NREM sleep in the rodent neocortex and hippocampus reflects excitable dynamics

University of Nottingham
UK | CHINA | MALAYSIA

Name: Shayan Shafquat
Student ID: 20595438

MATH4046, Department of Mathematical Sciences

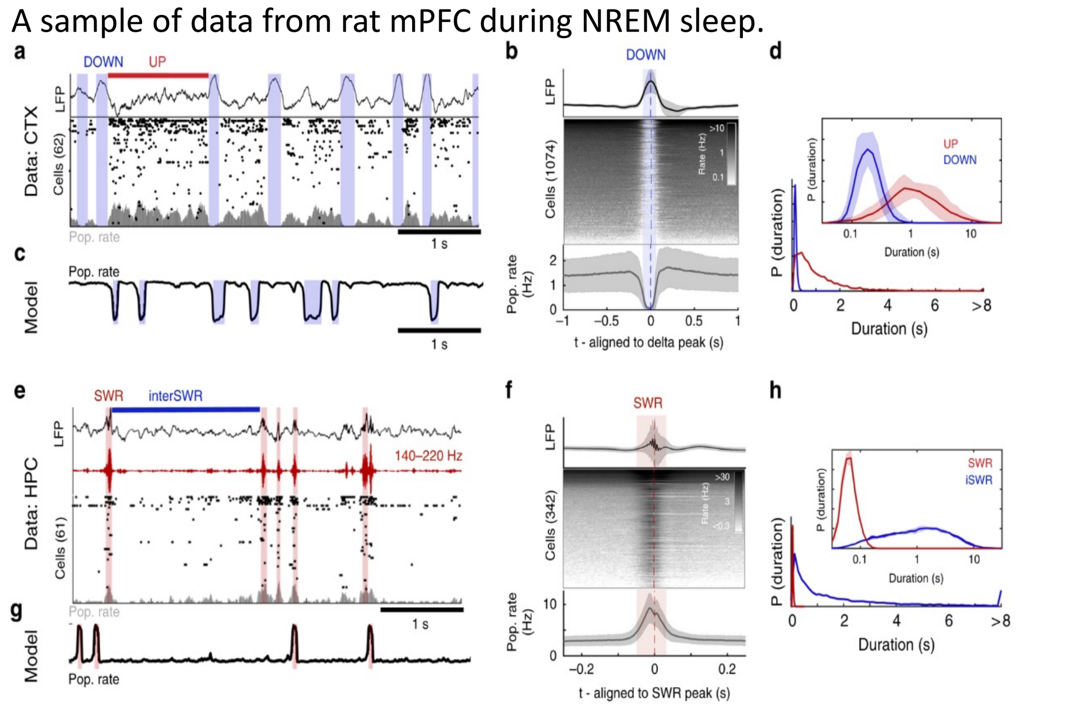
1. Introduction

Sleep function relies on internally-generated dynamics in neuronal populations. In the mammalian forebrain, during non-rapid eye movement (NREM) sleep, neural populations oscillate between active spiking and quiet states. Known as slow oscillations in the neocortex and sharp wave-ripples in the hippocampus, these dynamic patterns, though typically studied in isolation, are both vital to the processes of NREM sleep.

The significance of these neural dynamics is clear: both slow waves and sharp wave-ripples (SWRs) play a role in the synaptic homeostasis [2] within their respective regions and their temporal coupling aids [3] memory consolidation [4]. Yet, the mechanisms by which the state of neuronal groups in these regions facilitates their distinct rhythms, and how such states enable the transfer of neural signals between areas, remain to be fully understood.

2. Motivation

A sample of data from rat mPFC during NREM sleep.



Source: (Levenstein et al., 2019, p. 2)

In the Neocortex, the local field potential (LFP) features slow waves, characterized by cycles of neuronal spiking (UP states) and hyperpolarization (DOWN states). The Hippocampus during NREM sleep is characterized by sharp wave-ripple events, which are bursts of neuronal activity (SWRs) interspersed with intervals of relative quiescence. Both brain structures exhibit a skewed distribution in the duration of these alternating states.

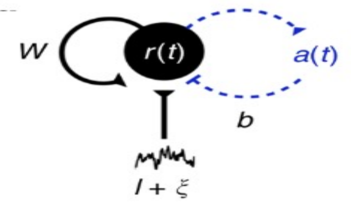
3. Methods

To study the state of hippocampal and neocortical populations during NREM sleep, we used a firing rate model that represents a neuronal population with positive feedback (recurrent excitation) and slow negative feed- back (adaptation). Wilson-Cowan-like model for a neural population with slow adaptive process

$$\tau_r \frac{dr}{dt} = -r + R_\infty(wr - ba + I + \xi(t))$$

$$\tau_a \frac{da}{dt} = -a + A_\infty(r)$$

$$R_\infty(x) = \frac{1}{1+e^{-(x-x_0)}} \quad A_\infty(r) = \frac{1}{1+e^{-k(r-r_0)}}$$



Ornstein-Uhlenbeck noise:

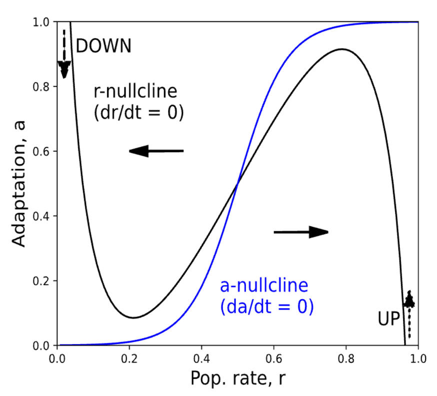
$$d\xi = -\theta\xi\, dt + \sigma\sqrt{2\theta dt}\, dW_t$$

Numerical and analytical methods from dynamical systems theory reveals how UP/DOWN dynamics in the model.

R-a phase plane plots determine number of fixed points.

Jacobian matrix to analyze stability of fixed points.

$$J = \begin{bmatrix} -1 + wr(1-r) & -br(1-r) \\ \frac{1}{\tau} - \frac{a(1-a)}{\tau} & -\frac{1}{\tau} \end{bmatrix}$$

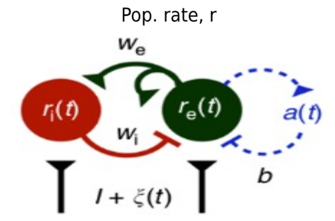


Adapting Inhibition-Stabilized Network (aISN)

$$\tau_e \frac{dr_e}{dt} = -r_e + R_{e,\infty}(w_{ee}r_e - w_{ei}r_i - ba + I_e + \xi_e(t)),$$

$$\tau_i \frac{dr_i}{dt} = -r_i + R_{i,\infty}(w_{ie}r_e - w_{ii}r_i + I_i + \xi_i(t)),$$

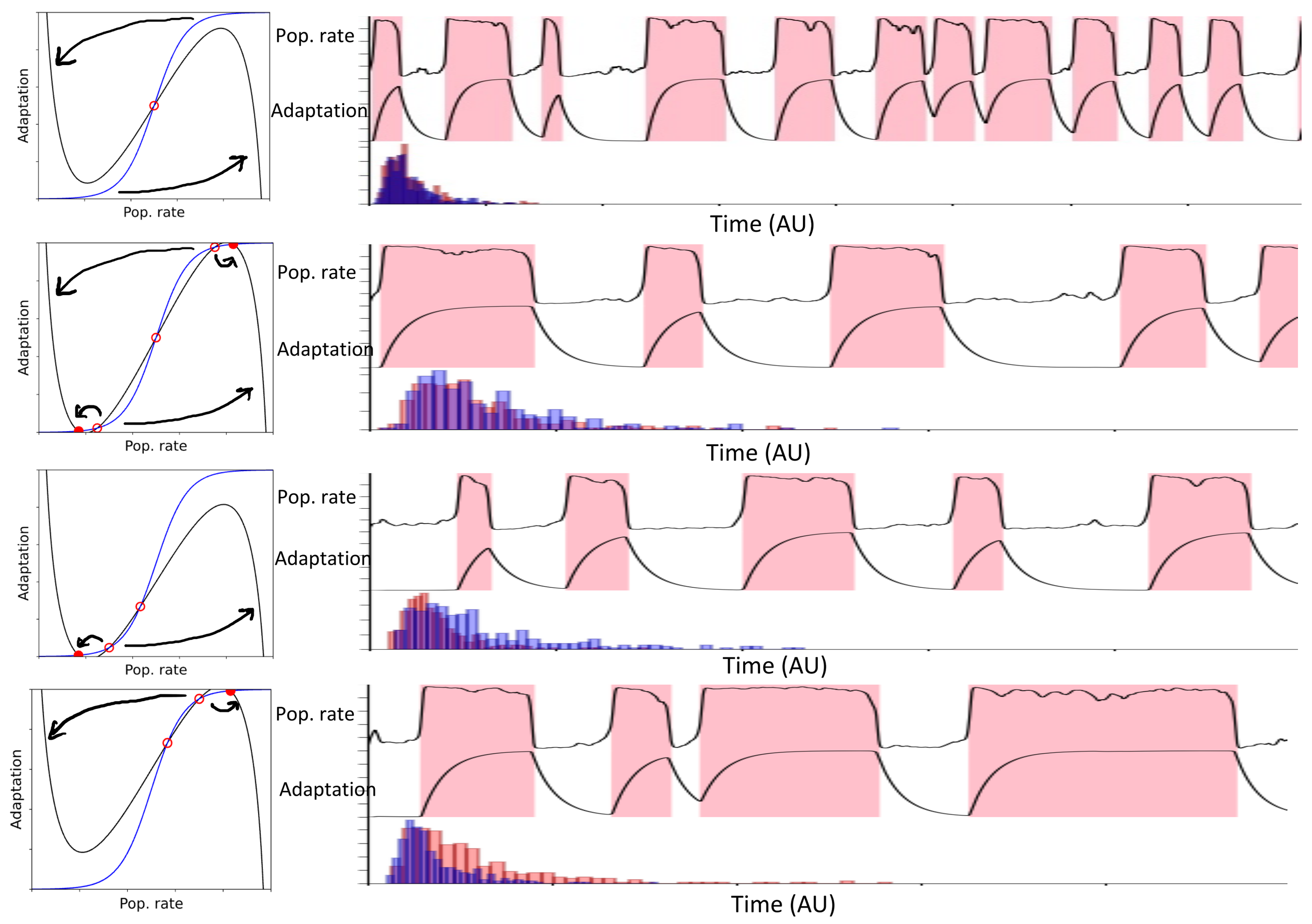
$$\tau_a \frac{da}{dt} = -a + A_\infty(r_e)$$



4. Results

UP/DOWN dynamics in an adapting excitatory population model

Depending on parameter values, the model can show four distinct regimes of UP/DOWN dynamics—distinguished by whether UP/DOWN transitions are noise- or adaptation-induced.

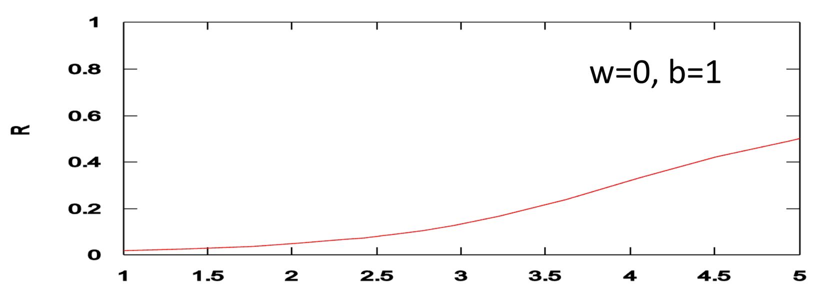


- Model shows four distinct regimes of UP/DOWN dynamics in the r-a phase plane.
- They are distinguished by whether UP/DOWN transitions are noise- or adaptation-induced and thus the stability or transient nature of the UP and DOWN states.
- Simulated time course and UP/DOWN state duration distributions for each regime.

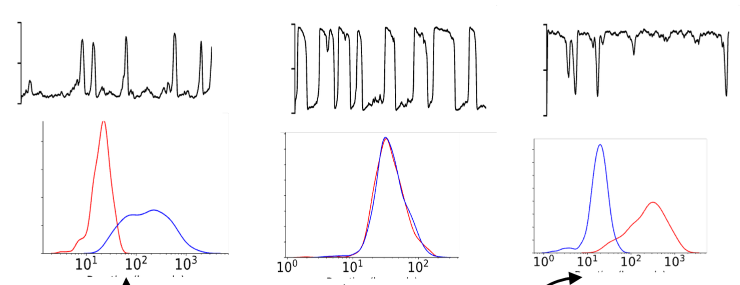
Recurrence, adaptation and drive determine dynamical regime and duration statistics

Considering the population's effective input/output relation (I/O curve) to know how the population rate fixed points, r_{ss} depend on the level of drive.

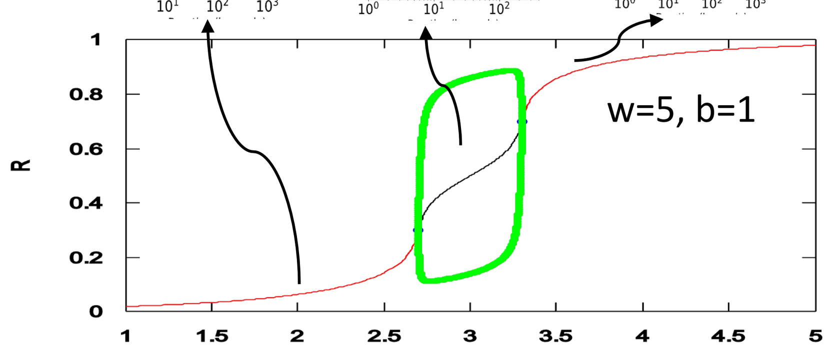
If recurrence is weak, the I/O curve increases monotonically with drive and no UP/DOWN alternations are possible.

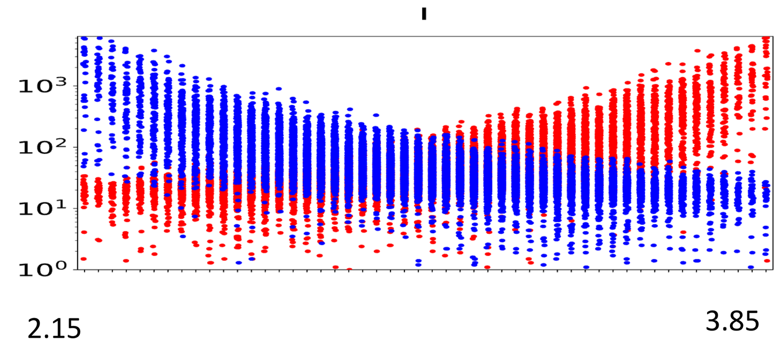


At a critical value of recurrent excitation the population is able to self-maintain an UP state and UP/DOWN alternations emerge between low-rate activity at weak drive and high-rate activity at strong drive.



Effects of noise on an oscillatory-centered I/O curve: Within the oscillatory regime, the simulated population rate alternates regularly between transient UP and DOWN states, and UP/DOWN state durations reflect the time scale of adaptation. As drive is further increased, the effective stability of the UP state increases and larger fluctuations are needed to end the UP state.

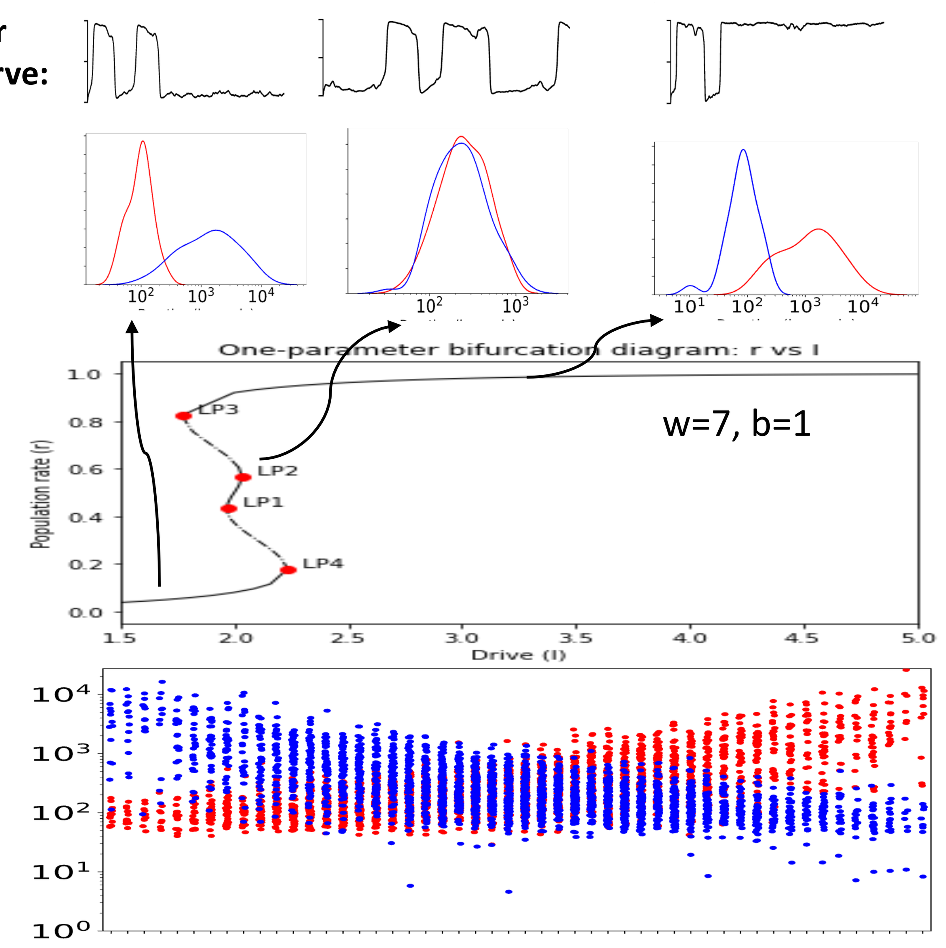




Response properties seen for the bistable-centered I/O curve:

Through pinpointing the parameters that prompt shifts in the dynamical regime at the midpoint of the input/output (I/O) curve, we observe that an oscillatory-focused I/O curve emerges with enhanced adaptation, while a bistable-focused I/O curve arises with increased recurrent activity.

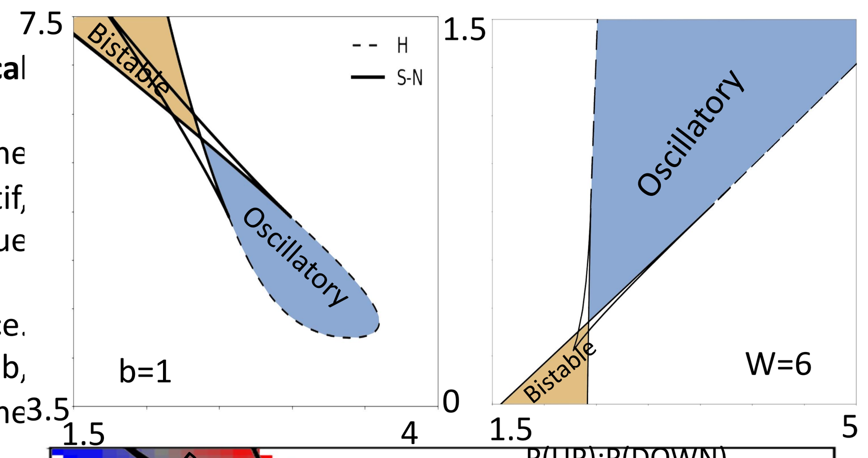
In either scenario, the duration distributions plotted vs. drive form a crossed-pair, with a center symmetrical portion.



Parameter space of dynamical regimes of the r-a model:

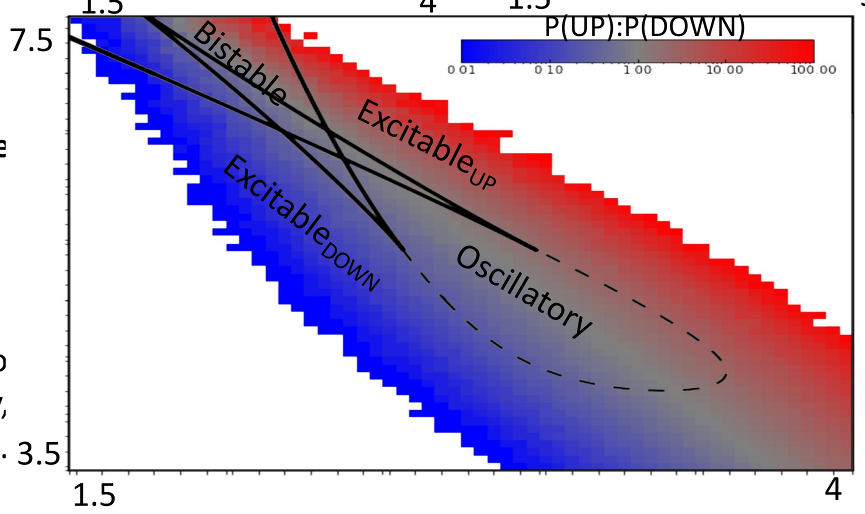
I-w bifurcation diagram reveals the "Butterfly Catastrophe" motif, yellow indicates bistability, blue indicates oscillations.

The I-b parameter space. Increasing adaptation strength, b, increases the domain of the oscillatory regime.



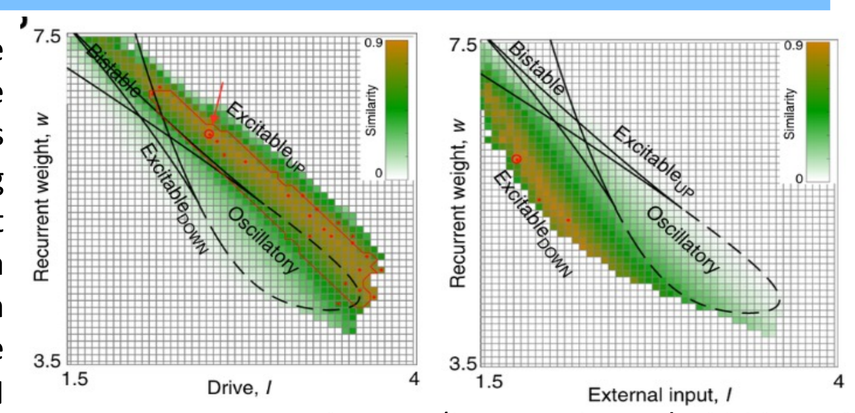
Analysis of simulated duration distributions to a representative parameter plane and I-b plane.

The statistics of UP/DOWN state durations reflect the underlying dynamical regime, allowing us to effectively distinguish oscillatory, bistable, and excitable dynamics.

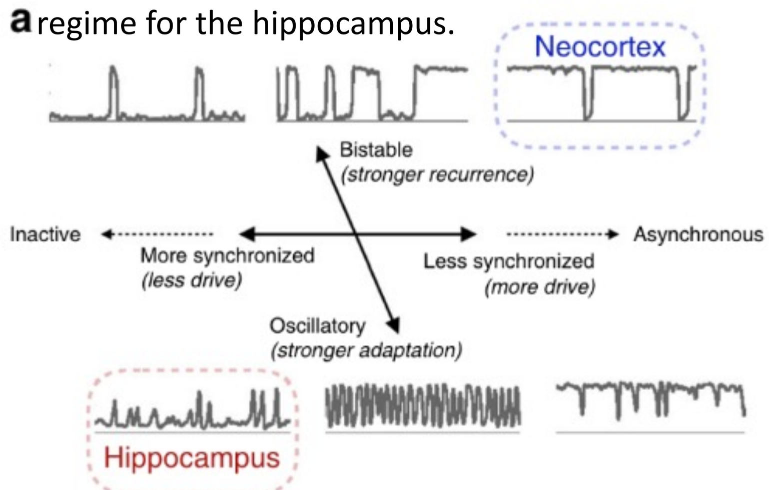


Neocortex is in Excitable$_{UP}$ and Hippocampus is in Excitable$_{DOWN}$ in NREM

The r-a model replicates the neuronal behaviour of the neocortex and hippocampus, as evidenced by the 25 top-fitting points. The areas of greatest congruence between empirical data and the model are located within the ExcitableUP regime for the neocortex and the ExcitableDOWN regime for the hippocampus.



Source: (Levenstein et al., 2019, p. 6)



Excitable dynamics of NREM sleep

UP/DOWN alternation dynamics are characterized by a spectrum of two effective axes: a degree of synchronization axis determined by the level of drive in the system and an oscillatory-bistable axis determined by the relative strength of recurrence and adaptation.

Source: (Levenstein et al., 2019, p. 9)

5. Future Work

1. UP/DOWN state duration matching that calculates similarity to plot the neocortical data of HPC and CTX on I-w space.
2. Plot Nullclines, time course and do the bifurcation analysis for the aISN model
3. Analysis on the duration variability which is measured by the coefficient of variation
4. Role of depth of NREM in the stability of states as the paper suggests that deeper stages of NREM reflect a less stable UP state

6. Conclusion

Our findings demonstrate that distinct excitability dynamics in the mammalian forebrain characterize NREM sleep, with concurrent neocortical slow oscillations and hippocampal SWRs. By applying a unified model with varied parameters, we captured diverse UP/DOWN dynamics akin to in vivo observations. The model suggests that key physiological parameters shape these dynamics. Specifically, neocortical oscillations correspond to an ExcitableUP regime with prevalent UP states interrupted by brief DOWN states, whereas hippocampal sharp waves align with an ExcitableDOWN regime where prevalent DOWN states are interspersed with brief UP states. This offers a cohesive view of neocortical and hippocampal activity during NREM sleep, indicating a potential mechanism for their interaction. Our analysis also highlights how neural drive and the balance between excitation and adaptation govern a range of dynamical regimes, characterized by the stability of UP and DOWN states, mirroring the asymmetrical durations seen in NREM sleep.

References

[1] Levenstein, D., Buzsáki, G. & Rinzel, J. NREM sleep in the rodent neocortex and hippocampus reflects excitable dynamics. *Nat Commun* **10**, 2478 (2019). https://doi.org/10.1038/s41467-019-10327-5

[2] Tononi, G. & Cirelli, C. Sleep and synaptic homeostasis: a hypothesis. Brain Res. Bull. 62, 143–150 (2003).

[3] Peyrache, A., Khamassi, M., Benchenane, K., Wiener, S. I. & Battaglia, F. P. Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. Nat. Neurosci. 12, 919–926 (2009).

[4] Siapas, A. G. & Wilson, M. A. Coordinated Interactions between Hippocampal Ripples and Cortical Spindles during Slow-Wave Sleep. Neuron 21, 1123–1128 (1998).

Acknowledgements

With thanks to:

1. Prof. Mark van Rossum for their advice and assistance on the topic and the poster.
2. Prof. Markus Owen for their guidance with numerical continuation methods and bifurcation plots.