Clusters synchronization: control





Task: Modify **A** to make $\mathcal{P}$ invariant **without** modyfying the dotted edges

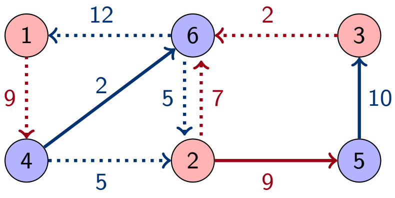


Task: Modify $\mathbf{A}$ to make $\mathcal{P}$ invariant **without** modyfying the dotted edges

$$\min_{\boldsymbol{\Delta}} \|\boldsymbol{\Delta}\|_F^2$$

$$\text{s.t. } (\mathbf{A} + \boldsymbol{\Delta}) \text{ respects } \mathbf{GEP}$$

$$\boldsymbol{\Delta} \in \mathcal{H} \quad \text{structural constraints}$$



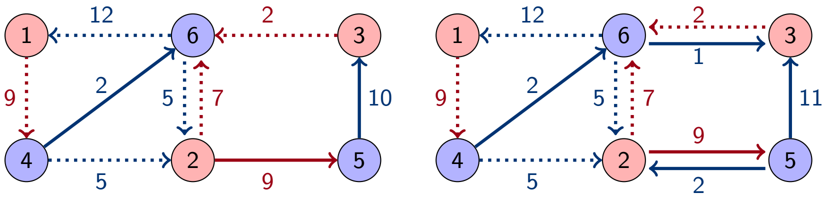
Task: Modify $\mathbf{A}$ to make $\mathcal{P}$ invariant **without** modyfying the dotted edges

$$\min_{\boldsymbol{\Delta}} \|\boldsymbol{\Delta}\|_F^2 \qquad \textbf{Frobenius norm}$$

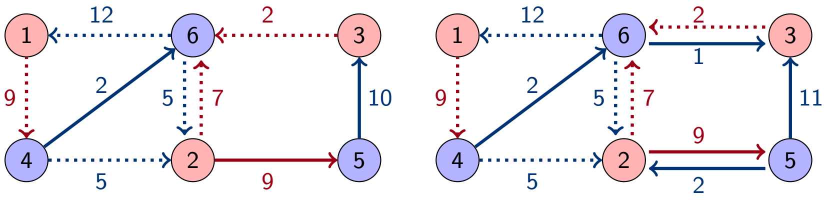
$$\text{s.t. } (\mathbf{A}+\boldsymbol{\Delta}) \text{ respects } \textbf{GEP}$$

$$\boldsymbol{\Delta} \in \mathcal{H} \quad \text{structural constraints}$$

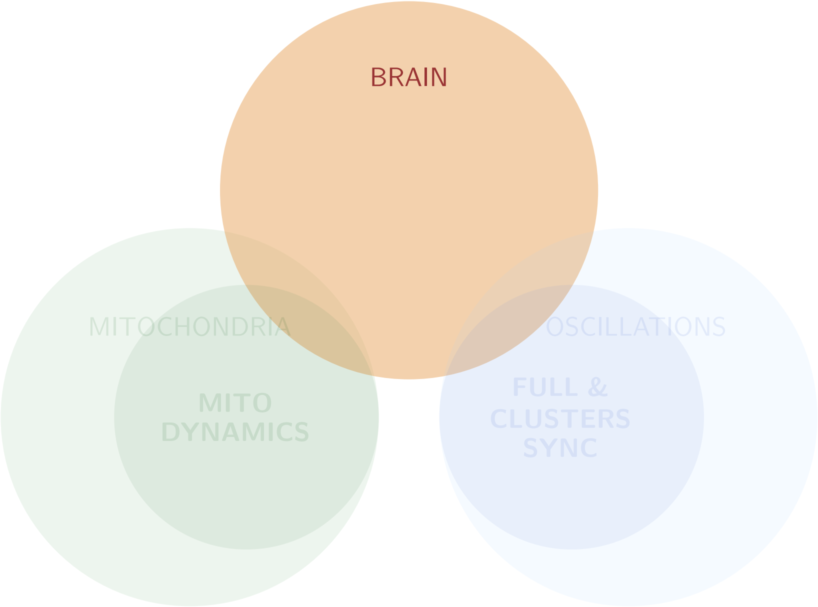
Clusters synchronization: control



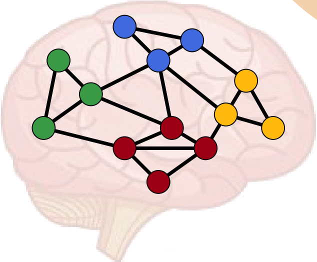
Clusters synchronization: control



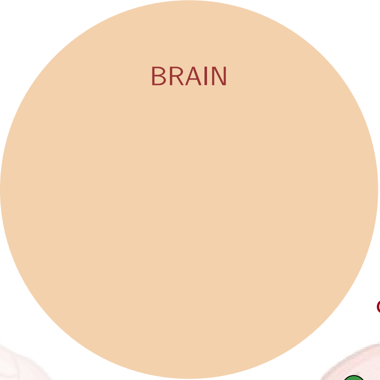
Brain


BRAIN
MITOCHONDRIA
MITO DYNAMICS
OSCILLATIONS
FULL & CLUSTERS SYNC

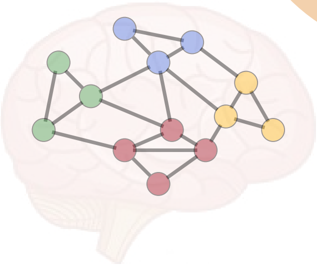
clusters of **nodes**



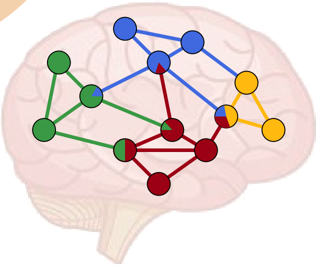
Brain



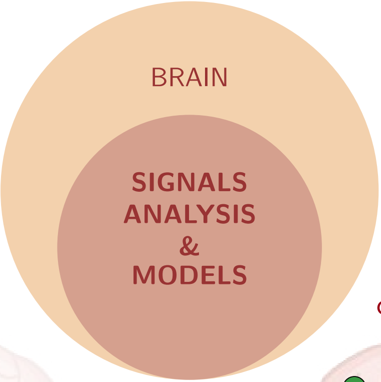
clusters of **nodes**



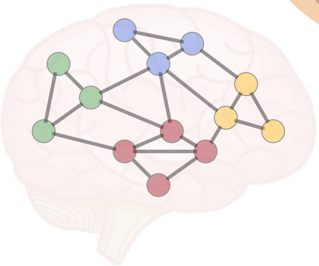
clusters of **links**



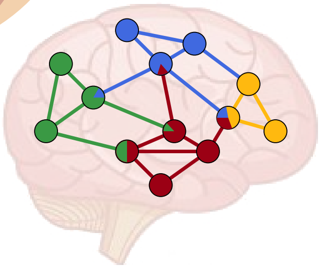
Brain



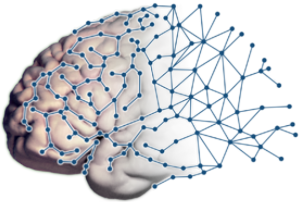
clusters of **nodes**



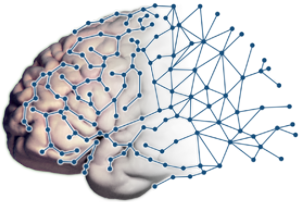
clusters of **links**



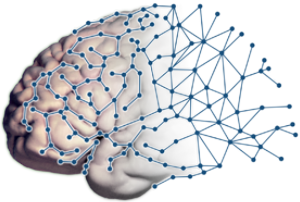
Brain: a complex system



Brain: a complex system



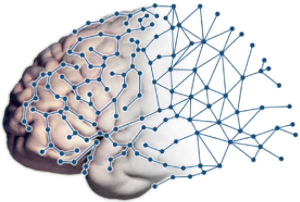
connectivity
matrix



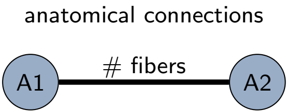
connectivity matrix

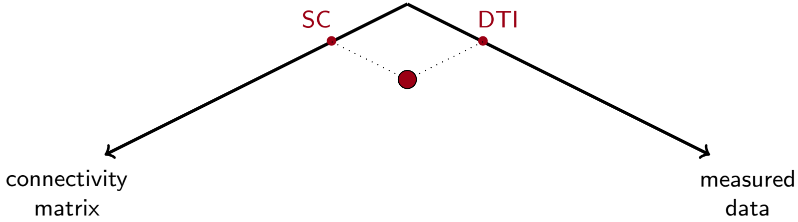
measured data

Brain: a complex system

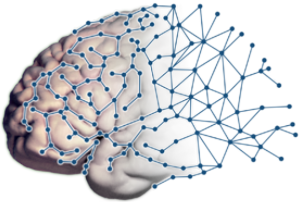


Structural Connectivity

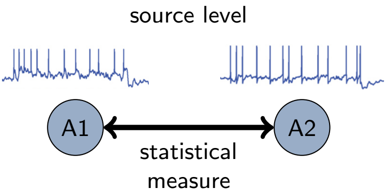


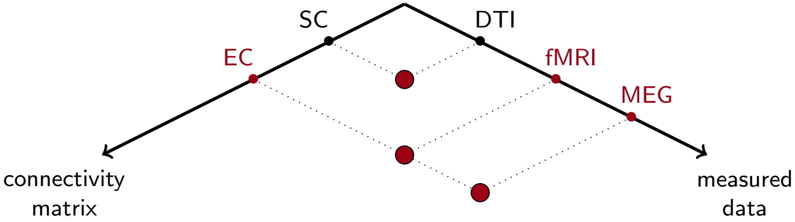


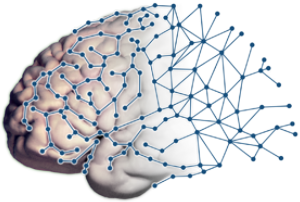
Brain: a complex system



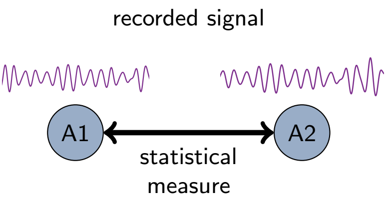
Effective Connectivity

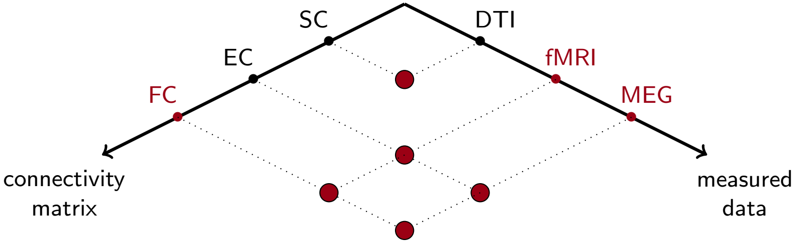




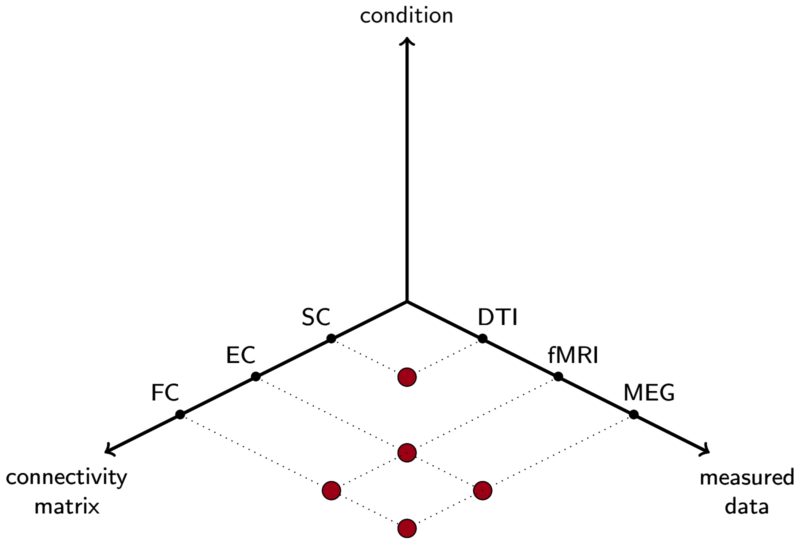


Functional Connectivity



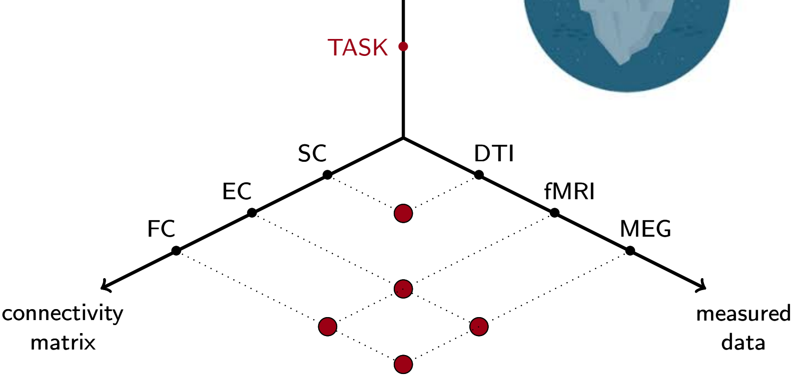


Brain: a complex system

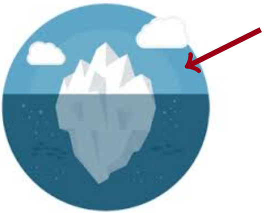


Task Activity

- any kind of activity
- only involved areas actived
- links: activity-dependent

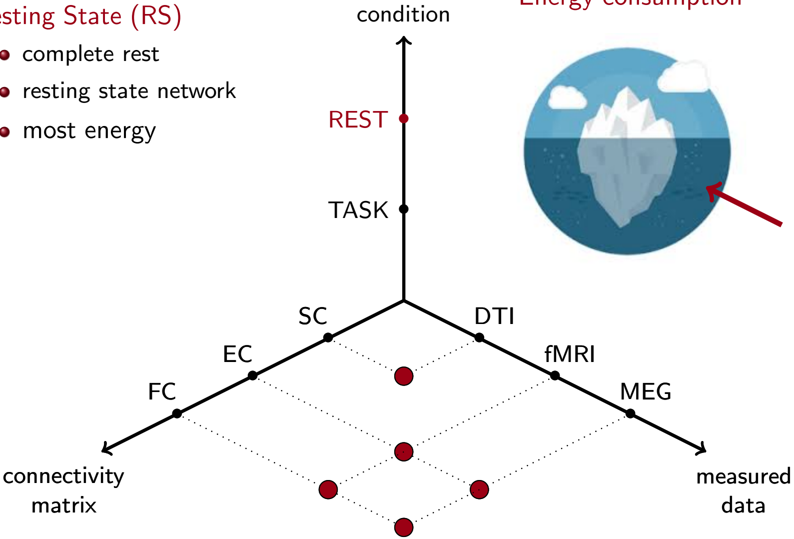


Energy consumption



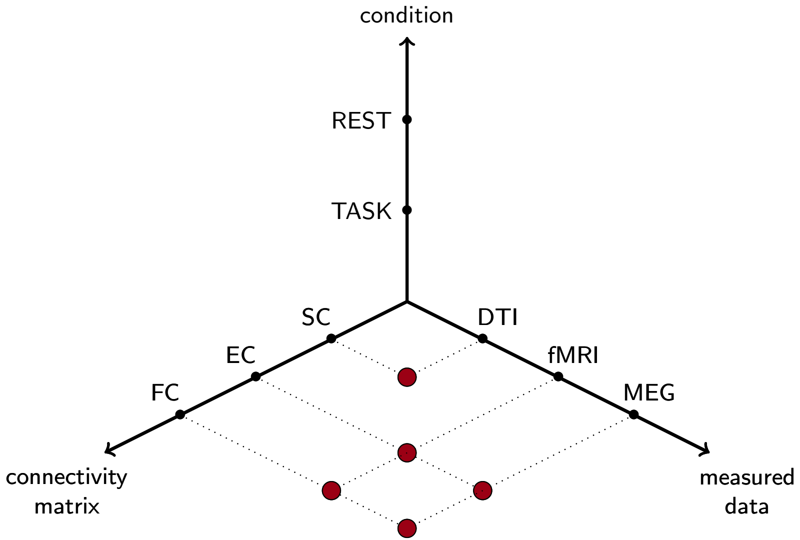
Resting State (RS)

- complete rest
- resting state network
- most energy



Energy consumption

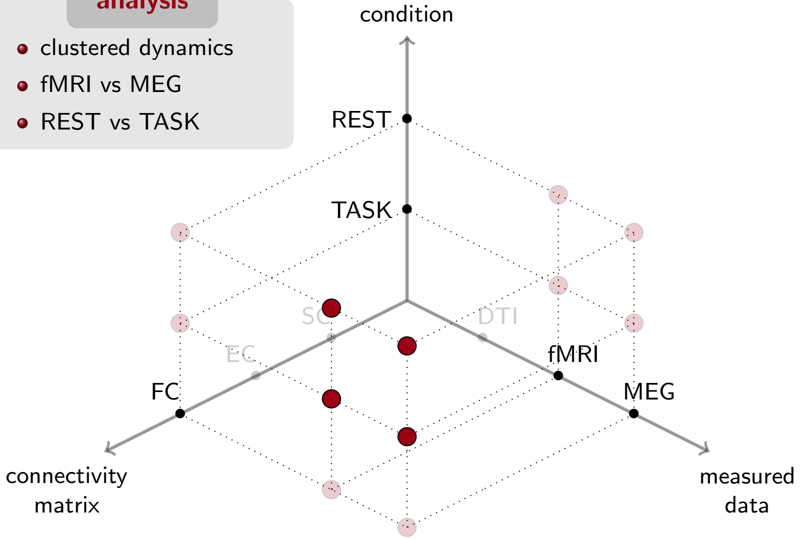
Brain: a complex system



Brain: a complex system

analysis

- clustered dynamics
- fMRI vs MEG
- REST vs TASK



analysis

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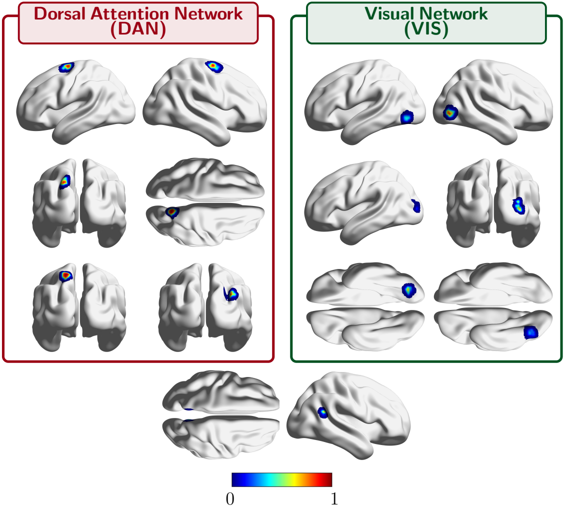

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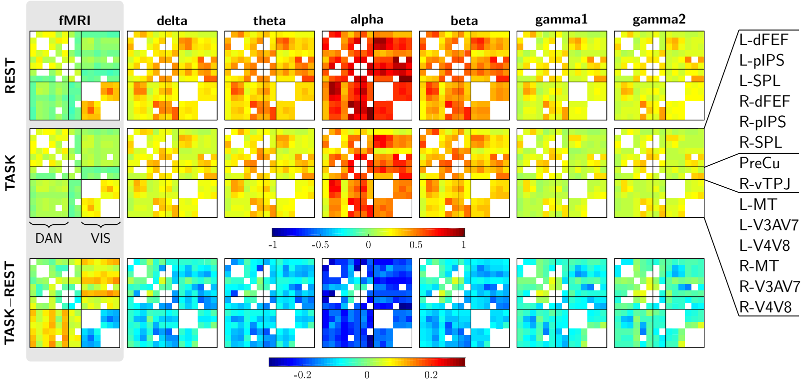

analysis

- clusters dynamics
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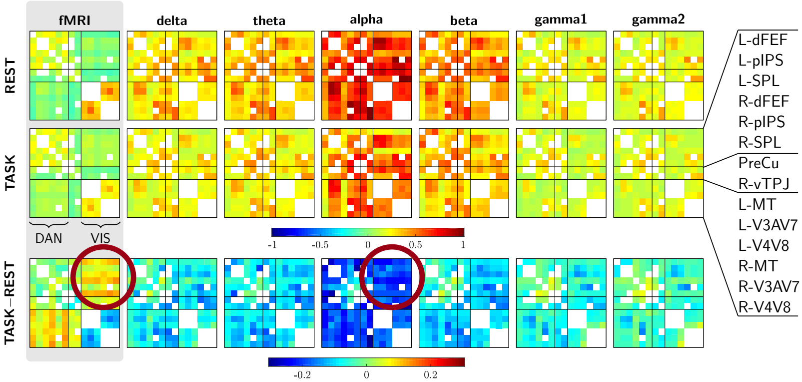
- REST vs TASK

- opposite behavior



analysis

- clusters dynamics
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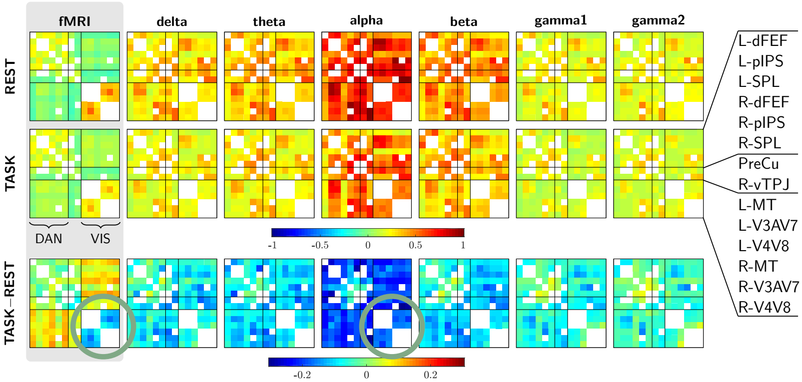
- REST vs TASK

- opposite behavior
- coherent behavior



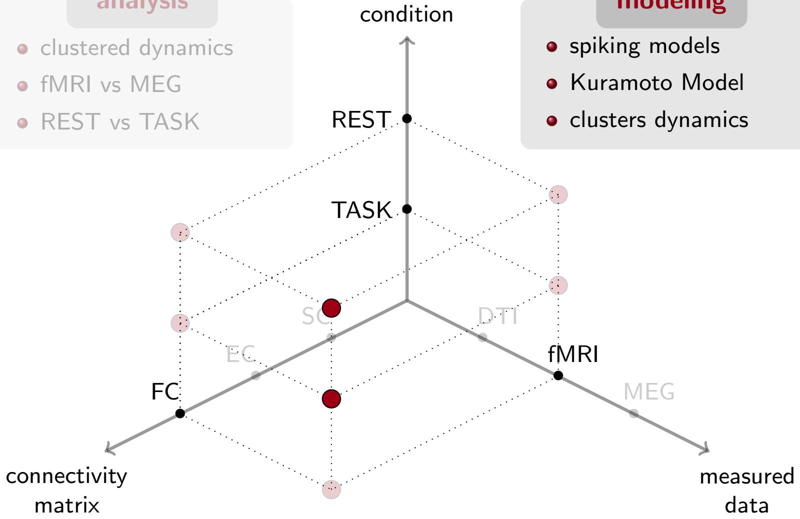
Brain: a complex system

analysis

- clustered dynamics
- fMRI vs MEG
- REST vs TASK

modeling

- spiking models
- Kuramoto Model
- clusters dynamics



Brain: a complex system

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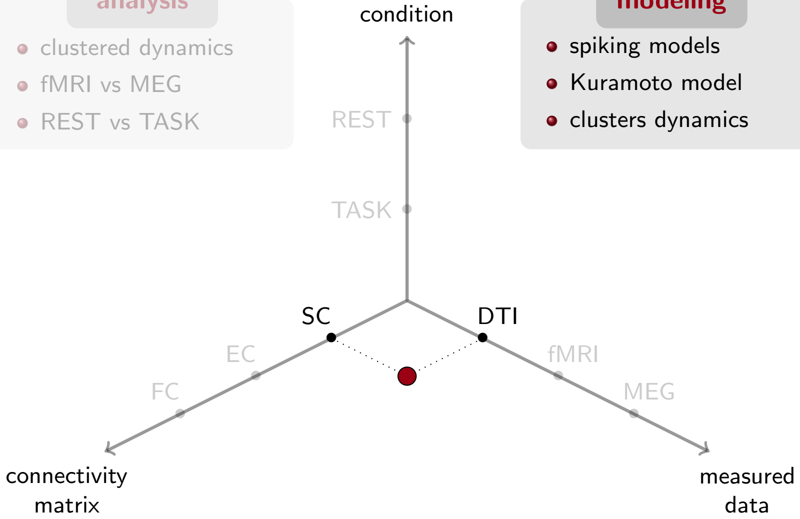


Structural connectivity

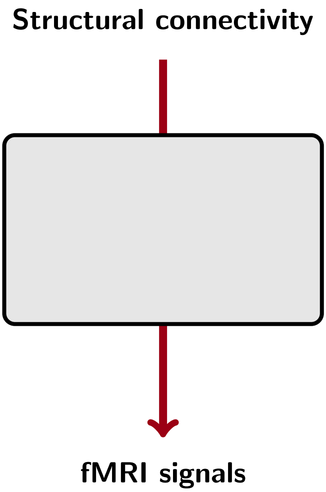
Structural connectivity

fMRI signals

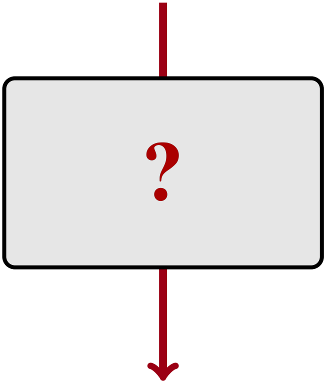
Structural connectivity

↓

fMRI signals


Structural connectivity
fMRI signals

Structural connectivity



fMRI signals

Structural connectivity

phase model

fMRI signals

Brain: a complex system

Structural connectivity

↓

- Rulkov Neuron Model
- **Kuramoto Model**
- Fitzhugh Nagumo Model

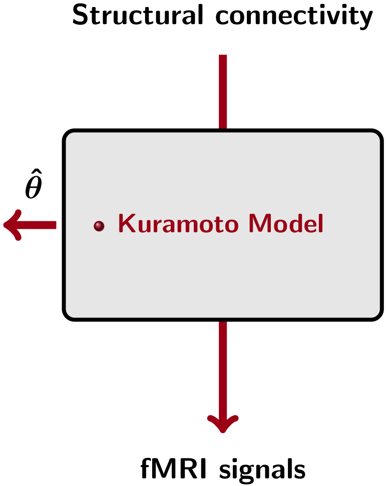
↓

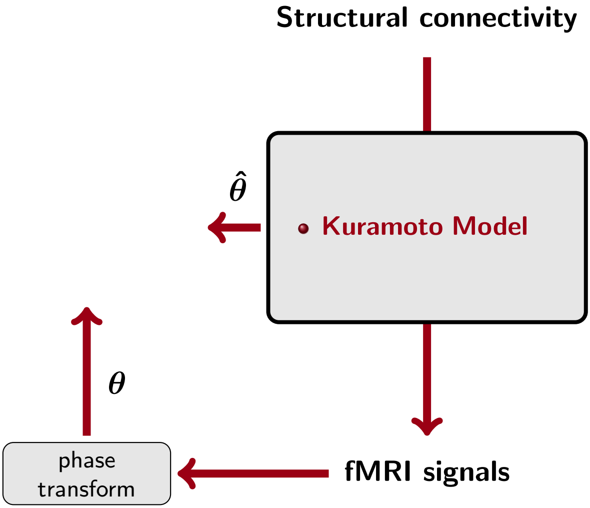
fMRI signals

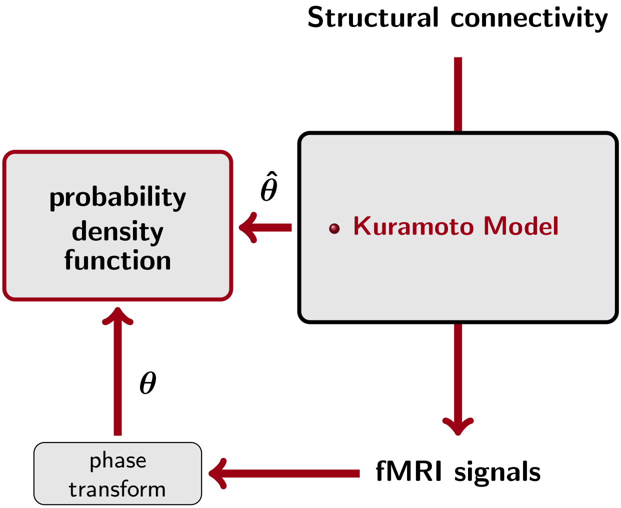
Structural connectivity

- **Kuramoto Model**

fMRI signals


Structural connectivity
$\hat{\theta}$
Kuramoto Model
fMRI signals


Structural connectivity
$\hat{\theta}$
Kuramoto Model
θ
phase transform
fMRI signals


Structural connectivity
Kuramoto Model
$\hat{\theta}$
probability density function
θ
phase transform
fMRI signals

Structural connectivity

- **Kuramoto Model**

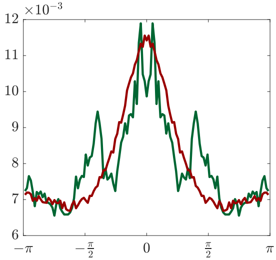
$\hat{\theta}$

probability density function

θ

phase transform

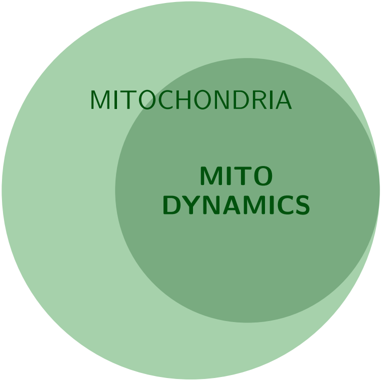
fMRI signals



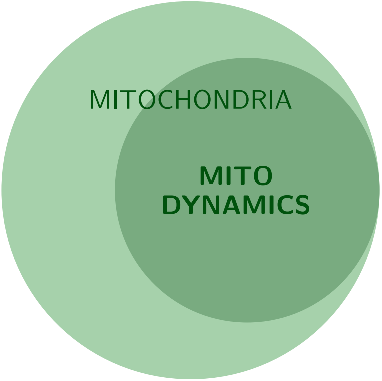
$\theta_j - \theta_i$

- real data
- model

Conclusion & ongoing research


MITOCHONDRIA
MITO
DYNAMICS

Conclusion & ongoing research



- population model
- mito dynamics + energy
- feedback regulation
- stability & sensitivity analyses

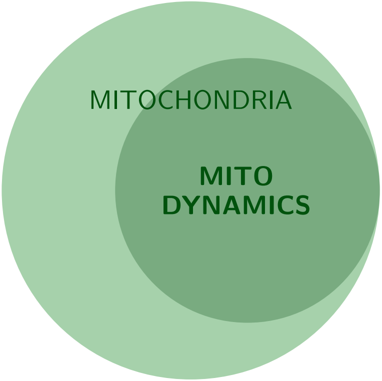
results

- population model
- mito dynamics + energy
- feedback regulation
- stability & sensitivity analyses

results

- non-linear feedback control
- damaged vs healthy model
- more classes

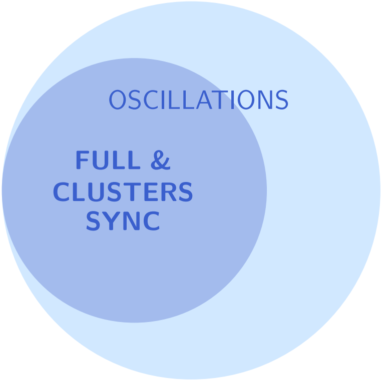
open research



Conclusion & ongoing research

results

- full phase cohesiveness
- clusters phase cohesiveness
- phase locking
- sync invariance

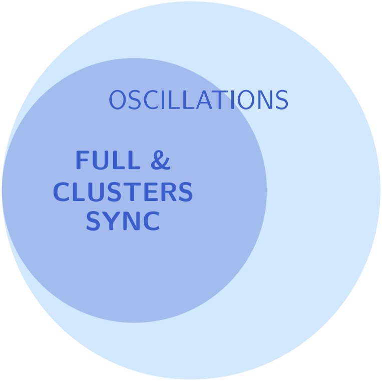


results

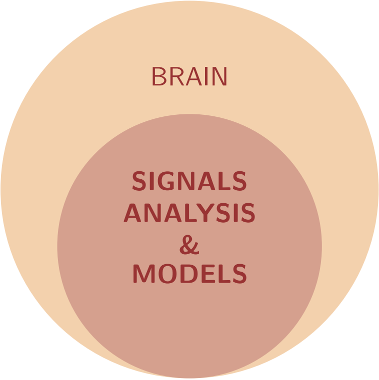
- full phase cohesiveness
- clusters phase cohesiveness
- phase locking
- sync invariance

open research

- clusters sync attractivity
- brain fitting

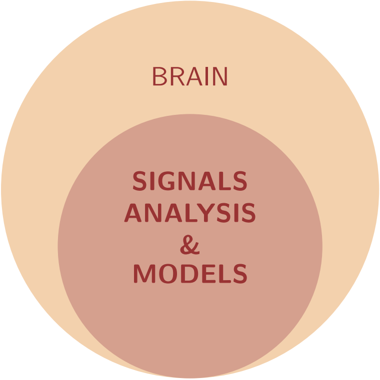


Conclusion & ongoing research



results

- data analysis
- modeling
- rest vs task
- fMRI vs MEG



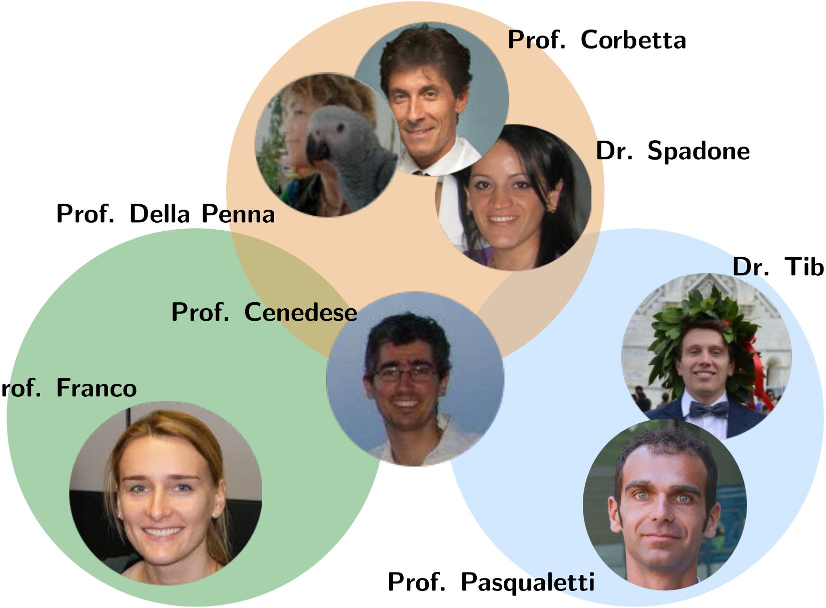
results

- data analysis
- modeling
- rest vs task
- fMRI vs MEG

open research

- stroke modeling
- rest vs task
- fMRI vs EEG
- FC dynamics

Thanks to...


Prof. Corbetta
Dr. Spadone
Prof. Della Penna
Dr. Tiberi
Prof. Cenedese
Prof. Franco
Prof. Pasqualetti

Thanks to...

... all of you for your attention!