Model-based inference on subject-specific mechanisms of (mal)adaptive learning and decision making

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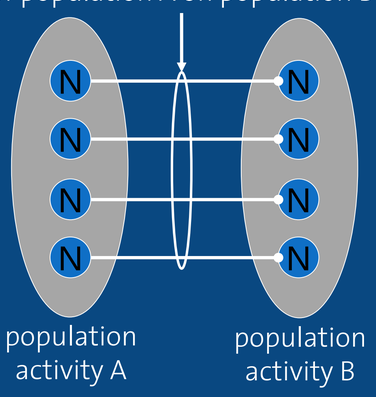
1 Synaptic plasticity and (mal)adaptive learning

- Synaptic plasticity is critical for reconfiguration of neuronal circles during normal learning and development but also for pathological learning and disorders.
- Synaptic plasticity at the level of neuronal populations leads to changes in the effective connectivity among these populations.
- Models of effective connectivity can, under experimentally well-controlled conditions, provide indices of the synaptic plasticity that underlies measured fMRI or EEG data.

- **fMRI & EEG/MEG:**
  - neural population activity
- **Effective connectivity:**
  - influence of one population over another
- **Synaptic plasticity:**
  - changes in effective connectivity, e.g. during learning

Under appropriate experimental control (!), change in effective connectivity = index for short-term plasticity

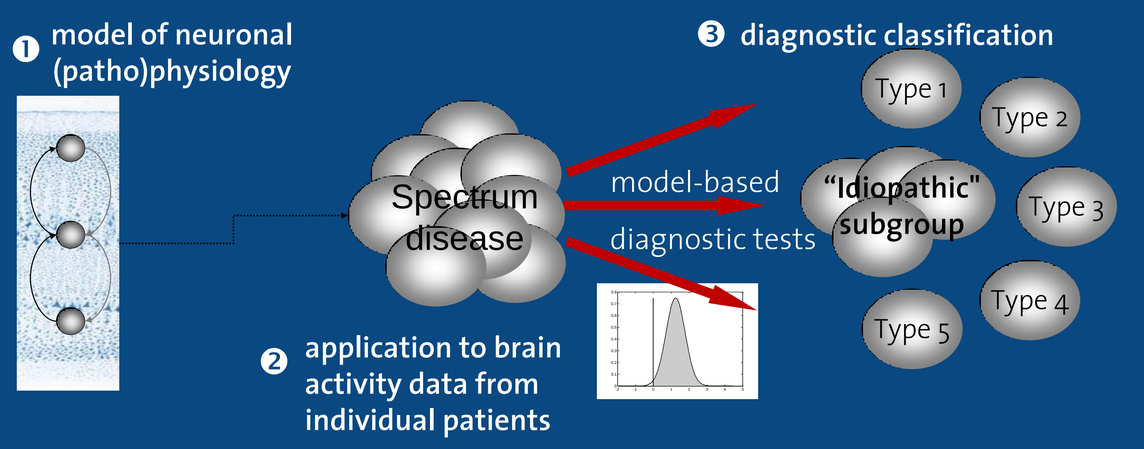
SP → change in the influence of population A on population B



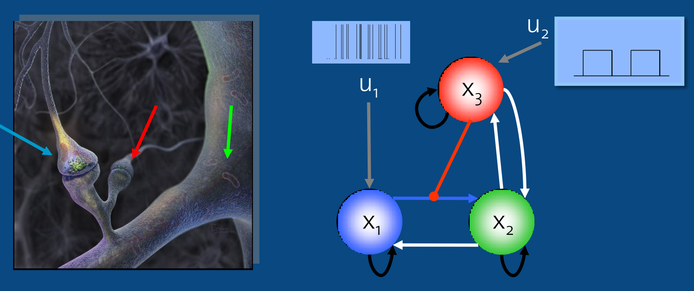
2 Model-based inference on synaptic plasticity

Model-based inference about synaptic plasticity during learning can be achieved by combining computational models of learning and neurophysiological models of changes in connectivity. We aim to develop individualised models, using anatomically and physiologically informed priors, that can be mechanistically interpreted.

This model-based approach can, in principle, quantify „hidden" physiological mechanisms in individual subjects or patients. This framework may serve to establish neurophysiologically grounded diagnostic classifications of spectrum diseases, such as schizophrenia or depression.



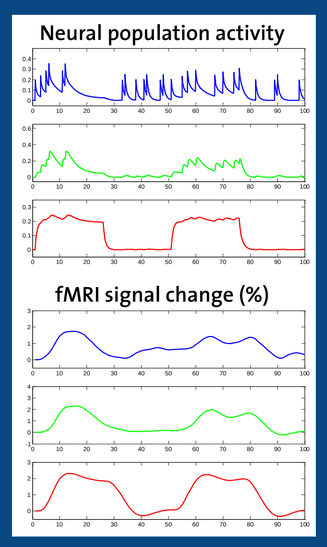
3 DCM & pharmacology

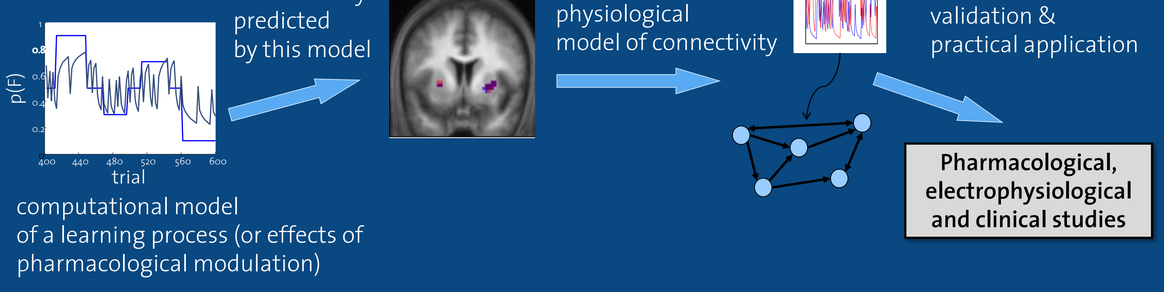


Nonlinear dynamic causal model (DCM) for fMRI

$$\frac{dx}{dt} = \left(A + \sum_{i=1}^{m} u_i B^{(i)} + \sum_{j=1}^{n} x_j D^{(j)}\right) x + Cu$$

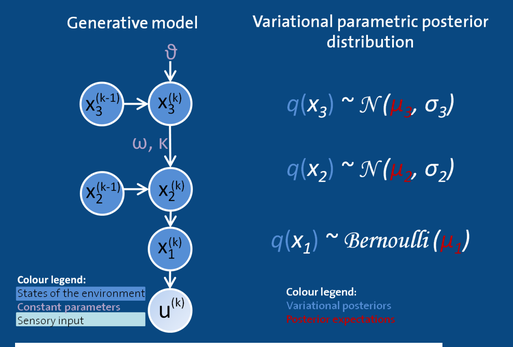
Stephan et al. 2008, *NeuroImage*

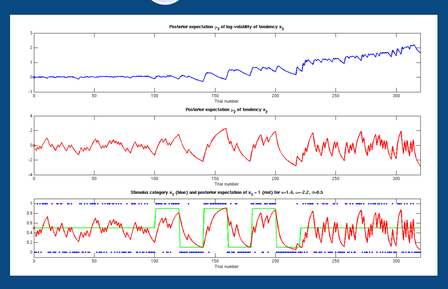




4 Computational models

Bayesian learning models prescribe an optimal way how agents learn under uncertainty, and they provide trial-wise prediction error estimates that can inform models of synaptic plasticity. However, they are computationally too complex for real-time learning and therefore biologically unrealistic. We have developed an extremely efficient variational approximation to ideal Bayesian learning; this allows for inference on an agent's belief about causal relations between stimuli in a changing world.





An agent is taken to receive a sequence of inputs u(1), u(2),... It uses these to make inferences on a hierarchy of hidden states x1, x2,... of its environment. While x1 is binary, all higher states are continuous. Continuous states change by performing Gaussian random walks that are hierarchically coupled (one state's step size is determined by the next higher state).

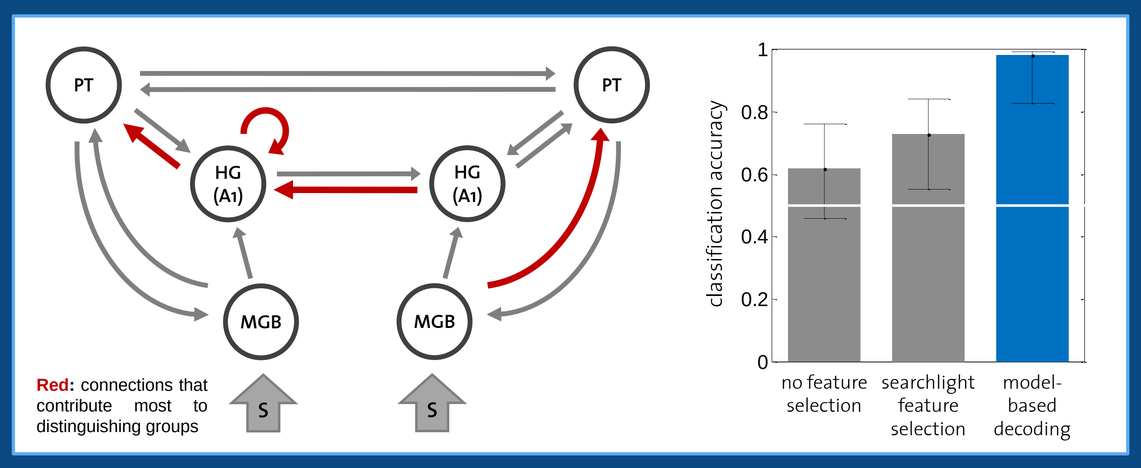
In a model with two coupled random walks, the nature of learning is determined by three parameters ϑ, κ, and ω. These parameters can be estimated from behavioural data.

ϑ is the step size of the random walk in x3. Reducing it leads to little learning in x3 due to agent's small uncertainty about x3's true value. ω regulates the step size in x2. Reducing it leads to little learning primarily in x2 and secondarily in x3 since this, representing the log-volatility in x2, cannot change much if x2 remains stable. κ determines how strongly x2 and x3 are coupled. Small κ diminishes learning in x3 despite great uncertainty while learning in x2 remains largely unaffected.

5 Model-based decoding

DCMs can not only serve to infer on (patho)physiological processes, but can also be used for diagnostic applications based on multivariate decoding techniques. The critical advantage of using DCM parameters for decoding is that the ensuing clinical classification becomes mechanistically interpretable.

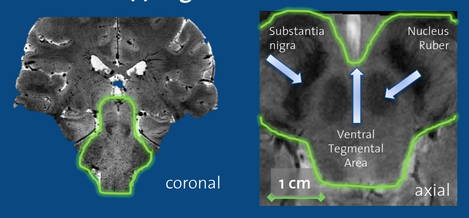
For example, patterns of effective connectivity, inferred by DCM, enable accurate model-based decoding of trial-by-trial perceptual states in rodents (Brodersen et al. 2010, *NeuroImage*), or diagnoses of aphasic patients (below). Our scheme outperforms conventional approaches and enables a biological interpretation of the results.



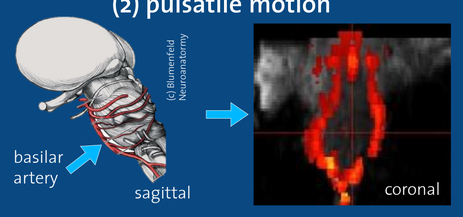
6 High-field fMRI (7 T)

Brainstem challenges

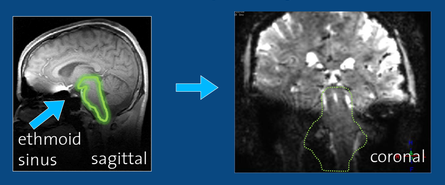
(1) high resolution



(2) pulsatile motion

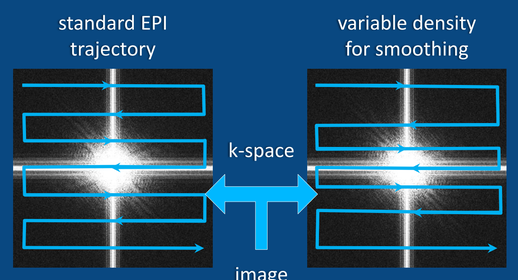


(3) susceptibility

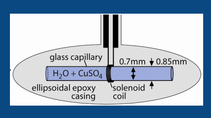


Brainstem solutions

SNR-optimal acquisition



field-monitoring with NMR probes



motion models: RETROICOR

$$y_{cardiac}(t) = \sum_n A_{c,n} \cdot \cos(n \cdot \varphi_c(t) + \varphi_c^0)$$

$$y(t) = y_{BOLD}(t) + y_{cardiac}(t) + y_{respiratory}(t)$$