Ca^{2+} modelling and TMS variability

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Outline

- Neural field modelling
  - Of calcium
- Modelling MEPs from a neural field scheme
- Consequences for variability

Neural field modelling of Calcium

$$V_a(t) = \sum_b V_{ab}(t),$$

$$Q_a(V_a) = \frac{Q_a^{\max}}{1 + e^{-(V_a - \theta_a)/\sigma_a}},$$

$$\left(\frac{1}{\gamma_{ab}}\frac{d}{dt} + 1\right)^2 \phi_{ab}(t) = Q_{ab}(t),$$

$$\left(\frac{1}{\alpha_{ab}}\frac{d}{dt} + 1\right)\left(\frac{1}{\beta_{ab}}\frac{d}{dt} + 1\right) V_{ab}(t) = \nu_{ab}(t)\phi_{ab}(t - \tau_{ab})$$

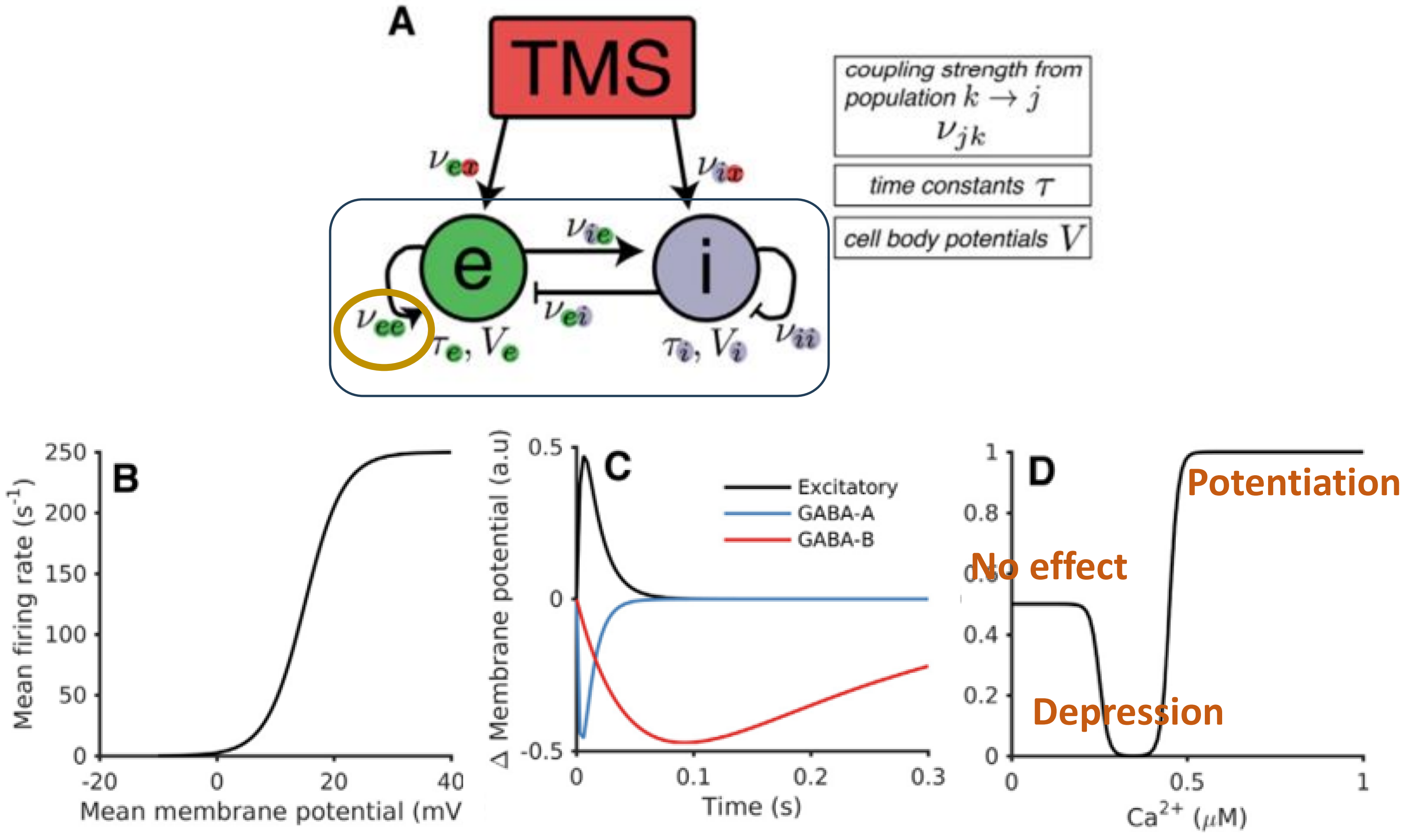
$$\frac{d\bar{\nu}_{ee}}{dt} = \eta([\mathrm{Ca}^{2+}]_e)\left(\nu_{\max}\Omega([\mathrm{Ca}^{2+}]_e) - \bar{\nu}_{ee}\right)$$

$$\frac{d[\mathrm{Ca}^{2+}]_e}{dt} = gB([\mathrm{glu}])H(V) - \frac{[\mathrm{Ca}^{2+}]_e}{\tau_{\mathrm{Ca}}},$$

$$\frac{d[\mathrm{glu}]}{dt} = \lambda_{\mathrm{glu}}\phi_{ee} - \frac{[\mathrm{glu}]}{\tau_{\mathrm{glu}}},$$

$$\frac{dg}{dt} = \frac{1}{\tau_{\mathrm{rec}}}(g_0 - g) - \frac{g_0}{\tau_{\mathrm{BCM}}}\left(\frac{\bar{\nu}_{ee}}{\nu_{ee}} - 1\right)$$

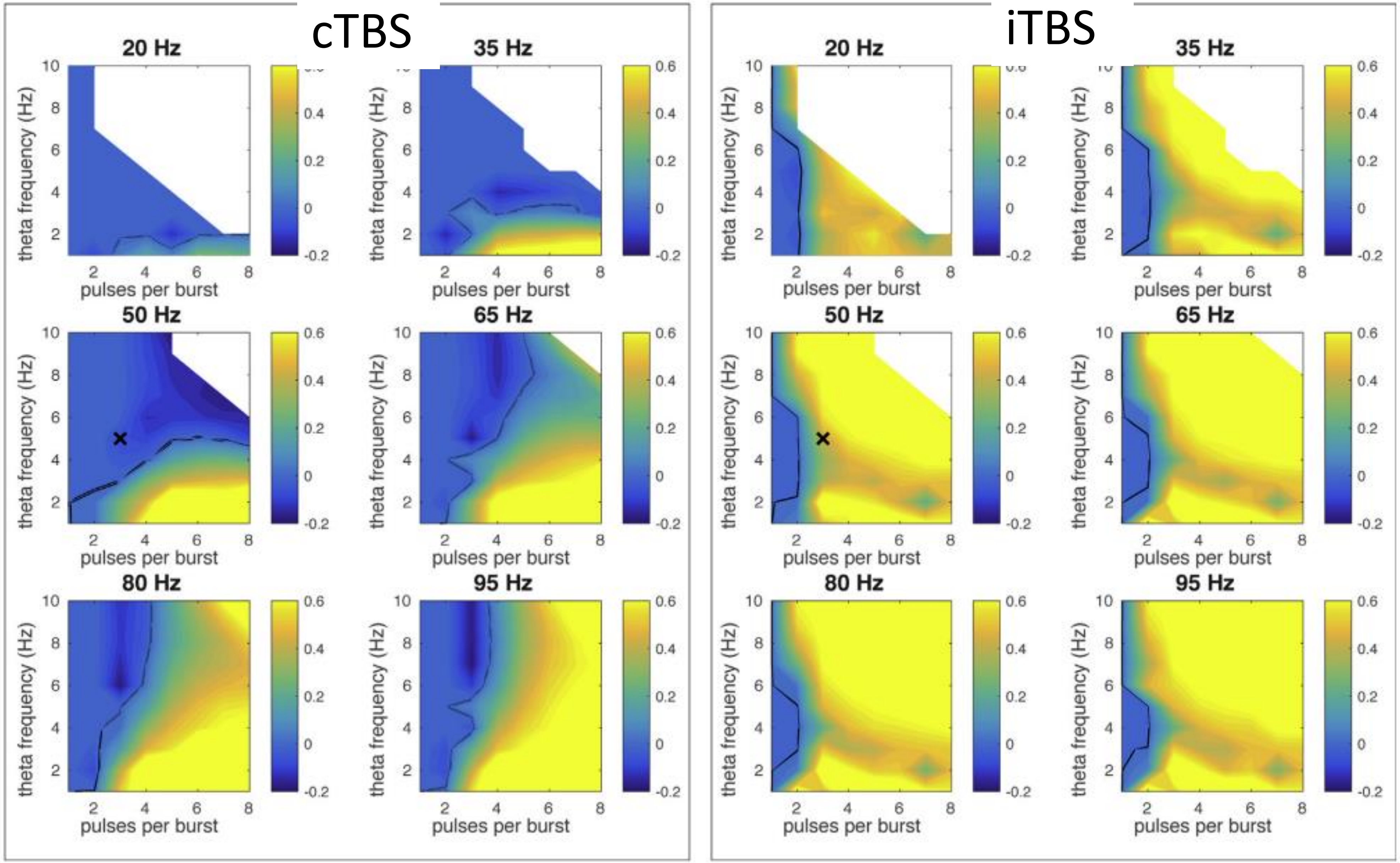
$$\left(z\frac{d}{dt} + 1\right)^2 \nu_{ee} = \bar{\nu}_{ee}.$$



M.T. Wilson et al. *Clinical Neurophysiology 129* (2018) 1230–1241, Figure 1

What can we do? Vary protocols

How does ν_{ee} change?



M.T. Wilson et al. *Clinical Neurophysiology 129* (2018) 1230–1241, Figure 4

Consequences for variability

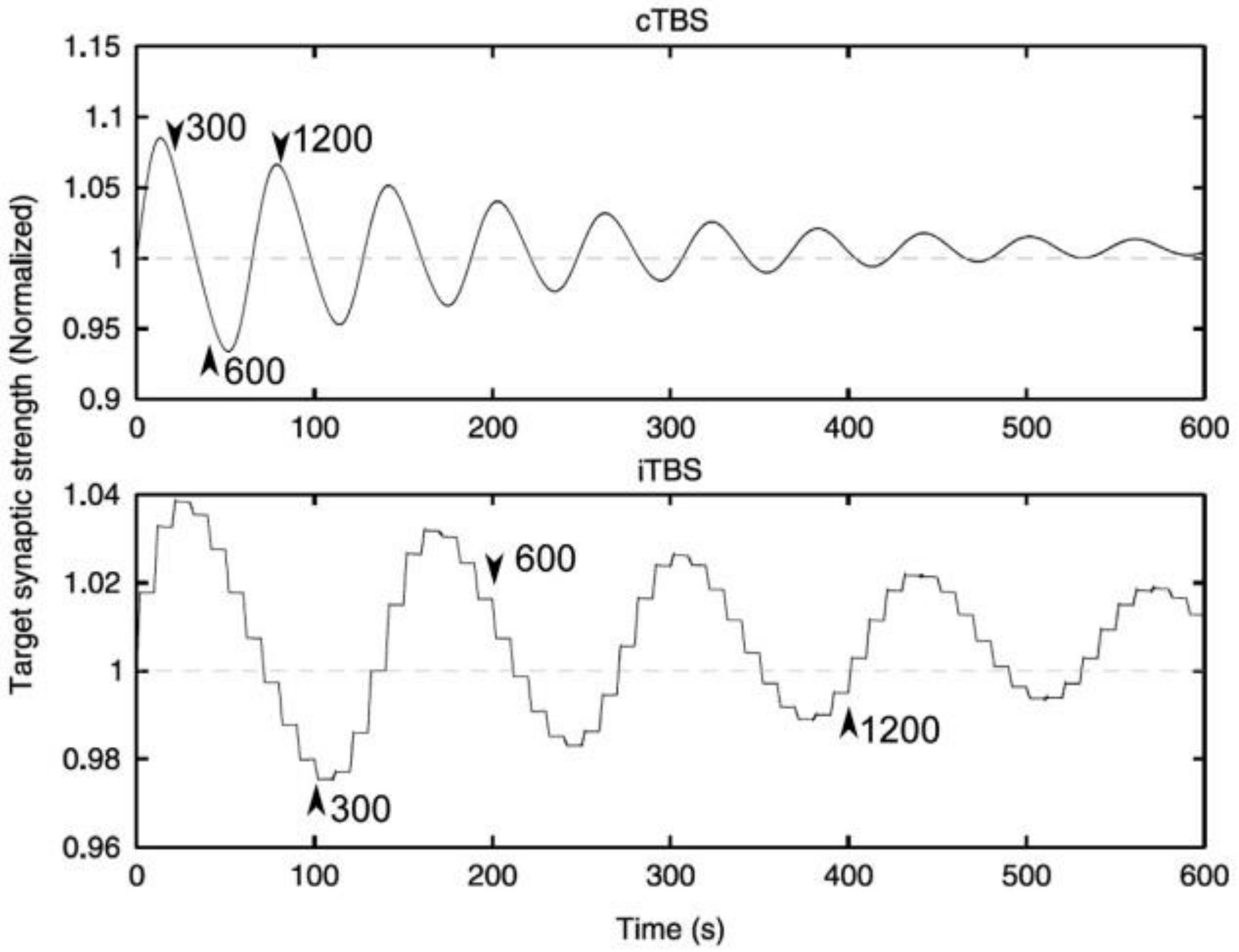
- Responses are variable because...

What you do

- Ultimate synaptic strength can oscillate with number of pulses
- Ultimate synaptic strength varies with strength of application

Where you start from

- Ultimate synaptic strength varies with initial strength of synaptic weight



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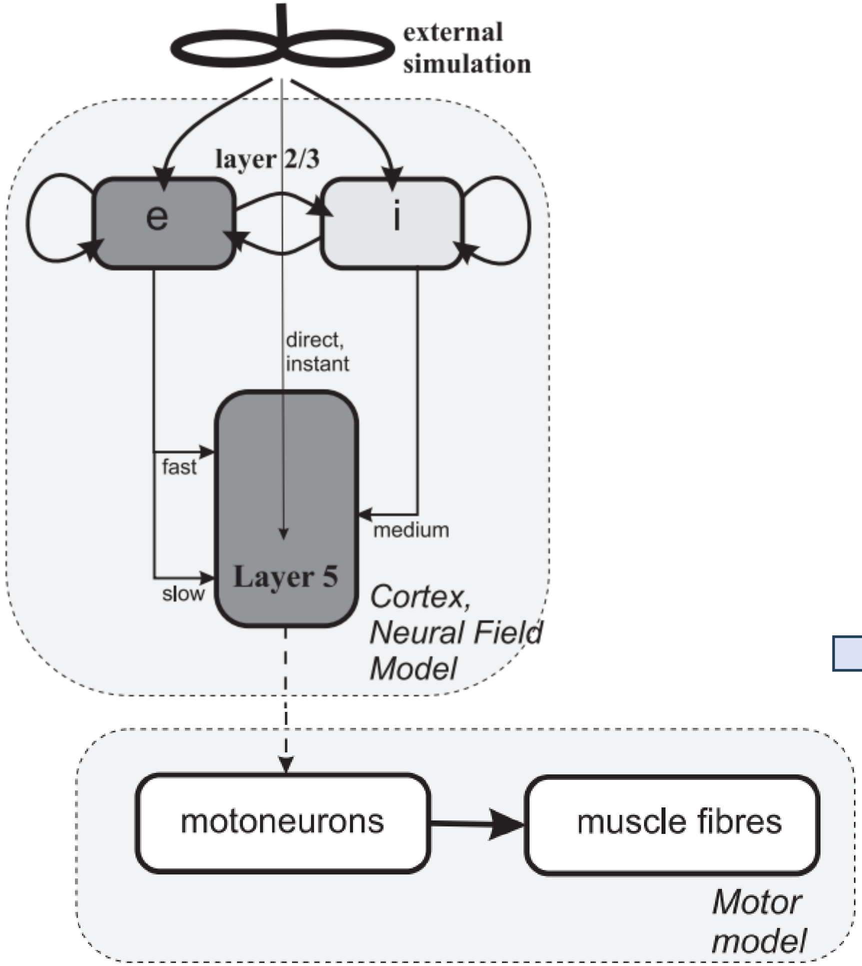
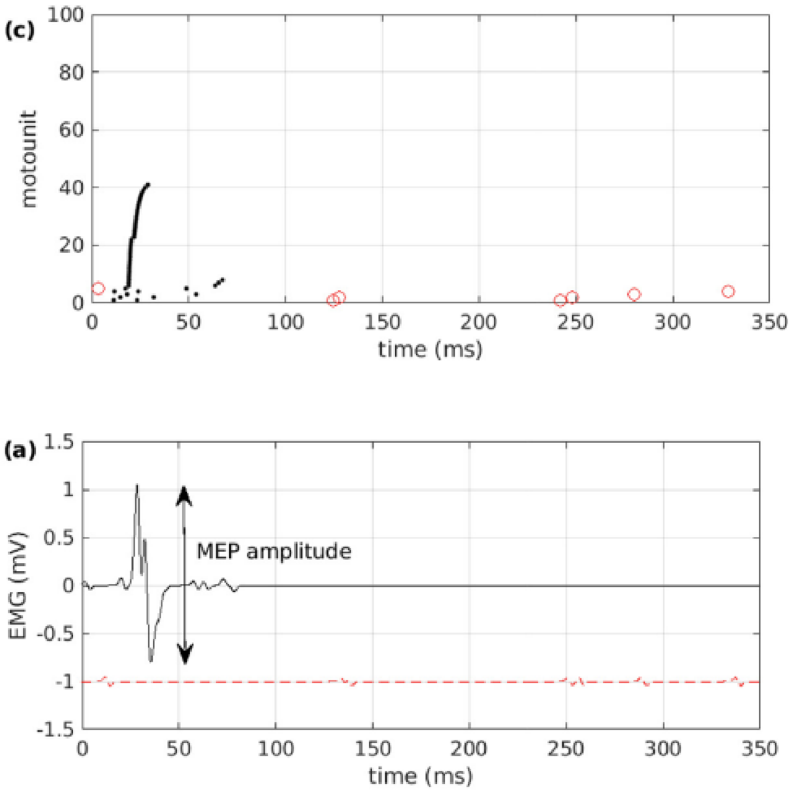
Modelling MEPs within neural field scheme

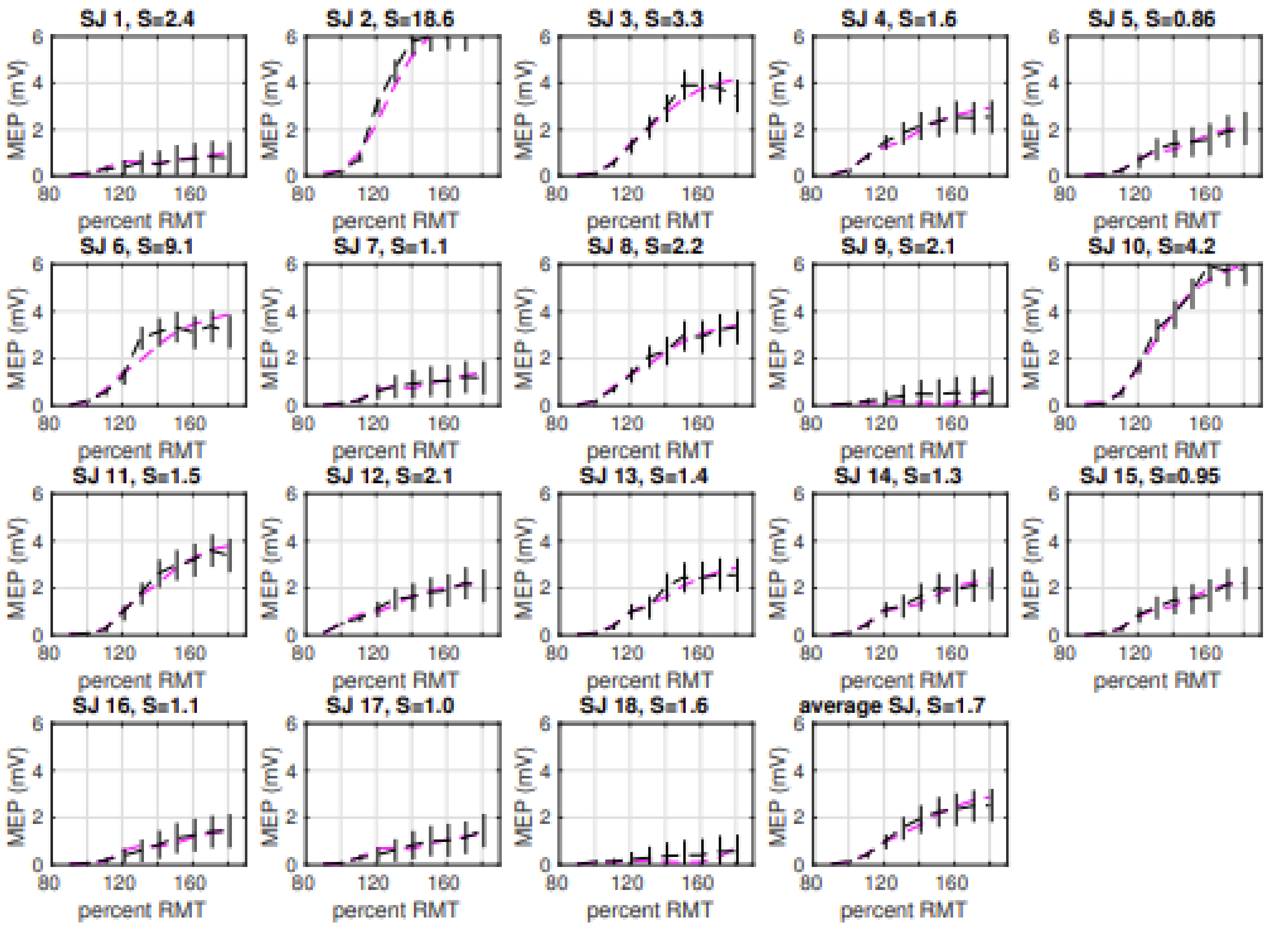


M.T. Wilson et al, *Clinical Neurophysiology* 132 (2021) 412–428. Figure 1



M.T. Wilson, B. Moezzi and N.C. Rogasch, *Clinical Neurophysiology 132* (2021) 412–428, Figure 3

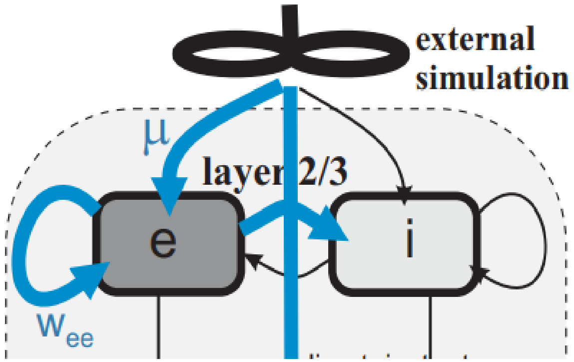
Fit model parameters to individual's input-output curves

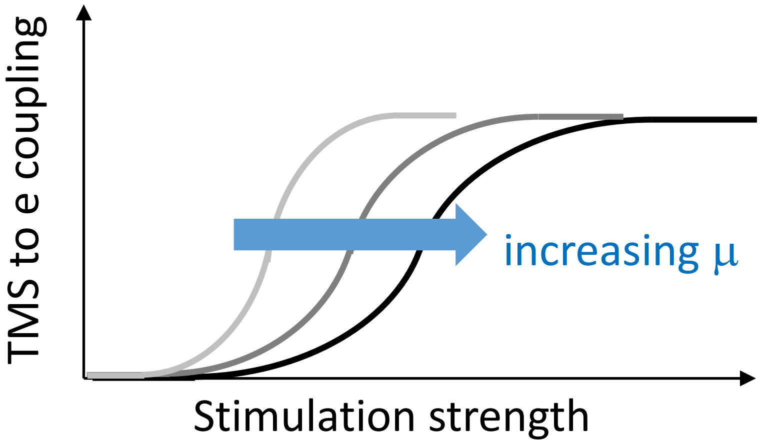


M.T. Wilson et al., Brain Research *1801* (2023) 148205, Figure 5

- Identify which parameters in model are most responsible for differences between individuals.

$$\nu_{ex} = \frac{\nu_{ex}^{max}}{e^{(\mu A - \phi_x)/\mu B} + 1}$$





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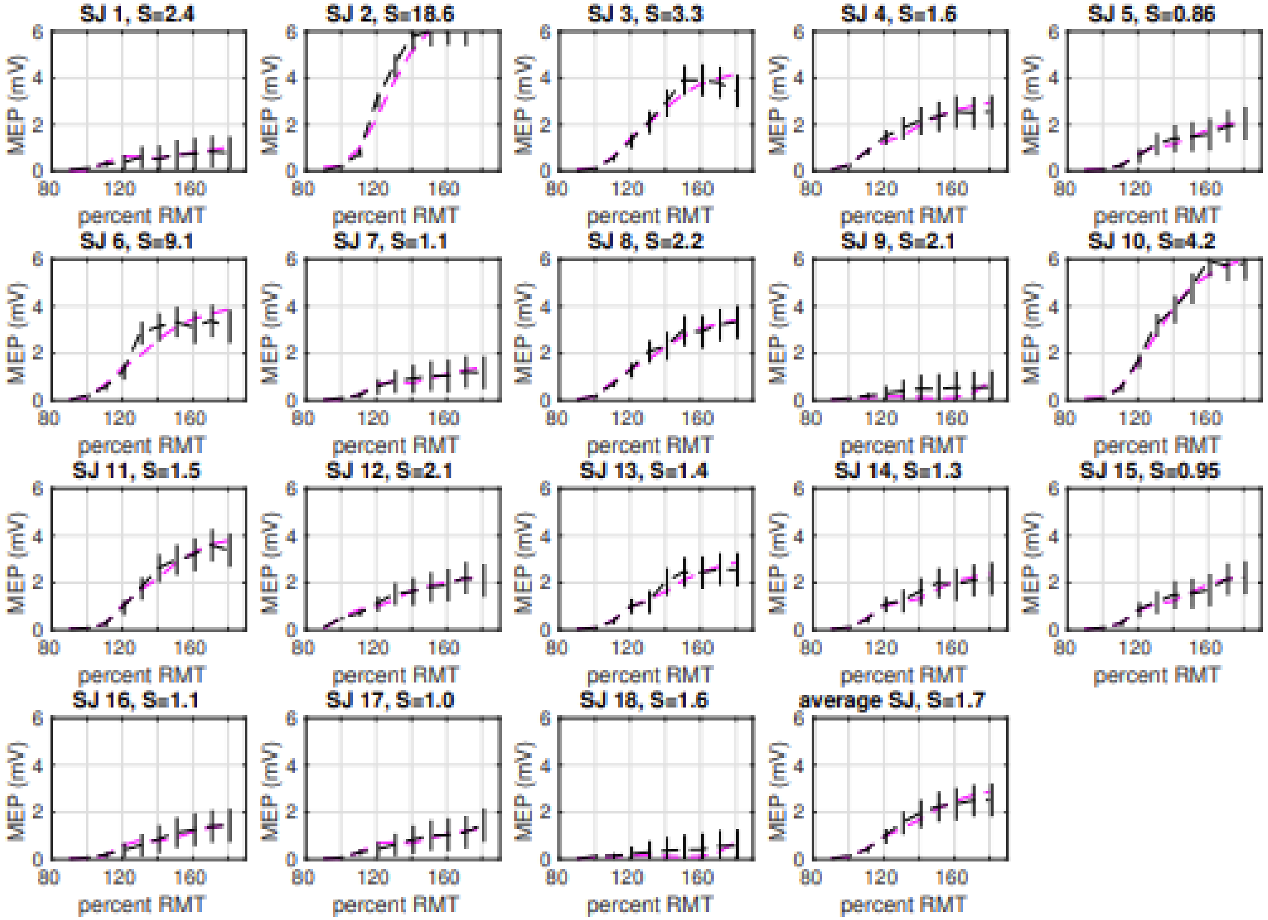

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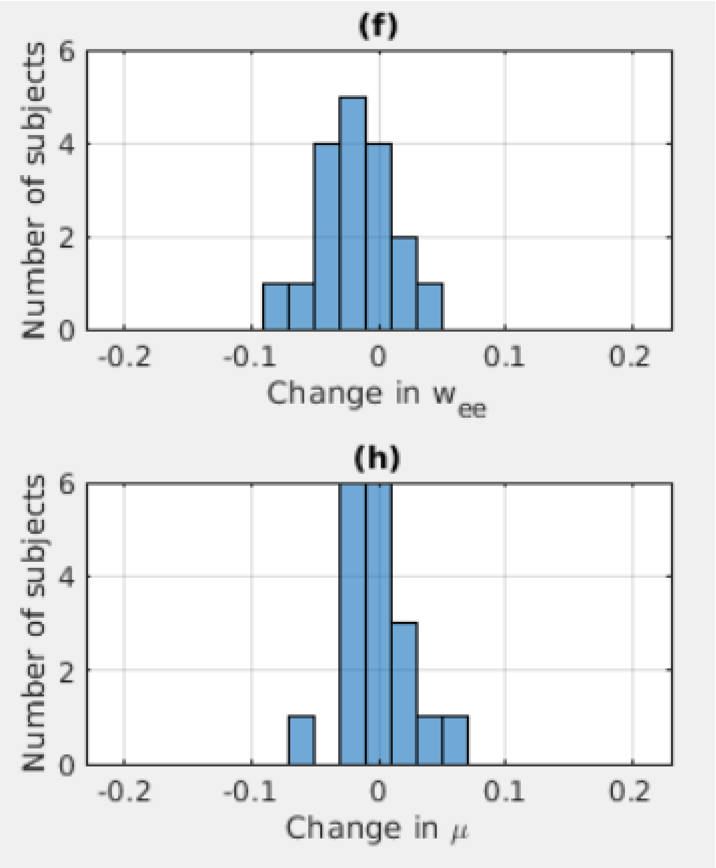
How do w_{ee} and μ change post-cTBS?



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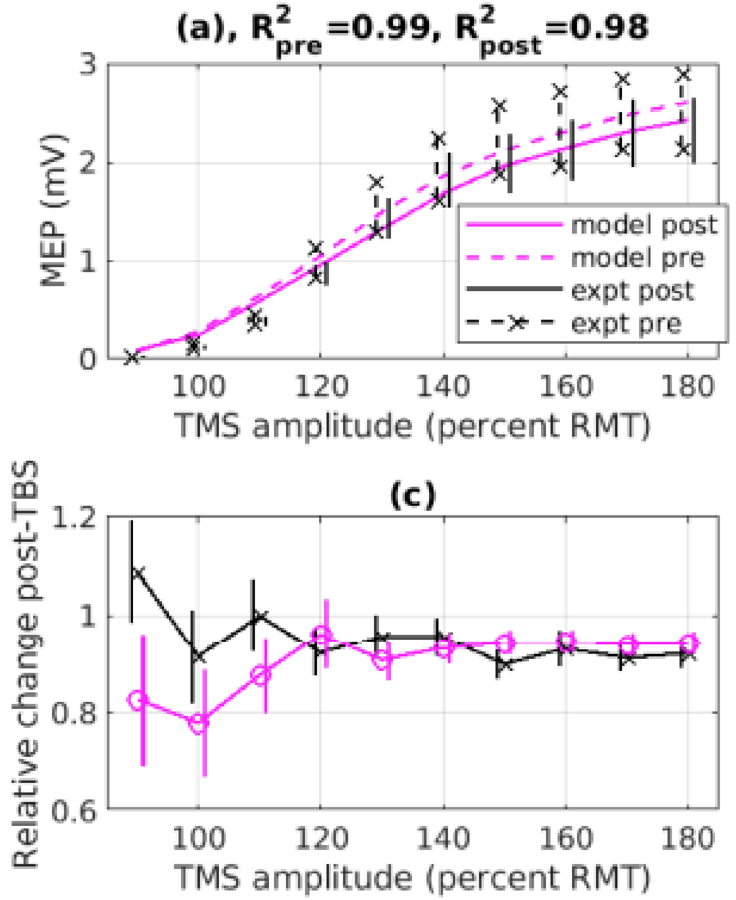
Consequences for variability

- MEPs vary according to:
  - TMS-to-e coupling strength (parameter μ) — Depends on subject and placement/orientation of coil
  - Excitatory-to-excitatory coupling strength w_{ee} — Depends on subject

Aside: Publish the raw data!

- MEPs often presented in terms of %RMT
- Modelling is more natural in terms of an actual amplitude
  - Electric field strength
  - %machine output (which machine?)
- Presenting input-output in terms of %RMT loses information unless the actual threshold is also quoted
- Makes comparison of model and literature-reported experimental data less direct



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Conclusions

- We have modelled Calcium-dependent plasticity with a Neural Field scheme
- Developed the approach further to modelling MEPs
- Identify what parameters might be to produce an individual IO curve
- In terms of variability of MEPs, the following are important:
  - TMS-to-e coupling strength (parameter μ)
  - Excitatory-to-excitatory coupling strength w_{ee}
  - Number of pulses / time since stimulation
- Include reporting of actual thresholds when %RMT is used (and raw data in general)