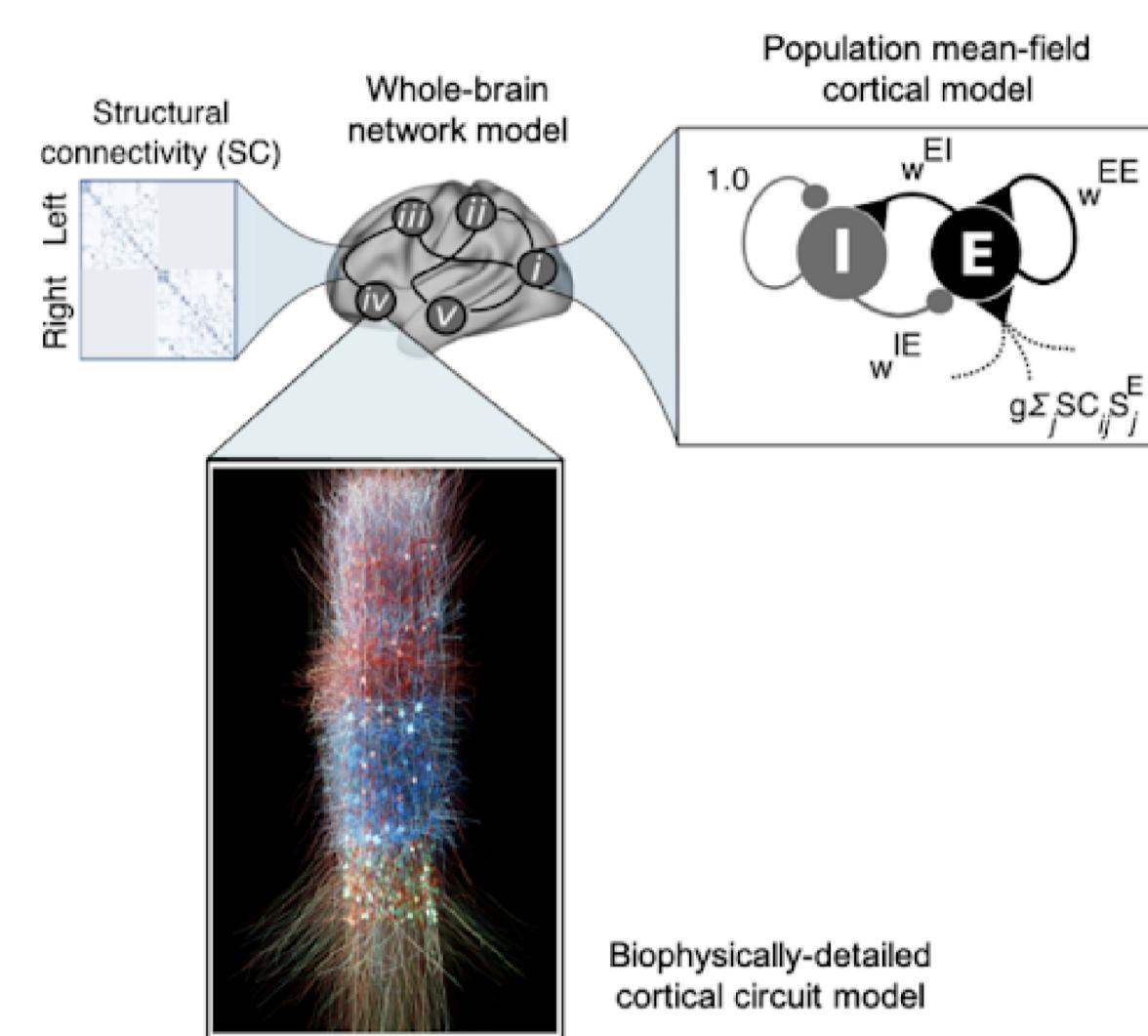


# Interfacing biophysical circuits with whole-brain networks using The Virtual Brain and NetPyNE

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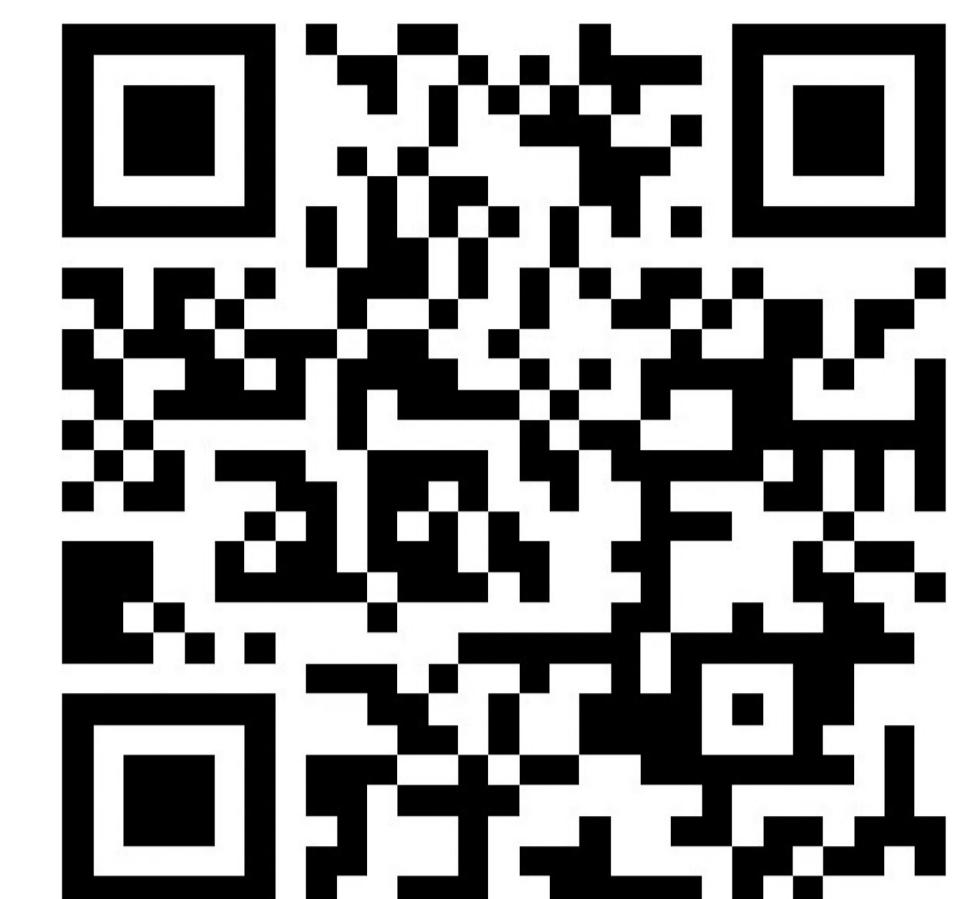
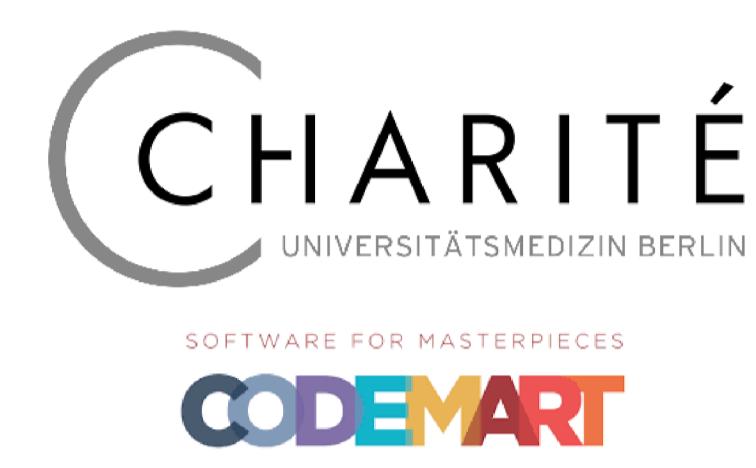
## Introduction



With the help of the TVB-multiscale toolbox, neural mass models can be interfaced with spiking models to achieve multiscale co-simulation. We introduce a new co-simulation interface between The Virtual Brain (TVB) and the NetPyNE/NEURON, achieving a new cross-scale coverage milestone: linking molecular chemical signaling to whole-brain network dynamics.



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## Components

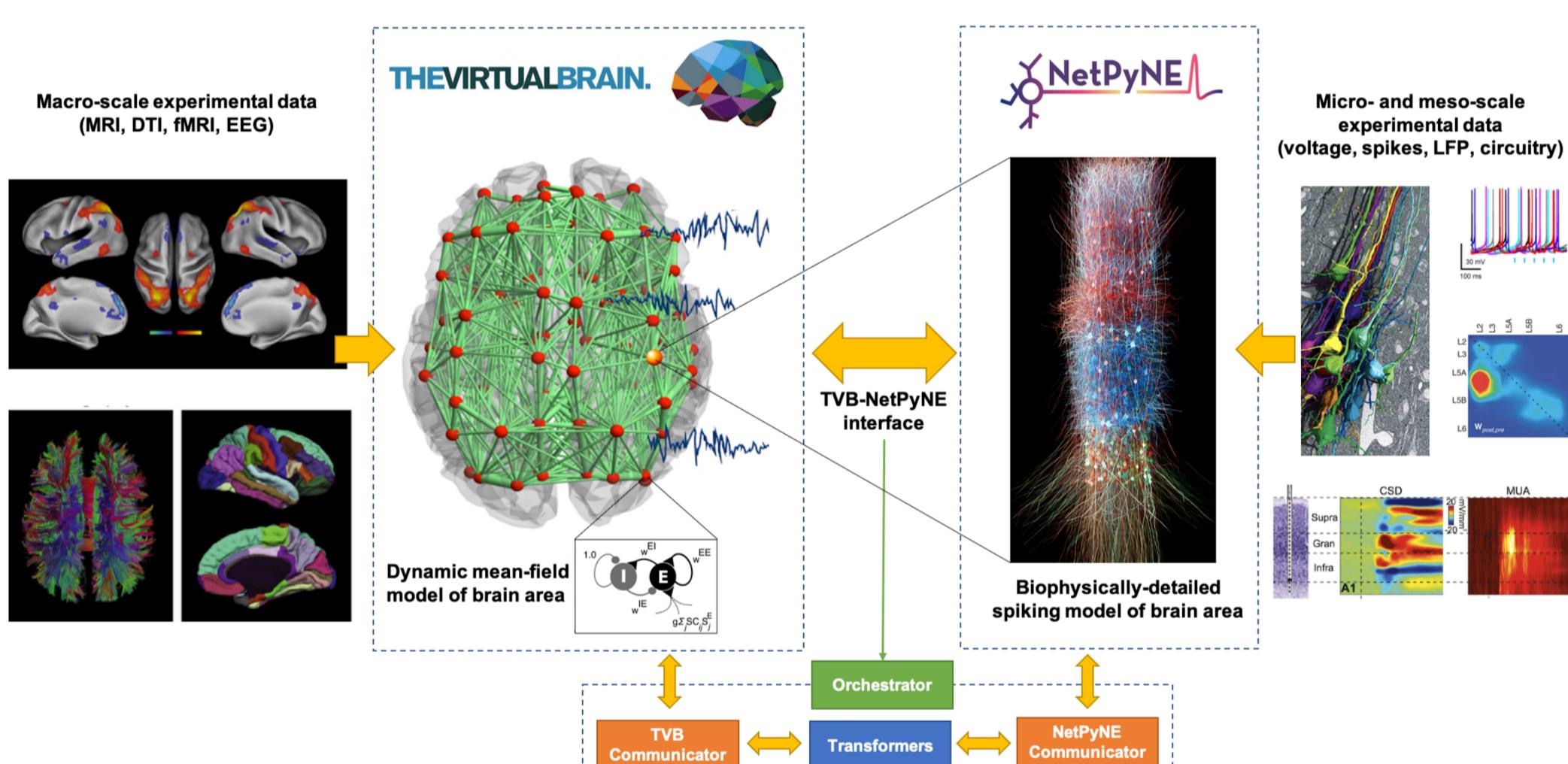


THE VIRTUAL BRAIN.

The Virtual Brain [2, 4] is a commonly-used reference tool for simulating macroscale whole-brain network models derived from multimodal MRI (anatomical, functional and diffusion) and electrophysiological datasets. TVB dynamics come from weighted interactions among network nodes, which are represented as neural mass models (mean-field models), whose state reflects the statistical average of the underlying neural population activity.



NetPyNE [1] provides a high-level interface to NEURON - the most widely used multiscale neural simulation engine [3] - to facilitate the development, parallel simulation and analysis of brain models covering the molecular, cellular and circuit scales. Additionally, NetPyNE/NEURON are unique compared to other neural circuit modeling tools in supporting the molecular reaction-diffusion (RxD) module.



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## Mechanism of co-simulation

With co-simulation approach [5], any of the TVB nodes can be replaced by a network of spiking neurons to establish bidirectional real-time transfer of information between the TVB network and the spiking network [Fig. A]. Each region modeled with the spiking network receives combined input from TVB mean-field nodes: the state variable that represents the firing rate of a TVB node is transformed into Poisson spike trains, which feed into the spiking network. Communication from NetPyNE to TVB is implemented by transforming the recorded spiking activity to instantaneous firing rates, which update the corresponding state variable in the respective TVB mean-field node that represents the given spiking population. The example on Fig. B shows the Reduced Wong-Wang mean-field model, operating with two state variables - S (average synaptic activity) and R (average firing rate). The latter can be bound to spiking populations activity.

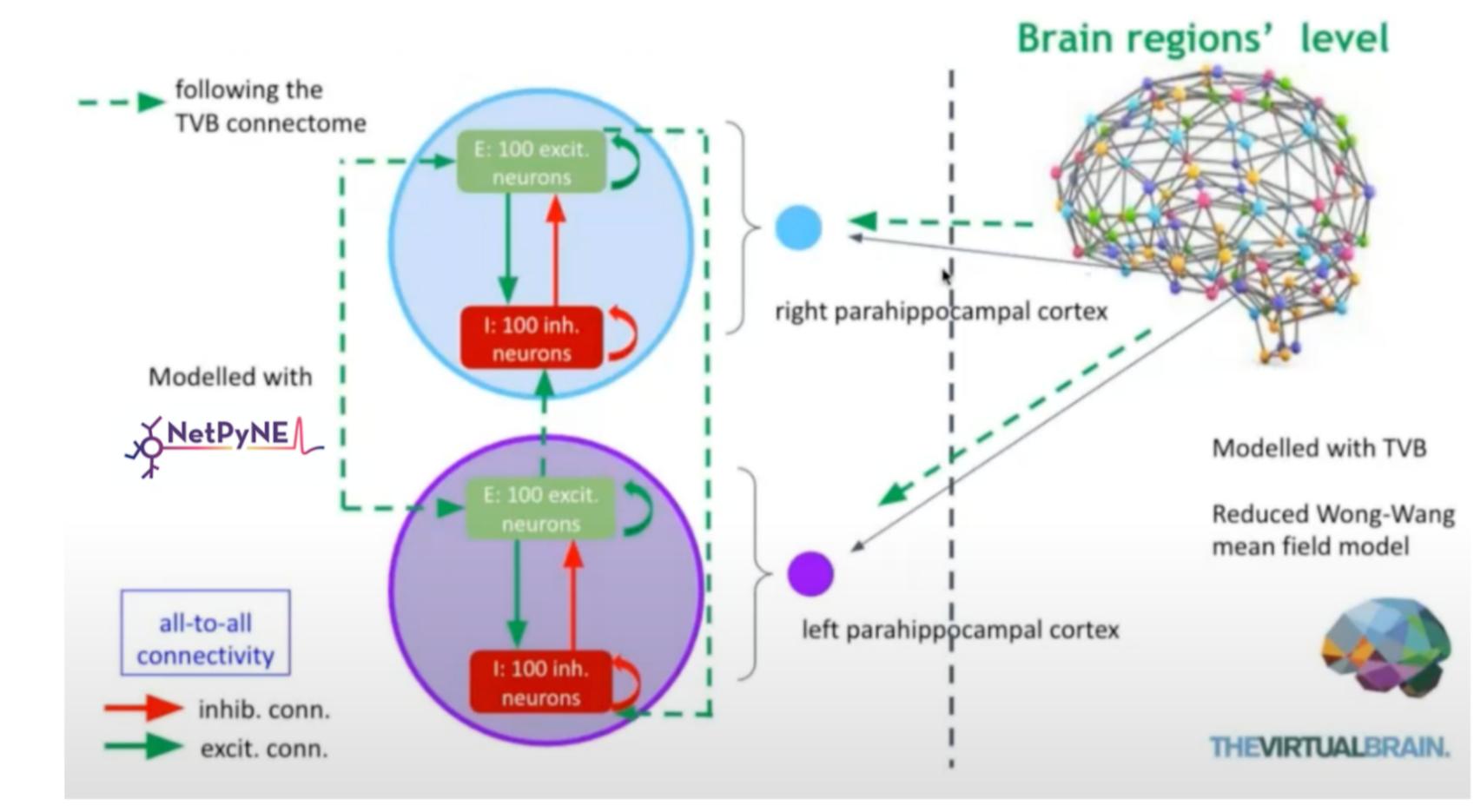


Fig. A

### Reduced Wong-Wang TVB mean field model

(Post)Synaptic gating dynamics (i.e., proportion of synapse channels open at any given time):  
 $S_{nr} = -\frac{1}{\tau} S_{nr}(t) + (1 - S_{nr}(t)) \gamma R_{nr}(t)$   
and  $R_{nr}(t)$  is the postsynaptic firing rate given by:  
 $R_{nr}(t) = H(I_{synnr}(t), a, b, d)$  where  
 $H(I_{synnr}(t), a, b, d) = \frac{a I_{synnr}(t) - b}{1 - e^{-d(I_{synnr}(t) - b)}}$   
is a sigmoidal activation function of the input presynaptic current.  
The total input presynaptic current to excitatory populations is given by:  
 $I_{synnr}(t) = I_o + w_{+} J_N S_{nr}(t) + G J_N \sum_{m \neq nr} C_{mnr} S_{mr}(t - \tau_{mnr})$

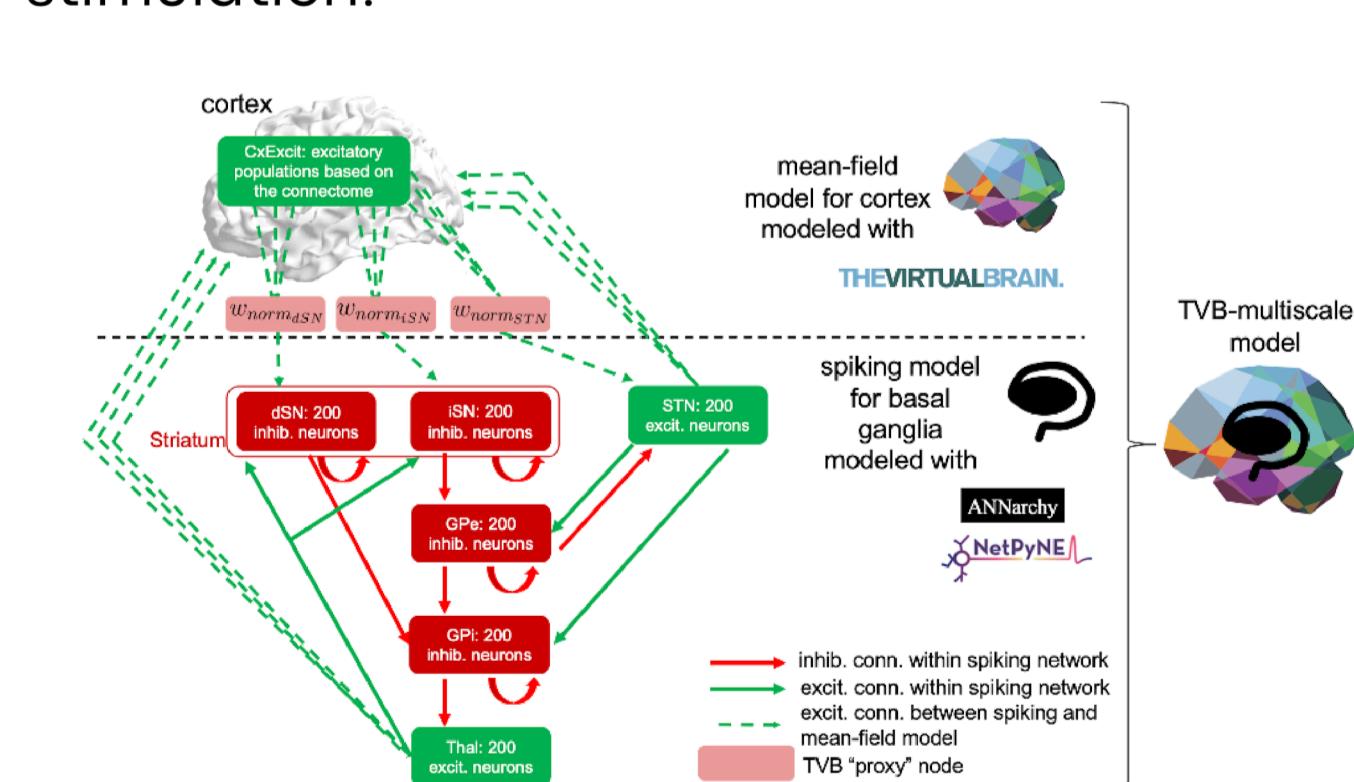
Fig. B

## Programmatic interface

Interface is described using standard python data structures. User provides the mapping of spiking network to the nodes of large scale network, and the interfaces for communication in both directions.

```
class DefaultExcIOInhBuilderInterface(NetpyneNetworkBuilder):  
    def set_default(self):  
        self.state_variable = 'R_e' # TVB state variable to couple to  
        self.set_cell_models()  
        self.set_synapse_models()  
        self.set_population()  
        self.set_population_connections()  
        self.set_nodes_connections()  
        self.set_output_devices()  
  
    def set_cell_model(self):  
        # spiking cell geometry and mechs  
        geom = NetpyneCellGeometry(diam=18.8, length=18.8, axialResistance=123)  
        mech = NetpyneMechanism(name='NH', gBar=0.12, gKBar=0.036, gLeak=0.003, gLeakmech=70)  
        cell_model = NetpyneCellModel(name='PNK', geom=geom, mech=mech)  
        self.cell_models = {cell_model}  
  
        self.cell_model_E = cell_model  
        self.cell_model_I = cell_model  
  
    def set_population(self):  
        self.populations = [  
            {'label': 'E', 'model': 'None', '# None means "all"'},  
            {'params': 'self.params',  
             'scale': 'self.scale_E'},  
            {'label': 'I', 'model': 'None', '# None means "all"'},  
            {'params': 'self.params',  
             'scale': 'self.scale_I'}]  
  
    def set_EE_population_connections(self):  
        connections = [  
            {'source': 'E', 'target': 'E',  
             'conn_spec': 'self.conn_spec_prob_low',  
             'delay': 'self.delay_low',  
             'receptor_type': 'self.receptor_type_E', 'nodes': None} # None means "all"  
        ]  
        return connections
```

network into a whole-brain mean-field network to investigate the essential tremor suppression through invasive or transcranial stimulation.



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## Work-in-progress applications

As a first demonstration of the capabilities of new interface, we are working on reproducing the results previously obtained with TVB-ANNarchy interface: multiscale co-simulation of a spiking basal ganglia model and a whole-brain mean-field model [6, figure]. Further on, this model can be actualized with morphological neurons of striatum and other areas.

Another ongoing study focuses on embedding a biophysically detailed cortico-cerebello-thalamo-cortical

## Summary

The TVB-multiscale toolbox enables to interface neural mass models with spiking models to achieve multiscale co-simulation. Previous studies have demonstrated the success of such interfaces using the NEST and ANNarchy spiking simulators [6] which operate with point neurons. We introduce the new co-simulation interface - between NetPyNE/NEURON and TVB - that achieves a new milestone for multiscale modeling: linking the whole-brain network dynamics to microscale characteristics of morphologically- and biophysically-

detailed cells and circuits, including molecular dynamics. In particular, this will enable unique studies of the effect that the molecular scale has on whole-brain activity and macroscale measures (fMRI, EEG, MEG). In turn, the whole-brain dynamics from different brain regions will interact with and affect the detailed biophysical circuit model, including its individual spiking neurons and underlying molecular dynamics. These complex multiscale interactions are essential to understand and treat various brain diseases.