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Structured E-I networks for movement generation

A salient property of neural population dynamics in motor cortex is the separation of neural activities into different subspaces, respectively traversed by the population during the preparation or execution of a movement pattern. Previous computational models used stabilized excitatory-inhibitory (E-I) networks to explain this separation. For these networks, inputs and readouts are trained to map target trajectories to the rich neural dynamics of a non-normal, stabilized E-I reservoir, which otherwise does not have any structured connectivity. Here, we instead suggest that motor circuits are much more regular, with different subspaces being implemented by specific cell types. We construct an E-I circuit that strongly amplifies activity in a preparatory subspace into an oscillatory subspace, corresponding to the difference and sum activity modes of recurrently connected excitatory and inhibitory neurons, respectively. Oscillatory dynamics is realized via uni-directional connections between excitatory neuron sub-types, reflecting the well-known connectivity structure between intratelencephalic (IT) and pyramidal tract (PT) neurons in cortical layer 5. Motivated by recent reports of a discrete set of temporal frequencies in motor-cortical neural activity during movement generation, we suggest that neurons precisely balance their synaptic inputs from different neuron subtypes to generate a limited number oscillatory modes. These modes provide different temporal basis functions whose weighted activation allows the composition of specific movement patterns. We explain how different oscillatory modes can be represented in the network in a distributed manner, while maintaining Dale's law, and demonstrate how complex movement trajectories can be triggered by the stimulation of even a single neuron, in line with experimental evidence. In summary, we present a general framework for the implementation of motor-cortical dynamics in recurrent networks. We suggest that oscillatory modes are realized by defined cell types and show how complex movement patterns can be stored in structured biological E-I circuits.

During movement initiation, the identity of a movement can be decoded from neural activity in the preparatory subspace, already before movement onset.[3] After movement onset neurons exhibit strong oscillatory dynamics (Fig. 1*A* & *B*). Recent reports suggest that this oscillatory activity contains distinct frequency modes[1] (Fig. 1*B* & *C*). We analysed activities generated from a popular network model of motor cortex[2] and instead observed a continuum of oscillatory modes, reflecting the random nature of the network's recurrent connectivity (Fig. 1*D*, i). While a large random network might still provide a sufficiently rich dynamics to produce trajectories in line with the observed dynamics, replicating the observed eigenspectrum, we asked how distinct oscillatory modes can be represented in more compact, structured networks.

To create a preparatory subspace that feeds into a single oscillatory mode we consider a linear E-I rate networks with the following dynamics

$$\dot{\mathbf{r}} \propto -\mathbf{r} + \mathbf{M}_\omega \mathbf{r}, \quad \mathbf{r} = \left(r_{E_1}, r_{I_1}, r_{E_2}, r_{I_2}\right)^\mathsf{T}, \qquad (1)$$

$$\mathbf{M}_\omega = \begin{pmatrix} w & -kw & \omega & 0 \\ w & -kw & \omega & 0 \\ 0 & -\omega & w & -kw \\ 0 & -\omega & w & -kw \end{pmatrix}, \mathbf{S} \propto \begin{pmatrix} 1 & 0 & 1 & 0 \\ -1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 1 \\ 0 & -1 & 0 & 1 \end{pmatrix},$$

where **r** is a vector of excitatory and inhibitory firing rates. Following previous work, we consider **r** to be the the difference from a firing rate baseline,[2] thus, **r** can be negative. We adhere to Dale's law and maintain the corresponding sign in the columns of the recurrent weight matrix **W** (Fig. 1*E* & *F*, top). Transforming **M** into a sum and difference basis reveals the non-normal amplifying, and oscillatory dynamics:[4]

$$\mathbf{S}^\mathsf{T}\mathbf{M}\mathbf{S} = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ w + kw & \omega & w - kw & \omega \\ \omega & w + kw & -\omega & w - kw \end{pmatrix},$$

where activity in the difference modes, corresponding to the preparatory subspace, quickly decays to zero (cf. Eq. 1), while they transiently amplify the oscillating sum modes[5] (Fig. 1*G*). The uni-directional connectivity from E_2 to E_1, provides the crucial asymmetry that is required to generate oscillatory dynamics. We speculate that this asymmetry corresponds to the uni-directional projections from IT to PT excitatory neurons.[6]

To generate more complex motor trajectories we combine a discrete set of oscillatory modes into a single network. The weight matrix becomes (Fig. 1*F*, centre)

$$\overline{\mathbf{M}} = \begin{pmatrix} \mathbf{M}_{\omega_0} & & \\ & \ddots & \\ & & \mathbf{M}_{\omega_4} \end{pmatrix},$$

where we chose ω_i according to the spectrum of the experimentally observed neural trajectories (Fig. 1*C*). We generated activities from random initial conditions and confirmed that the spectrum resembled the experimentally reported values (Fig. 1*D*, ii & iii). The different oscillatory modes can also be understood as temporal basis functions. By initialising the system from preparatory states with appropriate weighting in each frequency mode, the network can generate precise neural trajectories (Fig. 1*H*). We speculate that different frequency modes may be facilitated by specific interneuron subtypes that selectively project

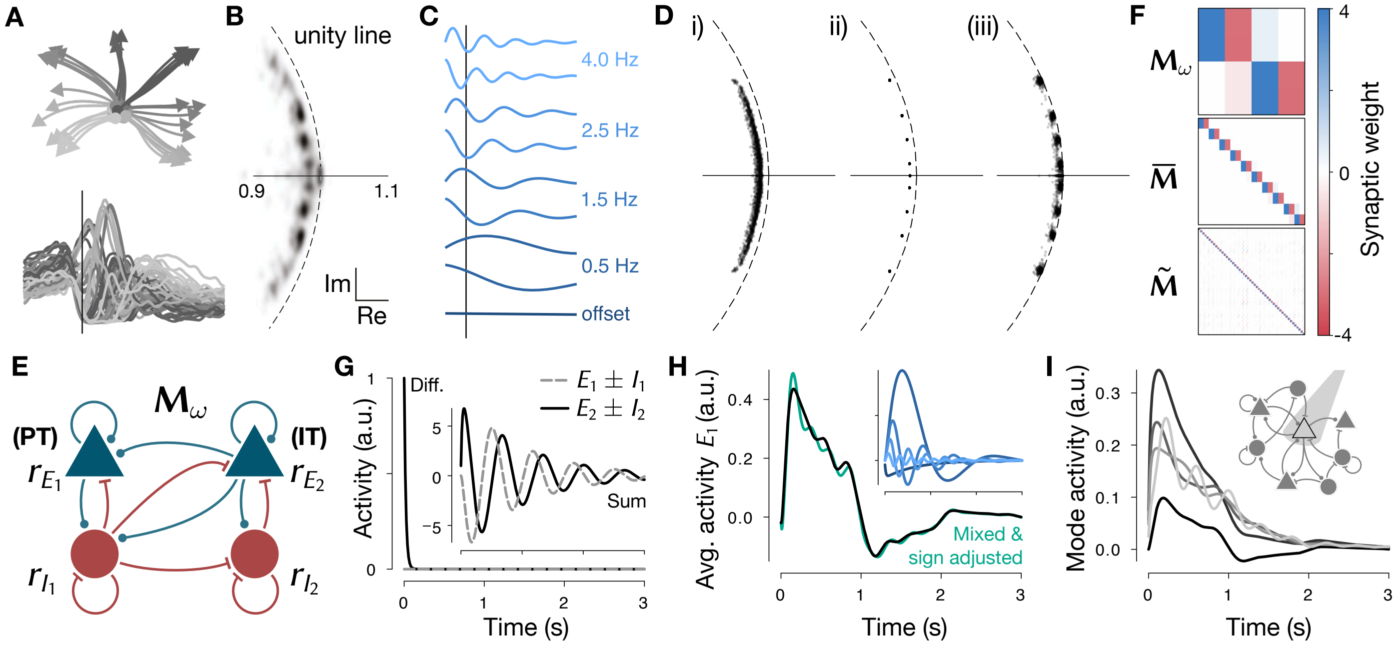

Figure 1. **(A)** Top: Macaque hand trajectories during a reaching task. Target locations varied across conditions, indicated by greyscale. Bottom: Single neuron recordings during different trials in *A*. Vertical line: movement onset. **(B)** Eigenvalue distribution of linear dynamical systems fitted to condition averaged trajectories.[1] **(C)** Discrete oscillatory modes corresponding to the clusters in *B*. **(D)** jPCA eigenvalue spectra of neural activities generated from different network models (Methods described in Sabatini and Kaufman[1]). i) Activity generated from random initial states in a stability-optimized network by Hennequin *et al.*[2] ii) Our network, initialised in different random initial states. iii) Same as ii), but with process noise. **(E)** E-I circuit structure to generate non-normal, oscillatory dynamics. **(F)** Different weight matrices with excitatory (blue) and inhibitory (red) synapses. See text for details. **(G)** Activity of difference and sum modes (inset) of the circuit in *E*. **(H)** Example trajectory composed out of multiple activated oscillatory modes of different frequencies (inset). Recovered trajectory after mixing and sign adjustment in green. **(I)** Activity trajectories of single output modes, initiated via single cell stimulation. The mixing matrix, **Q**, was constructed to produce the same trajectory as in *H* (black). Panels *A*, *B* & *C* adapted from Sabatini and Kaufman.[1]

to different excitatory subtypes,[7] as is required in our model (cf. Eq. 1 and Fig. 1*F*, center).

So far, our networks are organized in a block diagonal structure (Fig. 1*F*, top & center), where different frequency modes form disassociated sub-networks and single neurons oscillate at a specific frequency (cf. Fig. 1*H*, inset). We also considered only one set frequency modes that can control only a single output mode (cf. Fig. 1*H*). This is different from cortical circuits, where neurons are more densely connected, show more complex dynamics (cf. Fig. 1*A*, bottom), and control hundreds of muscles. To distribute and mix different oscillatory modes, we introduce a change of variables such that the recurrent weight matrix becomes less sparse, while the connectivity structure between presumed PT and IT neurons is maintained:

$$\tilde{\mathbf{M}} = \mathbf{Q}^{-1}\left(\mathbb{1}_{N\times N}\otimes\overline{\mathbf{M}}\right)\mathbf{Q}, \quad \mathbf{Q} = \overline{\mathbf{Q}}\otimes\mathbb{1}_{4\times 4},$$

where we now consider $5 \times N$ frequency modes that together control N output degrees of freedom, and **Q** mixes all $5 \times N$ oscillatory modes, i.e., $\overline{\mathbf{Q}} \in \mathbb{R}^{5N\times 5N}$. This allows to store specific motor primitives into the network that can be recalled by stimulating just a single neuron (Fig. 1*I*), reminiscent of complex movements triggered by cortical microstimulation.[8,9]

A change of variables does in general not maintain the sign structure of a matrix, i.e., we violate Dale's law. However, when E-I difference modes quickly decay to zero after movement onset (cf. Fig. 1*G*), excitatory and inhibitory neuron pairs have very similar activity and we can replace a negative excitatory (or positive inhibitory) connection by a negative inhibitory (or positive excitatory) connection originating from the corresponding E or I neuron. (Fig. 1*H*).

In summary, we present a general framework for the design of structured recurrent E-I circuits based on established dynamical motifs (non-normal and oscillatory dynamics), where experimental observations (discrete eigenspectra) together with biologically plausible connectivity structures (Dale's law) provide the necessary constraints to relate different cortical cell types to computational function.

References: ***1***. D. A. Sabatini, M. T. Kaufman, *Nature Communications* (2024). ***2***. G. Hennequin *et al.*, *Neuron* (2014). ***3***. M. M. Churchland, K. V. Shenoy, *Nature Reviews Neuroscience* (2024). ***4***. G. F. Elsayed *et al.*, *Nature communications* (2016). ***5***. B. K. Murphy, K. D. Miller, *Neuron* (2009). ***6***. A. Baker *et al.*, *Journal of Neuroscience* (2018). ***7***. S. J. Wu *et al.*, *Neuron* (2023). ***8***. M. S. Graziano *et al.*, *Neuron* (2002). ***9***. S. A. Overduin *et al.*, *Neuron* (2012).