

Analytical and computational approach to structure-function relationship in neural networks

Arthur Légaré,^{1,2} Antoine Légaré,^{3,4} Paul De Koninck,^{3,4} Nicolas Doyon,^{2,4,5} Patrick Desrosiers^{1,2,4}

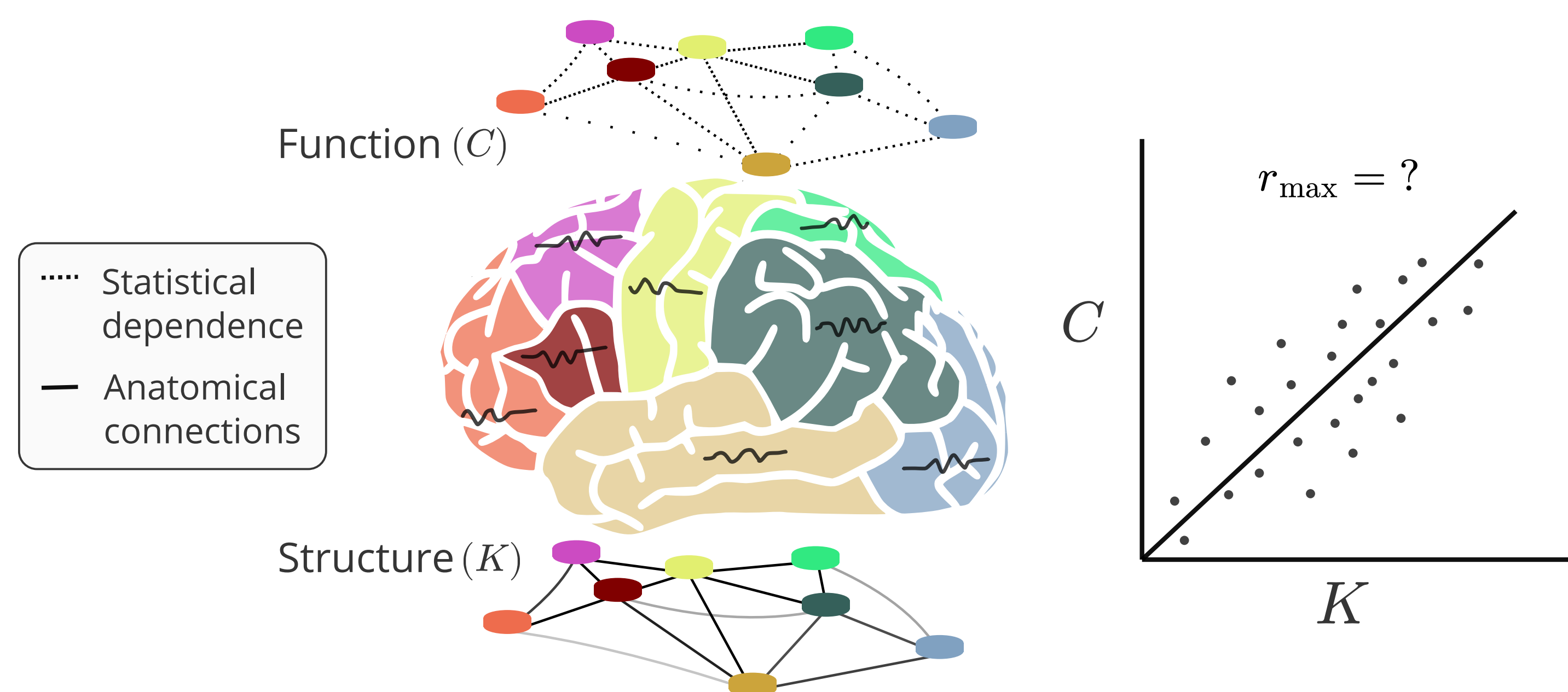
1. Département de physique, génie physique et d'optique, Université Laval, Québec, Canada
2. Centre Interdisciplinaire en Modélisation Mathématique de l'Université Laval, Québec, Canada
3. Département de biochimie, de microbiologie et de bio-informatique, Université Laval, Québec, Canada
4. Centre de recherche CERVO, Québec, Canada
5. Département de mathématiques et statistiques, Université Laval, Québec, Canada

arthur.legare.1@ulaval.ca



Structure-function relationship

Functional connectivity (FC) describes statistical dependencies between the activity of neurons or groups of neurons [1]. Comparing FC with anatomical or structural connectivity (SC) has emerged as a promising avenue to study how brain structure supports function and how both change in disease or with cognition [2]. However, empirical studies across species and recording modalities have reported a wide range of FC-SC correspondence values, typically assessed using Pearson correlation [1,3]. Recent theoretical work further suggests that fundamental limits on the information shared among structure and dynamics may constrain our ability to relate FC to SC [4,5].



Interpreting structure-function relationships thus remains challenging and raises key questions: *how expected is a strong FC-SC correspondence*, and *how do different dynamical models shape the nature and strength of this relationship?*

Project goals and methods

This project aims to identify specific dynamical regimes in which the structure-function correspondence is maximized, using established models of neural activity. It further seeks to determine how this relationship depends on the underlying dynamical model and to characterize it through nonlinear measures that go beyond simple correlations.

Computational framework. We developed a computational framework (see SIMBA library) that systematically simulates the ordinary differential equations governing these models. By sweeping across relevant parameters, randomizing initial conditions, and monitoring observables from spectral graph theory and order parameters [6], we identified and characterized regimes exhibiting strong structure-function correspondence.

Analytical investigations. To evaluate how structural connectivity shapes functional dependencies, we derived approximate nonlinear relationships between the covariance of neural activity and the underlying SC across different models.

Models of neural activity

a) Kuramoto's coupled oscillators:

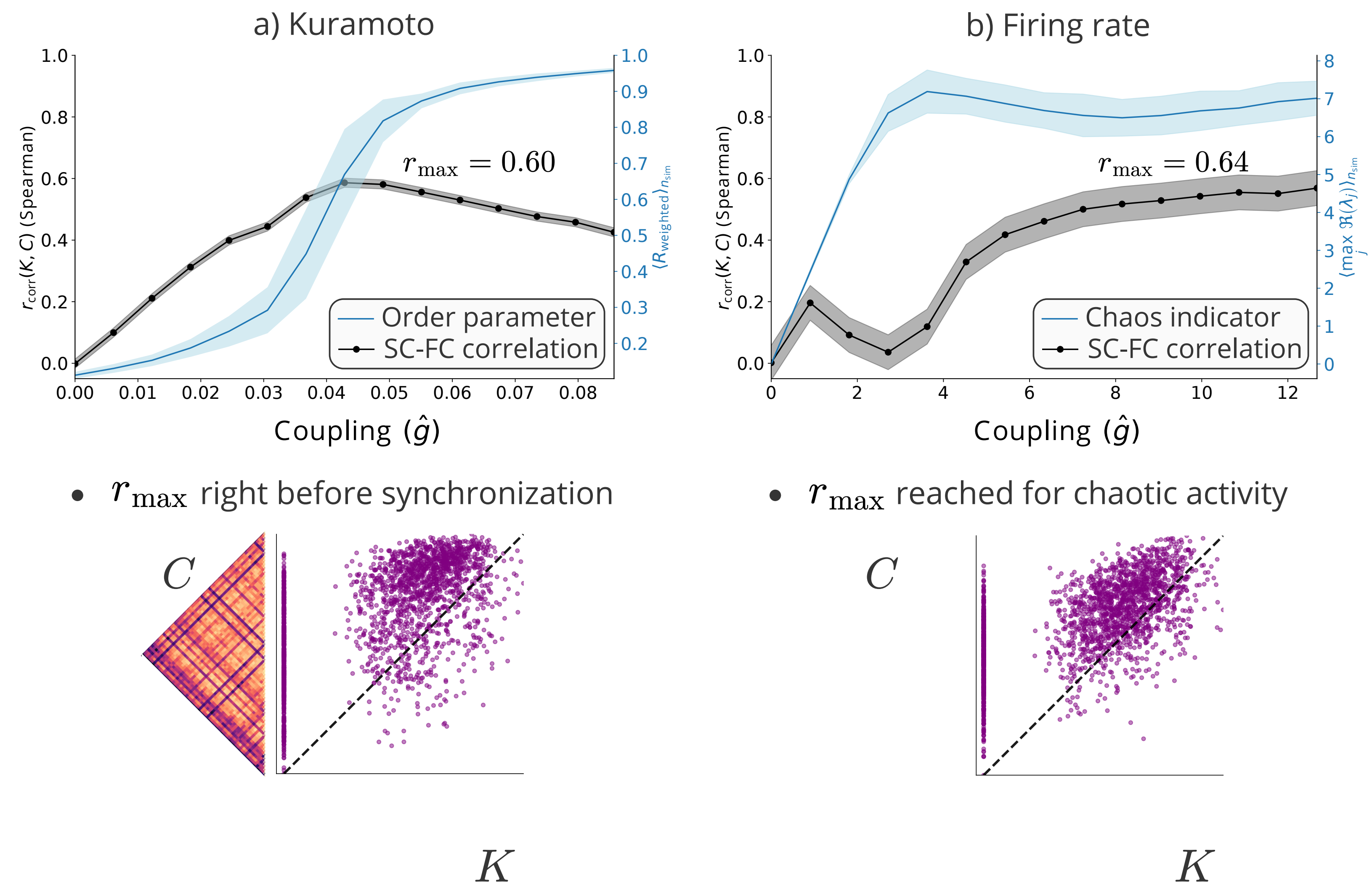
$$\frac{dx_j}{dt} = \omega_j + \hat{g} \sum_{l=1}^N K_{jl} \sin(x_l - x_j), \quad \omega_j : \text{natural frequency}$$
$$\hat{g} = \frac{g}{N} : \text{reduced coupling}$$

b) Firing rate with **excitatory** and **inhibitory** connections:

$$\frac{dx_j}{dt} = -x_j + \hat{g} \sum_{l=1}^{2N} W_{jl} \sigma(x_l) + \eta_j(t), \quad \eta_j : \text{noise process}$$
$$\sigma(\cdot) = \frac{2}{\pi} \arctan(\cdot)$$
$$\hat{g} = \frac{g}{\sqrt{2N}}$$

Numerical simulations

Example. SC-FC simulated on zebrafish mesoscale networks comprising 70 brain regions [6]



Analytical predictions

a) Kuramoto (low coupling):

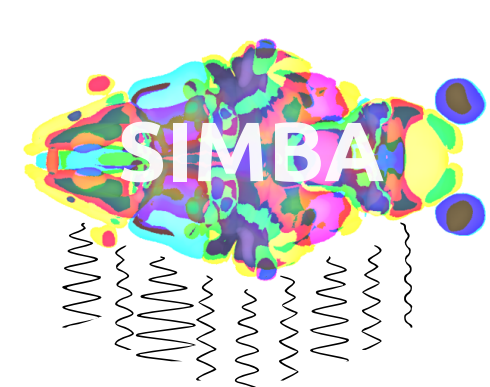
$$\text{Covariance of sinus.} \quad C_{jk}(T) \approx \frac{1}{2} \text{sinc}(\Delta_{jk}T) + \frac{\hat{g}^2}{8} \sum_{l=1}^N \frac{K_{jl}}{\Delta_{lj}} \frac{K_{kl}}{\Delta_{lk}} \bar{\delta}_{lj} \bar{\delta}_{lk} \quad T : \text{duration}$$
$$\Delta_{jk} = \omega_j - \omega_k$$
$$\bar{\delta}_{jk} = 1 - \delta_{jk}$$
$$\text{Phase coherence.} \quad C_{jk}^2(T) \approx \text{sinc}^2(\Delta_{jk}T/2) \left(1 + \hat{g}^2 \sum_{l=1}^N \left(\frac{K_{jl}}{\Delta_{lj}} \bar{\delta}_{lj} - \frac{K_{kl}}{\Delta_{lk}} \bar{\delta}_{lk} \right)^2 \right) \quad \text{sinc}(x) = \frac{\sin(x)}{x}$$

b) Firing rate (covariance):

$$\text{Weak coupling.} \quad C \approx \alpha (W^{-1})^2 \quad (\text{Stochastic}) \quad \epsilon = \frac{1}{\hat{g}} : \text{inverse coupling}$$
$$\alpha : \text{noise amplitude}$$
$$\text{Strong coupling.} \quad C \sim WW^T \quad (\text{Mean-field}) \quad C \approx \mathbb{I} + \frac{\epsilon^2}{4} (WW^T)^{\circ-1} \quad (\text{Chaotic})$$

Takeaways and future work

- Each model has its own optimal dynamical regimes for strong SC-FC correspondence.
 - Kuramoto: FC correlates most with SC before transition to synchronization [7].
 - Firing rate: FC globally aligns more with SC as interneuronal coupling increases, except near the transition to chaos where this alignment reaches minimum.
- What's next:
 - How do such SC-FC relationships evolve according to bioplausible plasticity rules [8]?
 - Within what structural limits do the closed-form expressions predict activity?



Python Library. Structure Influence on Models of Brain Activity, for simulation of many other models of neural activity.



[1] P. Fotiadis et al., "Structure-function coupling in macroscale human brain networks," *Nat. Rev. Neurosci.*, 2024.
[2] F. Zamani Eshfahani et al., "Local structure-function relationships in human brain networks across the lifespan," *Nat. Commun.*, 2022.
[3] A. I. Luppi et al., "An engine for systematic discovery of cause-effect relationships between brain structure and function," 2025.
[4] B. Prasse et al., "Predicting network dynamics without requiring the knowledge of the interaction graph," *Proc. Natl. Acad. Sci. U.S.A.*, 2022.
[5] C. Murphy et al., "Duality between predictability and reconstructability in complex systems," *Nat. Commun.*, 2024.

[6] A. Légaré et al., "Structural and genetic determinants of zebrafish functional brain networks," *Sc. Adv.*, 2025.
[7] M. Schröder et al., "A universal order parameter for synchrony in networks of limit cycle oscillators," *Chaos*, 2017.
[8] C. W. Lynn et al., "Heavy-tailed neuronal connectivity arises from Hebbian self-organization," *Nat. Phys.*, 2024.