Neuronal mechanisms for different gamma oscillators in the hippocampus

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Abstract (10 lines)
Self-localization is essential to animal survival. In rodents, this ability relies on functional interactions between interconnected structures in the temporal lobe. Communication between these structures is facilitated by oscillations of neuronal activity notably in the gamma frequency range (30-120 Hz, 1) allowing the formation of transiently synchronized neuronal assemblies (2). Recent work notably in the Dupret group in Oxford shows that, in the hippocampus, gamma oscillations can be separated into distinct narrow frequency bands (transient Spectral Components or TSCs) each allowing communication of specific neuronal assemblies between specific structures and supporting specific functions in spatial memory (3). Importantly, rapid transitions between neuronal assemblies and associated tSCs are experimentally observed but the cellular and network mechanisms are poorly understood. In this proposal we propose to address this question at the cellular level using dual intracellular/extracellular recordings in the hippocampus of awake mice navigating virtual environment and at the network level using neuropercolation models based on automata networks.

Keywords Gamma oscillations, Place cells, Hippocampus, Virtual reality, Patch-clamp, Neuropercolation, CA1, automata networks

Objectives (5 lines)

To better understand mechanisms of fast transition between different gamma tSCs at the cellular level, our first objective is to record gamma oscillations simultaneously both extracellularly and intracellularly in awake behaving mice in the Epsztein lab using analytical tools developed in the Dupret lab (3) to decipher the tSCs of gamma oscillations. Our second objective is to develop modular neuropercolation models based on automata networks (4) in the Perrot lab to understand the network mechanisms allowing such fast transitions between gamma tSCs.

Proposed approach (experimental / theoretical / computational) (10 lines)

We will combine high density silicon probe recordings of gamma rhythm in the extracellular space with intracellular patch-clamp recordings of neuronal membrane potential of neurons in head-fixed mice exploring virtual environments as performed in the Epsztein lab. Specific cue manipulation will be used to push the system toward different gamma tSCs.

Analytical tools already developed in the Dupret lab (3) will be used to decipher the tSCs of recorded gamma oscillations. In parallel we will implement neuropercolation models based on automata networks developed in the Perrot lab. Indeed, current models of gamma oscillations based on differential equations fail to reproduce rapid transitions between stable oscillatory states as observed experimentally (3). Conversely, neuropercolation which describes evolution of activity at criticality through a sequence of metastable states is well suited to model such fast transitions. These models have been successfully used to reproduce transitions between different oscillatory states in the cortex.

Interdisciplinarity (10 lines)

This project lies at the interface between neuroscience and computer science. Large-scale neuronal recordings combined with intracellular recordings as performed in the Epsztein lab using multi-shank electrodes (up to 128 recording sites) make now possible to record simultaneously intracellular and extracellular activity. The data generated will be used to assess the validity of a newly developed model of gamma rhythm generation using neuropercolation based on automata networks developed in the Perrot lab. Neuropercolation combines: (i) complexe dynamics and intermittent chaos; (ii) geometric graphs and percolation theory; and (iii) phase transition at critical states. Network in different tSCs components may be approximated as metastable self-organized criticality while rapid transitions between tSCs states are percolation processes. The main components of the project will therefore be 1- experiments performed in the Epsztein lab, 2- analysis of experimental results using tools developed in (and in collaboration with) the Dupret lab, 3- neuropercolation model development in the Perrot lab, 4- model validation and 5- model adaptation to match experimental results in the Perrot lab (in collaboration with the Epsztein lab).

Expected profile (5 lines)

We seek to recruit a highly motivated and versatile candidate with a background in experimental biology but willing to learn computer modeling. The candidate should be interest in network dynamics and have good programming skills (e.g. Python). Some knowledge in spatial cognition, in vivo patch clamp recordings and/or computational neuroscience would be a plus.

Is this project the continuation of an existing project or an entirely new one?
In the case of an existing project, please explain the links between the two projects (5 lines)

This is an entirely new project and new collaboration.

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2 to 5 references related to the project

1. Mechanisms of gamma oscillations. Buzsáki G, Wang XJ. Annu Rev Neurosci. 2012.

2. Theta phase segregation of input-specific gamma patterns in entorhinal-hippocampal networks. Schomburg EW, Fernández-Ruiz A, Mizuseki K, Berényi A, Anastassiou CA, Koch C, Buzsáki G. Neuron. 2014.

3. Parsing Hippocampal Theta Oscillations by Nested Spectral Components during Spatial Exploration and Memory-Guided Behavior. Lopes-Dos-Santos V, van de Ven GM, Morley A, Trouche S, Campo-Urriza N, Dupret D. Neuron. 2018.

4. Random graph theory and neuropercolation for modeling brain oscillations at criticality. Kozma R, Puljic M. Curr Opin Neurobiol. 2015

3 main publications from each PI over the last 5 years

Jérôme Epsztein

1. Synaptic dysregulation and hyperexcitability induced by intracellular amyloid beta oligomers. Fernandez-Perez EJ, Muñoz B, Bascuñan DA, Peters C, Riffo-Lepe NO, Espinoza MP, Morgan PJ, Filippi C, Bourboulou R, Sengupta U, Kayed R, **Epsztein J**, Aguayo LG. Aging Cell. 2021

2. Kv1.1 contributes to a rapid homeostatic plasticity of intrinsic excitability in CA1 pyramidal neurons in vivo. Morgan PJ, Bourboulou R, Filippi C, Koenig-Gambini J, **Epsztein J**. Elife. 2019

3. Dynamic control of hippocampal spatial coding resolution by local visual cues. Bourboulou R, Marti G, Michon FX, El Feghaly E, Nouguier M, Robbe D, Koenig J*, **Epsztein J***. Elife. 2019

David Dupret

1. El-Gaby M, Reeve HM, Lopes-dos-Santos V, Campo-Urriza N, Perestenko PV, Morley A, Strickland L, Lukács IP, Paulsen O and **Dupret D**. An Emergent Neural Coactivity Code for Dynamic Memory. Nat Neurosci. 2021.

2. Gava GP, McHugh SB, Lefèvre L, Lopes-dos-Santos V, Trouche S, El-Gaby M, Schultz SR and **Dupret D**. Integrating new memories into the hippocampal network activity space. Nat Neurosci. 2021.

3. Barron HC, Reeve HM, Koolschijn RS, Perestenko PV, Shpektor A, Nili H, Rothaermel R, Campo-Urriza N, O'Reilly JX, Bannerman DM, Behrens TEJ and **Dupret D**. Neuronal computation underlying inferential reasoning in humans and mice. Cell. 2020.

Kevin Perrot

1. Maximum sensitivity to update schedule of elementary cellular automata over periodic configurations. **Perrot K**, Montalva-Medel M, de Oliveira P. P. B. and Ruivo E. L. P. Natural Computing, 2020

2. On the emergence of regularities on one-dimensional decreasing sandpiles. **Perrot K** and Rémila E. Theoretical Computer Science, 2020

3. Complexity of Maximum Fixed Point Problem in Boolean Networks. Bridoux F, Durbec N, **Perrot K** and Richard A. Proceedings of CiE'2019, 2019