Perceptual rivalry as a window into cognition

IPAM: Computational Psychiatry

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Laboratory of Biological Modeling
NIDDK, National Institutes of Health

Challenges for objective clinical psychiatry

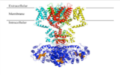
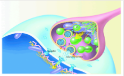
Major historical challenge for psychiatry

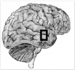
- What is the state space?

Major challenges for biological modeling of psychiatry

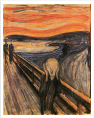
- What biological scale?
- What are the important non-linearities?

Microscopic (molecular):
genes,
ion channels,
synapses, ...


Macroscopic:
social and language dysfunction,
altered perception,
information processing, and
behavioral outcomes



Challenges to objective clinical psychiatry

Psychophysics + electrophysiology is useful for making this tractable.

National Institute of Mental Health

Kennedy Krieger Institute

DSM ??

cognitive differences – executive dysfunction, weak central coherence

underconnectivity, EI-imbalance, minicolumn abnormalities, channelopathies, …

Zimmerman*, Minshew, Ozonoff, Frith, Casanova, others

My starting point 2007

$\rightarrow$ partnered with Carson C Chow (Laboratory of Biological Modeling, NIDDK, NIH)

working memory differences in autism with minicolumn differences (bridging channel and histological findings with behavior)

Vattikuti and Chow (2009) A computational model for cerebral cortical dysfunction in autism spectrum disorders. Biological Psychiatry

$\rightarrow$ rivalry modeling

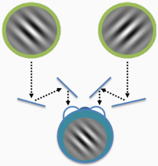
$\rightarrow$ general framework for simple cognitive traits

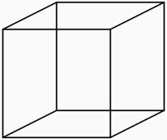
Binocular (static) Rivalry

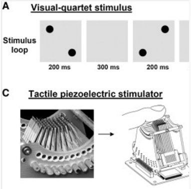
Rivalry - phenomena

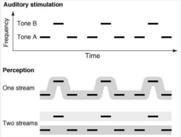
Changes in perception independent of the stimulus.

binocular rivalry

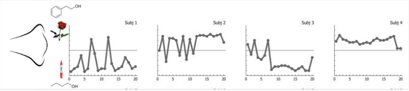




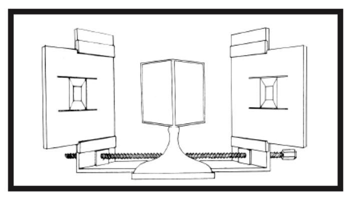




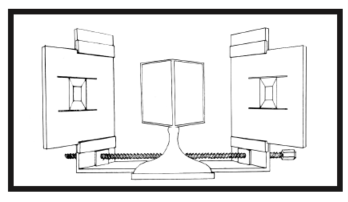
banana
tokei

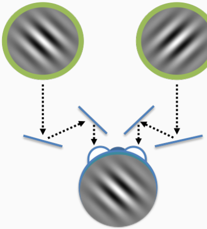


Sir Charles Wheatstone 1838 - invents the **stereoscope**, and observes stereoscopic (3D) illusion

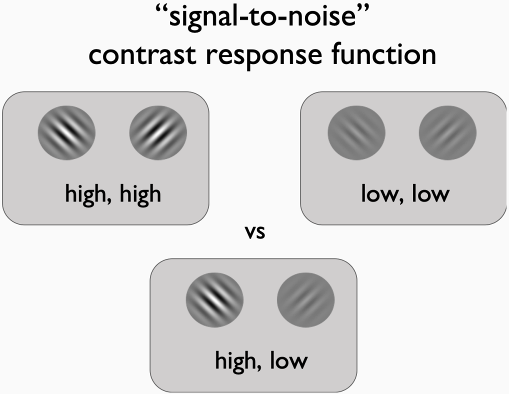


Sir Charles Wheatstone 1838 - invents the **stereoscope**, and observes stereoscopic (3D) illusion and **binocular rivalry**

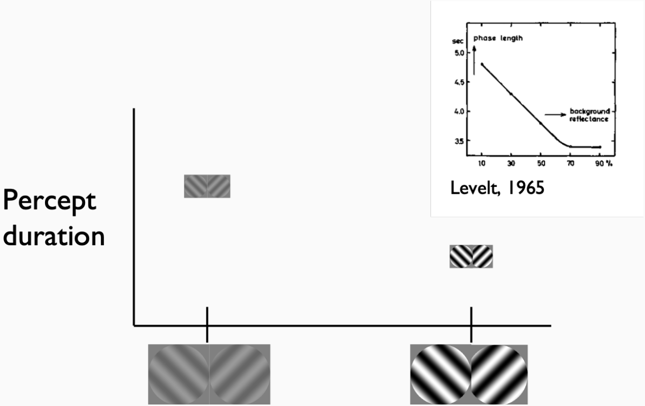




Levelt's propositions - stereotypical and non-obvious changes in percept dynamics with change in stimulus

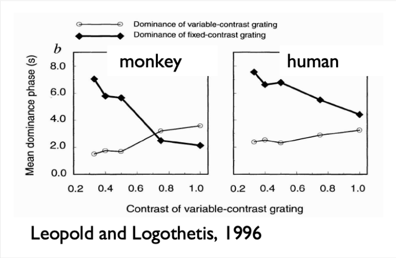


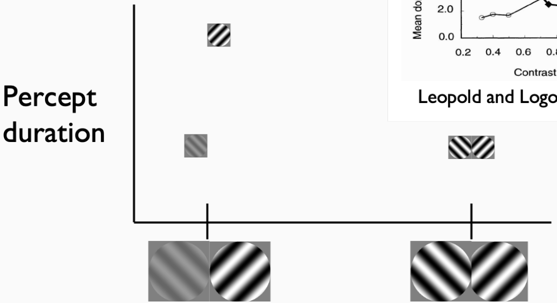
Levelt's 4th proposition



Binocular rivalry - phenomena

Levelt's 2nd proposition



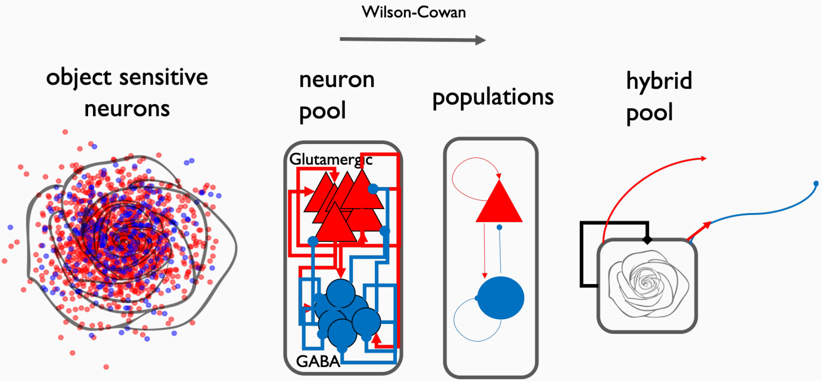


History

- Challenge for mutual inhibition models for many decades (1960s to 2002)
- Laing and Chow (2002) explain how a physiological neuronal model based on a general cortical architecture can explain this (rediscovery and expansion of point in Arrington thesis with Grossberg, 1993)

Stimulus (object) - sensitive populations act like neurons (Wilson and Cowan, 1973) - 1960s-90s Mountcastle, Hubel, Weisel, Albright, Tanaka (MT, IT, etc.)

Pool at different descriptive scales

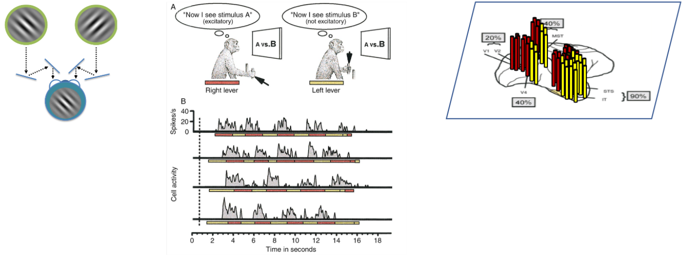


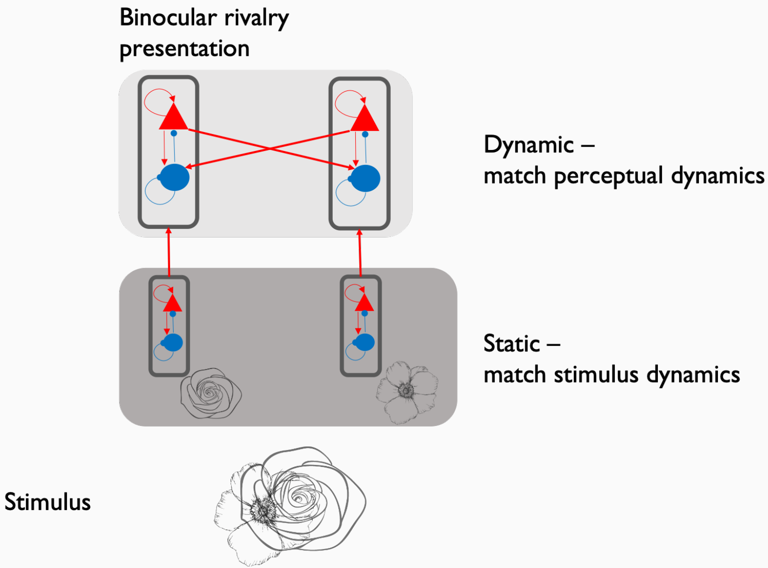
Binocular Rivalry model- electrophysiology

Pools are also correlated with perception, not just stimuli.

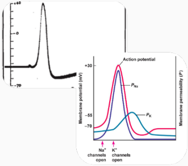
Leopold and Logothetis 1990s -
Binocular rivalry neuronal spiking correlated with perception in higher processing areas

(Also evidence from memory experiments by Funahashi, Goldman-Rakic, Colby, others.)

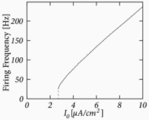



Binocular rivalry
presentation
Dynamic –
match perceptual dynamics
Static –
match stimulus dynamics
Stimulus

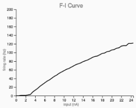
Binocular Rivalry model - electrophysiology



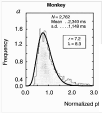
Type 2



Type 1

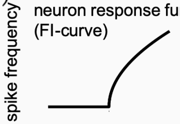


$$C\frac{dV}{dt} = I_{\text{ext}} - I_{\text{mem}}(V, n, h) - I_{\text{AHP}}(V, [Ca]) - I_{\text{syn}}$$
$$I_{\text{mem}} = g_L(V - V_L) + g_K n^4(V - V_K) + g_{Na} m_\infty^3 h(V - V_{Na})$$
$$I_{AHP} = g_{AHP}[Ca]/([Ca] + 1)(V - V_K)$$
$$\dots$$

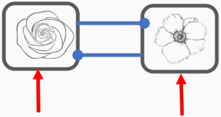


Leopold and Logothetis, 1996

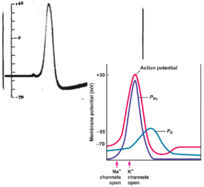
$g(x)$ neuron response function (FI-curve)



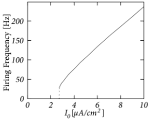
$$\tau_u \dot{u}_i = -u_i + g(S - \beta u_j - \gamma a_i)$$
$$\tau_a \dot{a}_i = -a_i + u_i$$
where $\tau_a >> \tau_u$
$$g(x) = \max(0, x)^\eta$$

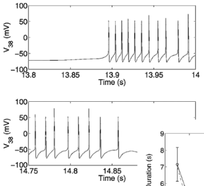


Laing and Chow, 2002



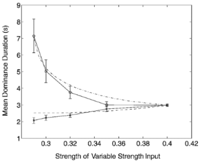
Type 2





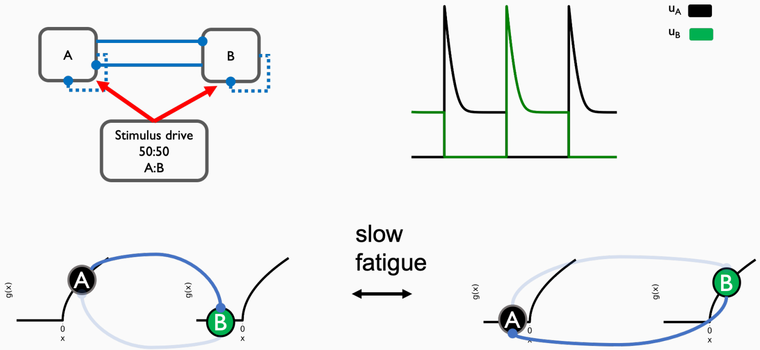
alternations

Levelt's 2nd

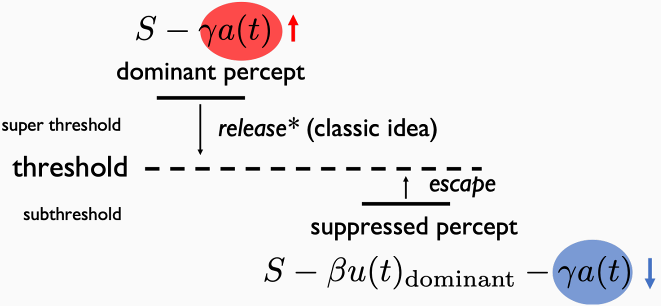


$$
\begin{aligned}
C\frac{dV}{dt} &= I_{\text{ext}} - I_{\text{mem}}(V,n,h) - I_{\text{AHP}}(V,[Ca]) - I_{\text{syn}} \\
I_{\text{mem}} &= g_L(V-V_L) + g_K n^4(V-V_K) + g_{Na} m_\infty^3 h(V-V_{Na}) \\
I_{AHP} &= g_{AHP}[Ca]/([Ca]+1)(V-V_K) \\
&\dots
\end{aligned}
$$

Binocular Rivalry model - mechanisms



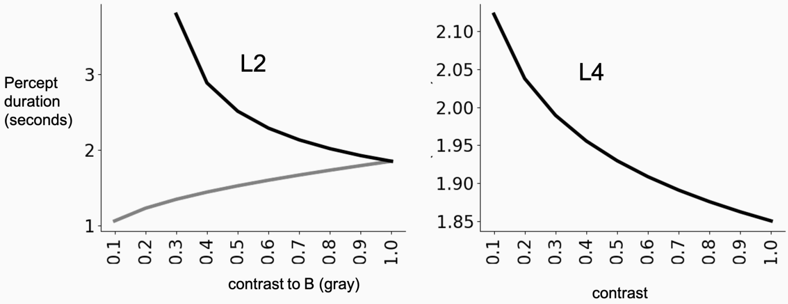
Release vs Escape



* shape of activation function strongly governs which predominates

Escape reproduces Levelt's propositions.

$$S - \beta u(t)_{\text{dominant}} - \gamma a(t)$$



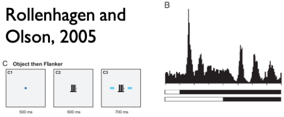
Binocular Rivalry model

- Variants - synaptic depression, complex architecture (eye effects, object disparity, etc.)
- General model used to explain alternative forced choice, normalization, flanker-suppressor, and short-term memory..

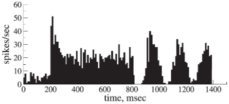
  ...and associated cryptic electrophysiology.

Flanker-suppressor task

Rollenhagen and Olson, 2005

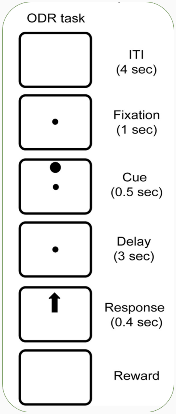


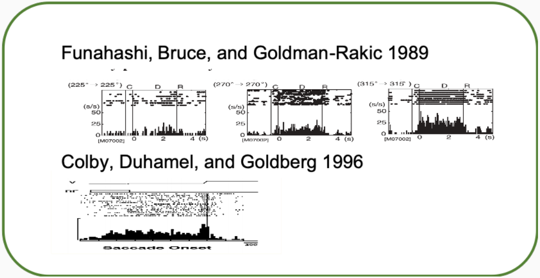
Moldakarimov, Rollenhagen, Olson, and Chow 2005



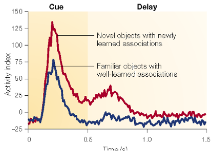
Short-term memory revisited: intermittent rivalry

Delay-period activity during memory tasks

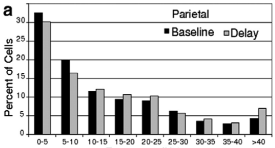




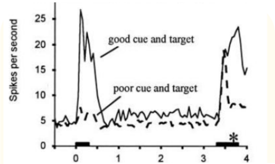
Debated - delay activity often highly variable and close to baseline



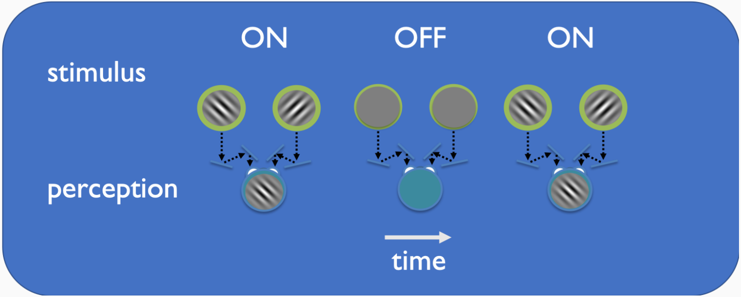
Miller 2000



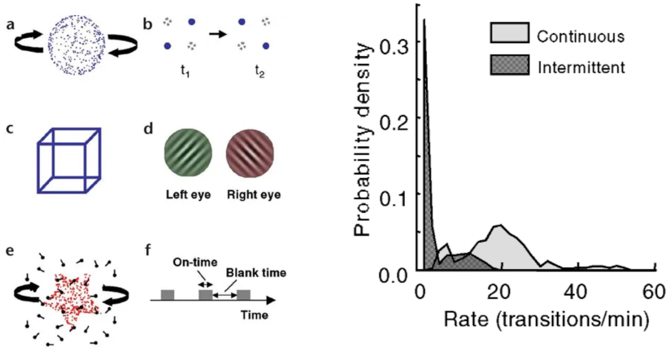
Shafi et. al, 2007



Desimone, Duncan (object memory)

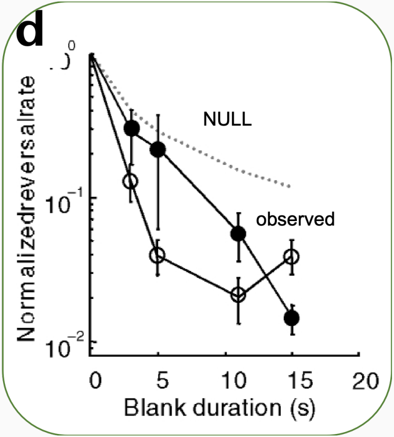

ON
OFF
ON
stimulus
perception
time

Many forms of rivalry have memory



Leopold, et. al 2002

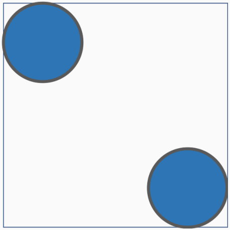
Percept (memory) is more stable with longer delays.



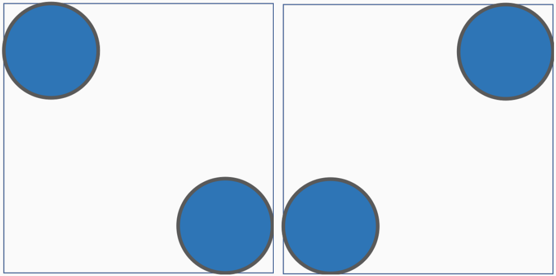
Leopold, et. al 2002

Experiment + modeling - Vattikuti S, Thangaraj P, Xie HW, Gotts SJ, Martin A, Chow CC. (2016) Canonical Cortical Circuit Model Explains Rivalry, Intermittent Rivalry, and Rivalry Memory. PLoS Comput Biol.

Quartet illusion captures these phenomena plus more.

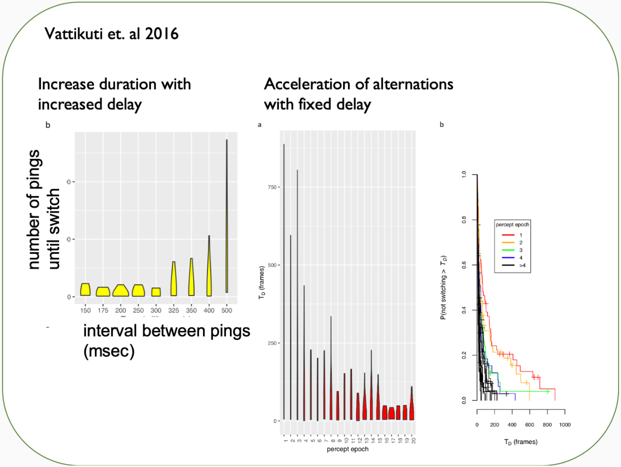


Drive occurs at the frame transition.



Intermittent rivalry and habituation in the quartet - phenomena

Quartet illusion captures these phenomena plus more.



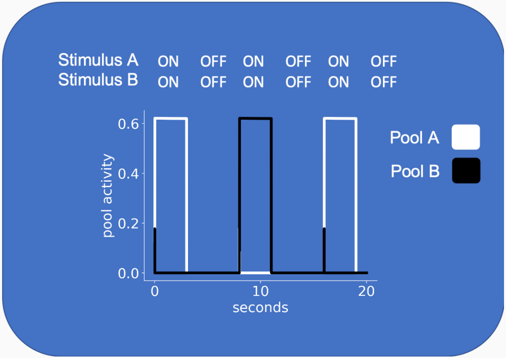
Intermittent rivalry and habituation in the quartet - phenomena

Phenomenological constraints

- delay period activity - variable amplitude
- increased percept stability with increased delay
- habituation with fixed parameters

Challenge for the standard rivalry model

- longtime variable in rivalry is fatigue → "anti-memory"



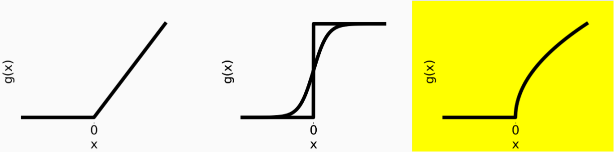
Solutions?

- positive feedback within pool - issue rhythmogenesis and amplitude
- add another positive variable like facilitation, subthreshold current - more complications but plausible
- ...

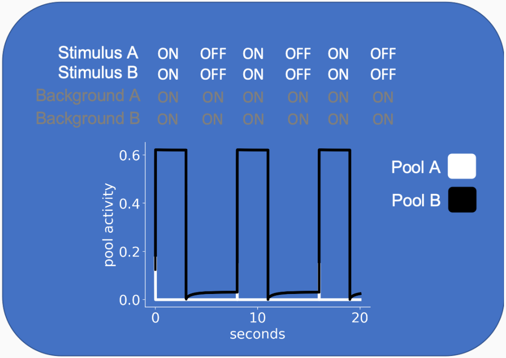
Our solution:
$\rightarrow$ **“topological memory”**

standard static rivalry model can do it if:

mutual inhibition + threshold-concave activation

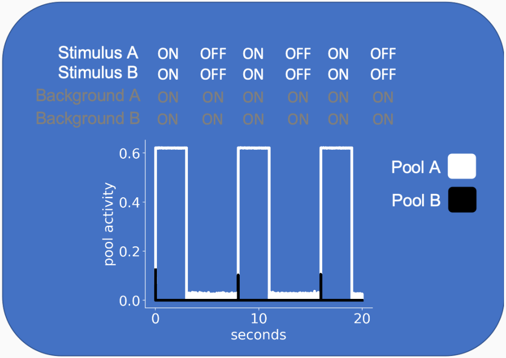


Drive memory with arbitrarily close to zero fixed drive.

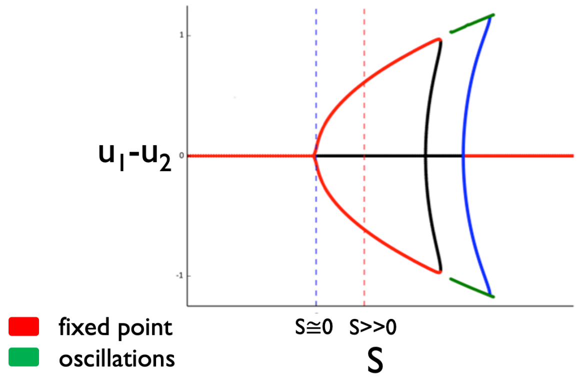


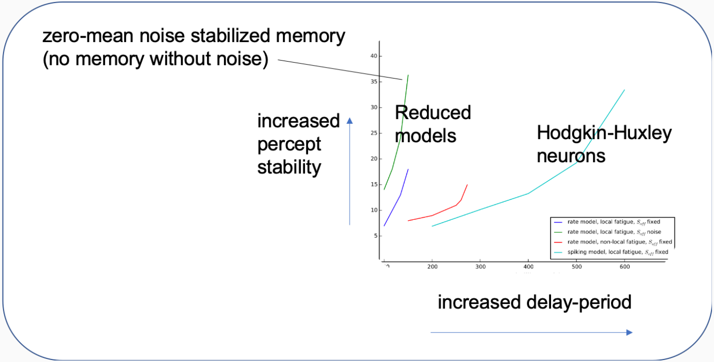
Intermittent Rivalry and habituation - model

Drive memory with zero-mean noise only.



Topological memory




zero-mean noise stabilized memory
(no memory without noise)
increased
percept
stability
Reduced
models
Hodgkin-Huxley
neurons
40
35
30
25
20
15
10
5
200
300
400
500
600
rate model, local fatigue, S_{off} fixed
rate model, local fatigue, S_{off} noise
rate model, non-local fatigue, S_{off} fixed
spiking model, local fatigue, S_{off} fixed
increased delay-period

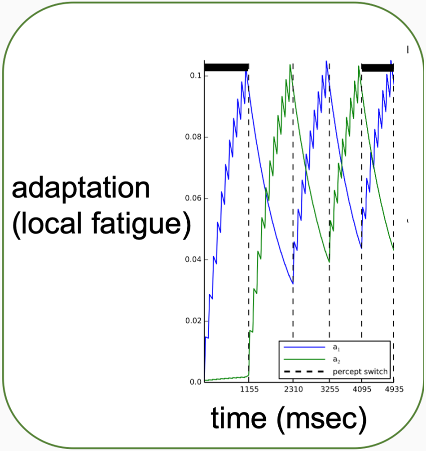
Intermittent Rivalry and habituation - model

Mechanism notes

- Activity u fixed point competes with fatigue variable.
- Low activity during off-state “stops” buildup of fatigue and stabilizes prior state.
- Mechanism is release, mutual inhibition strength does not factor into percept duration.
- Fatigue variable explains why stability is increased with bigger breaks and scales nonlinearly; slower build up.
- Complex relationship between noise, off-state activity, and fatigue.

Open analysis problems

Acceleration (habituation) is explained by release due to local fatigue such as spike frequency adaptation or synaptic depression in the dominant percept pool.



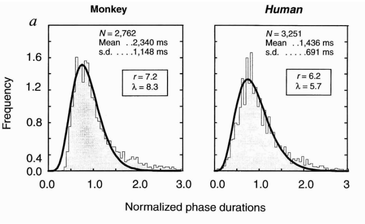
Summary 1

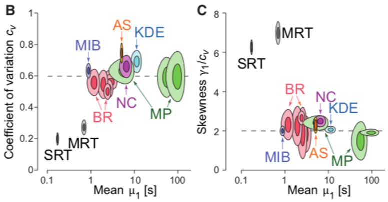
- Static and intermittent rivalry explained by same simple mutual inhibition type models.
- Threshold and shape of activation function important for both.
- Static rivalry most consistent with escape (durations depend on mutual inhibition strength).
- Intermittent rivalry most consistent with release (durations do not depend on mutual inhibition strength).
- Breaks are good for dynamic-memory as well as noise (?)

These models have a major flaw.
Rivalry is fundamentally stochastic.

Noise model for rivalry

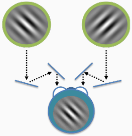
Robust statistics for rivalry - data

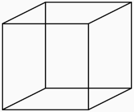


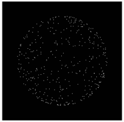


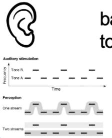
Leopold and Logothetis, 1996

Cao, et. al 2016





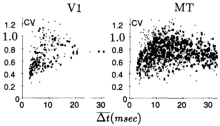




. . .

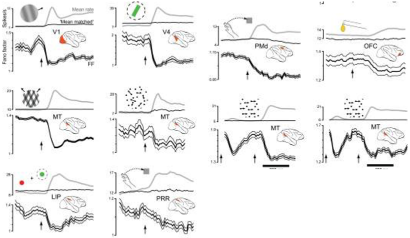
Balanced-state - attractor state theory for intrinsic variability in the brain (van Vreeswijk and Sompolinksy, 1996).
Explains the robust **Poisson-like** spike statistics of neuronal action potentials, despite many inputs.

Softky and Koch 1993



$$\mathrm{CV_{ISI}} = \frac{\text{spike interval standard deviation}}{\text{spike interval mean}} \approx 1$$

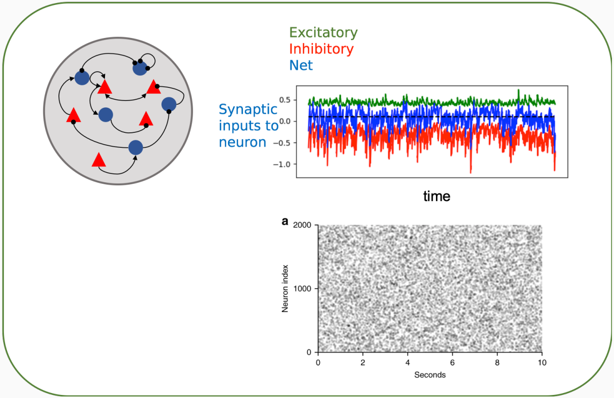
Churchland, et. al 2010
Spike count Fano factor
spontaneous >1
evoked ~1



Balanced-state

Balanced-state based on excitatory and inhibitory neurons balancing such that:

- mean input is at threshold
- spike generation is fluctuation driven

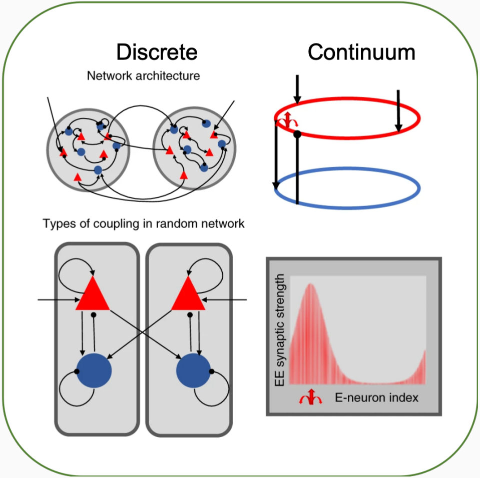


Mutual inhibition vs the balanced-state

Can balanced-state and mutual inhibition (net negative) coexist as a model for perceptual rivalry?

Cohen BP, Chow CC, Vattikuti S. (2019) Dynamical modeling of multi-scale variability in neuronal competition. Commun Biol.

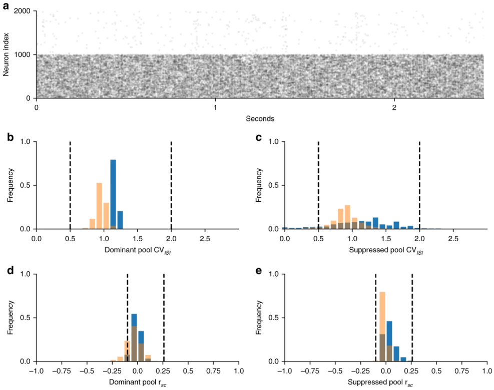
Two candidate rivalry (mutual inhibition) and balanced-state frameworks.



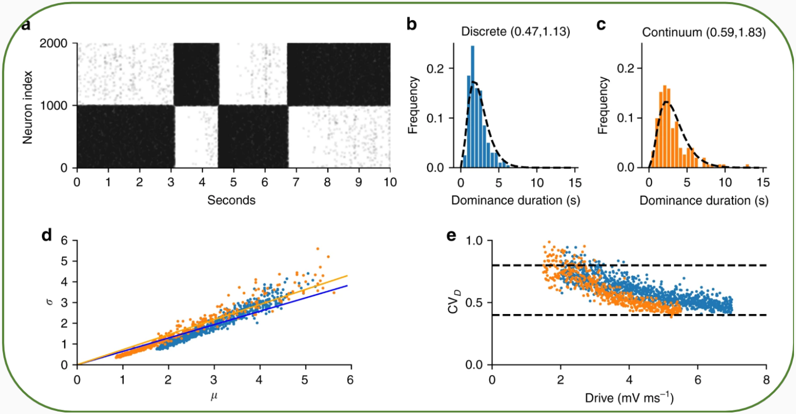
Models reproduce realistic spiking with no added noise term.

Irregular spiking

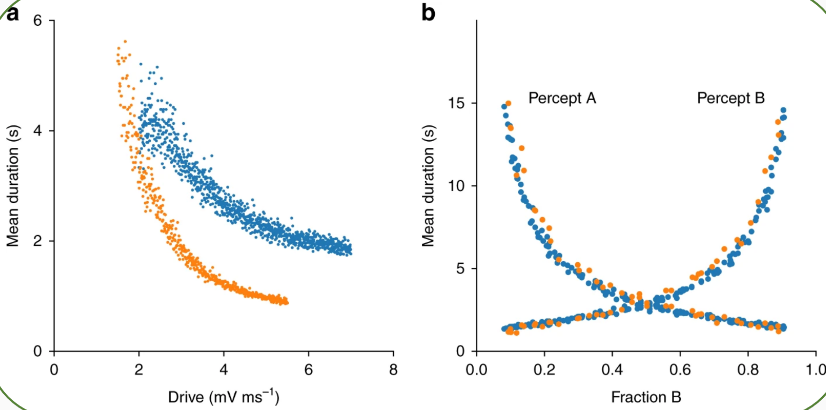
Asynchronous spiking



Models reproduces realistic percept duration variability with no added noise term.



Models capture mean dynamics.



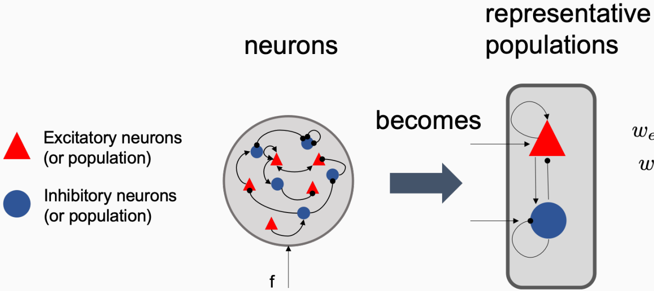
Mutual inhibition vs the balanced-state

What is the mechanism for variability?
Balanced-state?

What is the mechanism for variability?
Balanced-state? Yes and no

Mutual inhibition vs the balanced-state

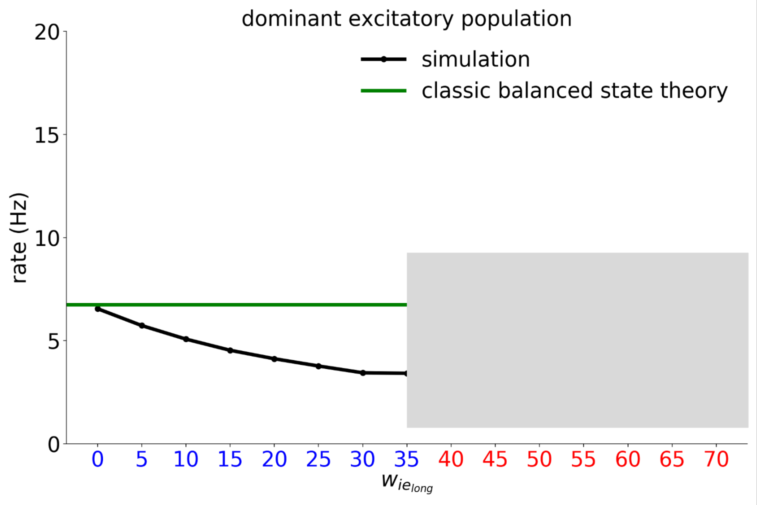
Under some conditions (that can be relaxed) in the limit of large N, balanced-state becomes a linear problem.



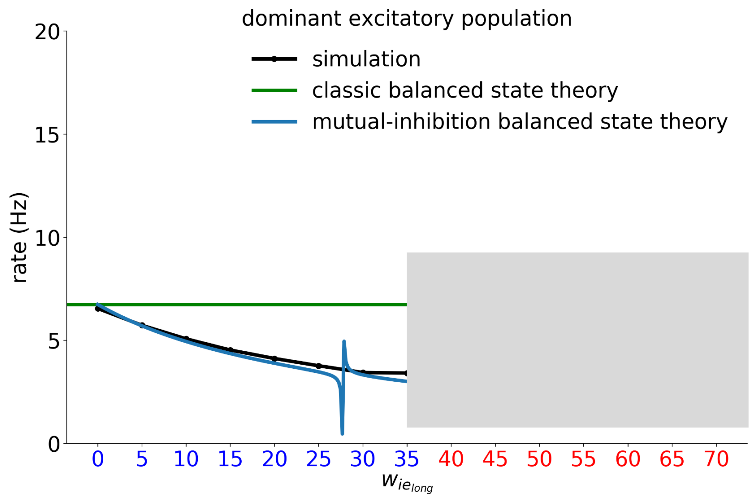
$$w_{ee}r_e - w_{ei}r_i + f_e = 0$$
$$w_{ie}r_e - w_{ii}r_i + f_i = 0$$

Mutual inhibition vs the balanced-state

How well does this fit?

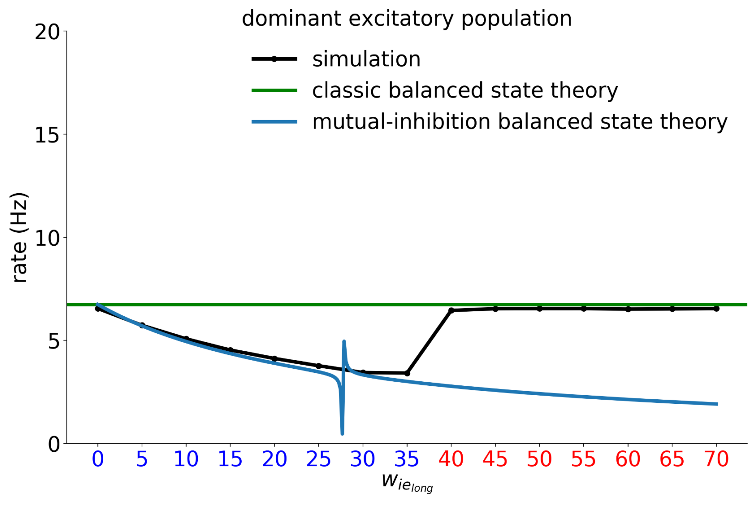


How well does this fit?

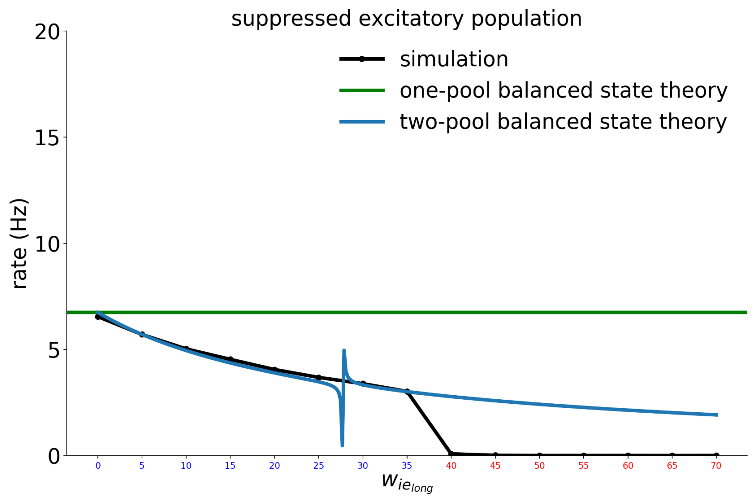


Mutual inhibition vs the balanced-state

How well does this fit?



How well does this fit?



Summary 2

- Self-consistent model explains spiking and perceptual variability and percept mean dynamics.
- Supports a noise model for rivalry that is cross-multiplicative from balanced-state dominant pool.
- Suggests mutual inhibition balanced-state model for none winner-take-all but competitive psychophysics.

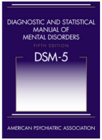
Clinical picture

Clinical Potential

Some clinically interesting features of rivalry:

- measure of cognitive stability
- assess structure of percept state-space
- capture effective biological parameters

Studied for many decades in many clinical contexts with many positive associations:



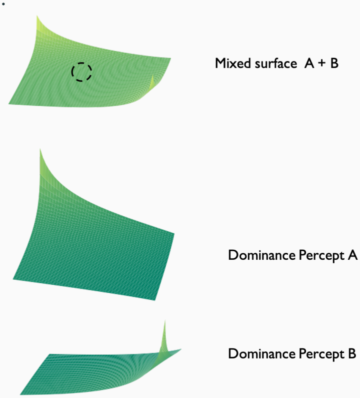
most major mental illnesses - schizophrenia, bipolar disorder, major depression, autism

many pharmacological agents - caffeine, benzodiazepine, catecholamine, psilocybin

<u>but</u> limited interpretation and utility due to task design

Need to modernize clinical studies

- Clinical studies are often point analyses.
- Need to capture the time-varying surface.
- Map the surface back to mechanistic model.



Machine learning

Dynamical systems look different depending on context.
Need to deconvolve test-condition transformation on brain circuit.

$b(\boldsymbol{\beta}, \quad)$	biological parameters of interest
$\mathbf{E}$	external (context dependent) parameters
$M(b(\boldsymbol{\beta}, \mathbf{E}))$	above embedded in report (measurement) function

$$\tau_{u_i}\frac{du_i}{dt} = -u_i + g(S_i - \beta_j u_j - \gamma_i a_i)$$

$$\text{where } g(x) = [\max(0,x)]^{\eta_i}$$

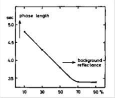
$$\tau_{a_i}\frac{da_i}{dt} = -a_i + u_i$$

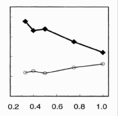
$$\tau_a >> \tau_u$$

$$u_i := \text{neural activity}$$

$M(b(\boldsymbol{\beta}, \{im1, im2, c1, c2\})) =$ dominance distribution T
$M(x) :=$ some report filter on $b(x)$ in context rivalry

Mathematical insight
of dynamical observations





$$T_i = -\tau_{aj} \ln\left(\frac{S_j - \beta_{ji}u_i}{\gamma_j u_j}\right)$$

Dominance activity:

$$u_{i(j)} = g(S_{i(j)} - \gamma u_{i(j)})$$

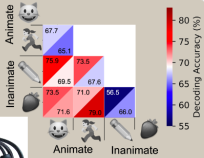
Rivalry alone can “theoretically” identify 14 parameters, with self-report.

ML notes

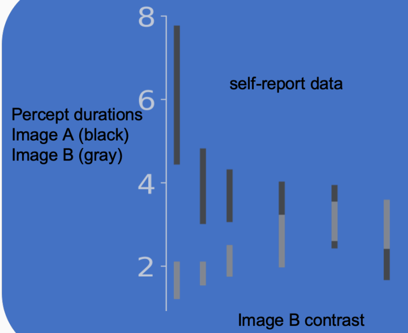
- Optimization scheme needs to account for different operating regimes of the circuit.
- Add data from other tasks to augment model fitting.

VR rig for psychophysical inputs

Report:
self-report (trackpad, head position)
neural recordings



Song and Vattikuti, 2019



$$\epsilon(p) = \sum_{i\in\{\text{conds}\}} \sum_{j=1}^{2} \frac{(D_j^i - T_j^i(p))^2}{\sigma_{ij}^2}$$

Derive gradients by hand
(Speeds up model fitting)

$$\frac{\partial T_i}{\partial \alpha_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(\frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial \alpha_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial \alpha_k} \right)$$

$$\frac{\partial T_i}{\partial \beta_{ik}} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \frac{u_i}{\gamma_j u_j} \delta_{ik} = \tau_{a_j} \frac{u_i}{S_j - \beta_{ji} u_i} \delta_{ik}$$

$$\frac{\partial T_i}{\partial \gamma_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(\frac{S_j - \beta_{ji} u_i}{\gamma_j^2 u_j} \delta_{jk} + \frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial \gamma_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial \gamma_k} \right)$$

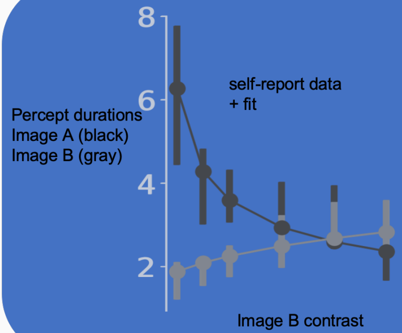
$$\frac{\partial T_i}{\partial \tau_{a_k}} = -\ln \frac{S_j - \beta_{ji} u_i(\infty)}{\gamma_j u_j(\infty)} \delta_{j,k}$$

$$\frac{\partial T_i}{\partial S_k^0} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(-\frac{1}{\gamma_j u_j} (1 - \delta_{i,k}) + \frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial S_k^0} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial S_k^0} \right)$$

$$\frac{\partial T_i}{\partial J_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(-\frac{1}{\gamma_j u_j} c_k (1 - \delta_{i,k}) + \frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial J_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial J_k} \right)$$

$$\frac{\partial T_i}{\partial \eta_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(\frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial \eta_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial \eta_k} \right)$$

CURRENT WORK



$$\epsilon(p) = \sum_{i \in \{\text{conds}\}} \sum_{j=1}^{2} \frac{(D^i_j - T^i_j(p))^2}{\sigma^2_{ij}}$$

Derive gradients by hand
(Speeds up model fitting)

$$\frac{\partial T_i}{\partial \alpha_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(\frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial \alpha_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial \alpha_k} \right)$$

$$\frac{\partial T_i}{\partial \beta_{lk}} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \frac{u_i}{\gamma_j u_j} \delta_{ik} = \tau_{a_j} \frac{u_i}{S_j - \beta_{ji} u_i} \delta_{ik}$$

$$\frac{\partial T_i}{\partial \gamma_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(\frac{S_j - \beta_{ji} u_i}{\gamma_j^2 u_j} \delta_{jk} + \frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial \gamma_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial \gamma_k} \right)$$

$$\frac{\partial T_i}{\partial \tau_{a_k}} = -\ln \frac{S_j - \beta_{ji} u_i(\infty)}{\gamma_j u_j(\infty)} \delta_{j,k}$$

$$\frac{\partial T_i}{\partial S_k^0} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(-\frac{1}{\gamma_j u_j} (1 - \delta_{i,k}) + \frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial S_k^0} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial S_k^0} \right)$$

$$\frac{\partial T_i}{\partial J_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(-\frac{1}{\gamma_j u_j} c_k (1 - \delta_{i,k}) + \frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial J_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial J_k} \right)$$

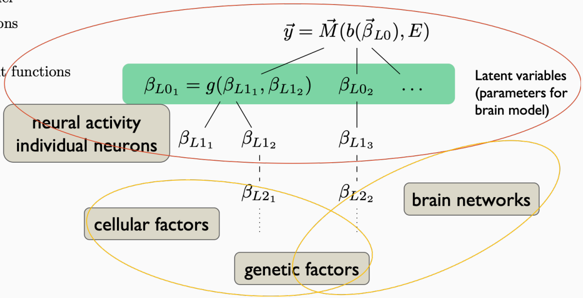
$$\frac{\partial T_i}{\partial \eta_k} = \tau_{a_j} \frac{\gamma_j u_j}{S_j - \beta_{ji} u_i} \left(\frac{S_j - \beta_{ji} u_i}{\gamma_j u_j^2} \frac{\partial u_j}{\partial \eta_k} + \frac{\beta_{ji}}{\gamma_j u_j} \frac{\partial u_i}{\partial \eta_k} \right)$$

Disjoint models "islands"

$b(x) :=$ nonlinear brain model

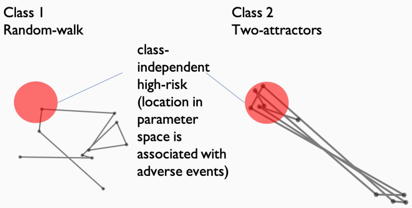
$\vec{E} :=$ environmental conditions (stimulus)

$\vec{M} :=$ vector of measurement functions (self-report, recordings)



The things we can do with these latent variables

1. Uncover patient trajectories in cognitive-biological space using <u>objective</u> parameters
   1. Learn about the course of disease
   2. Learn about interventions
   3. Predict risk of adverse event



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