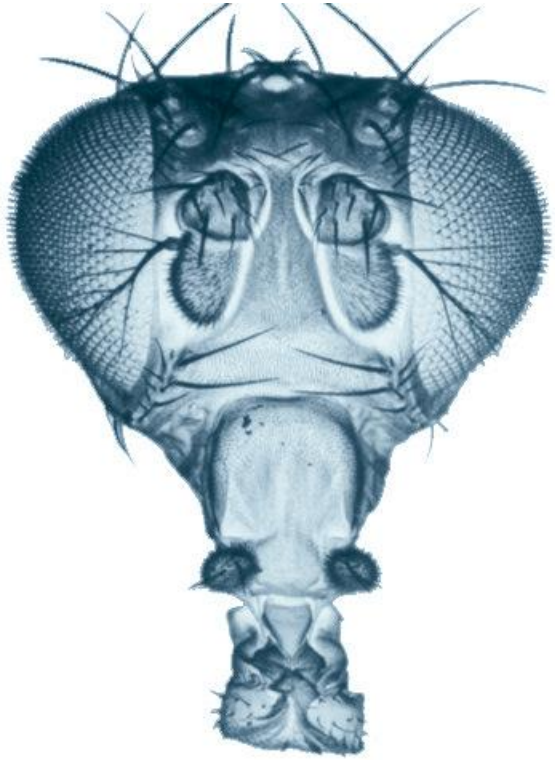
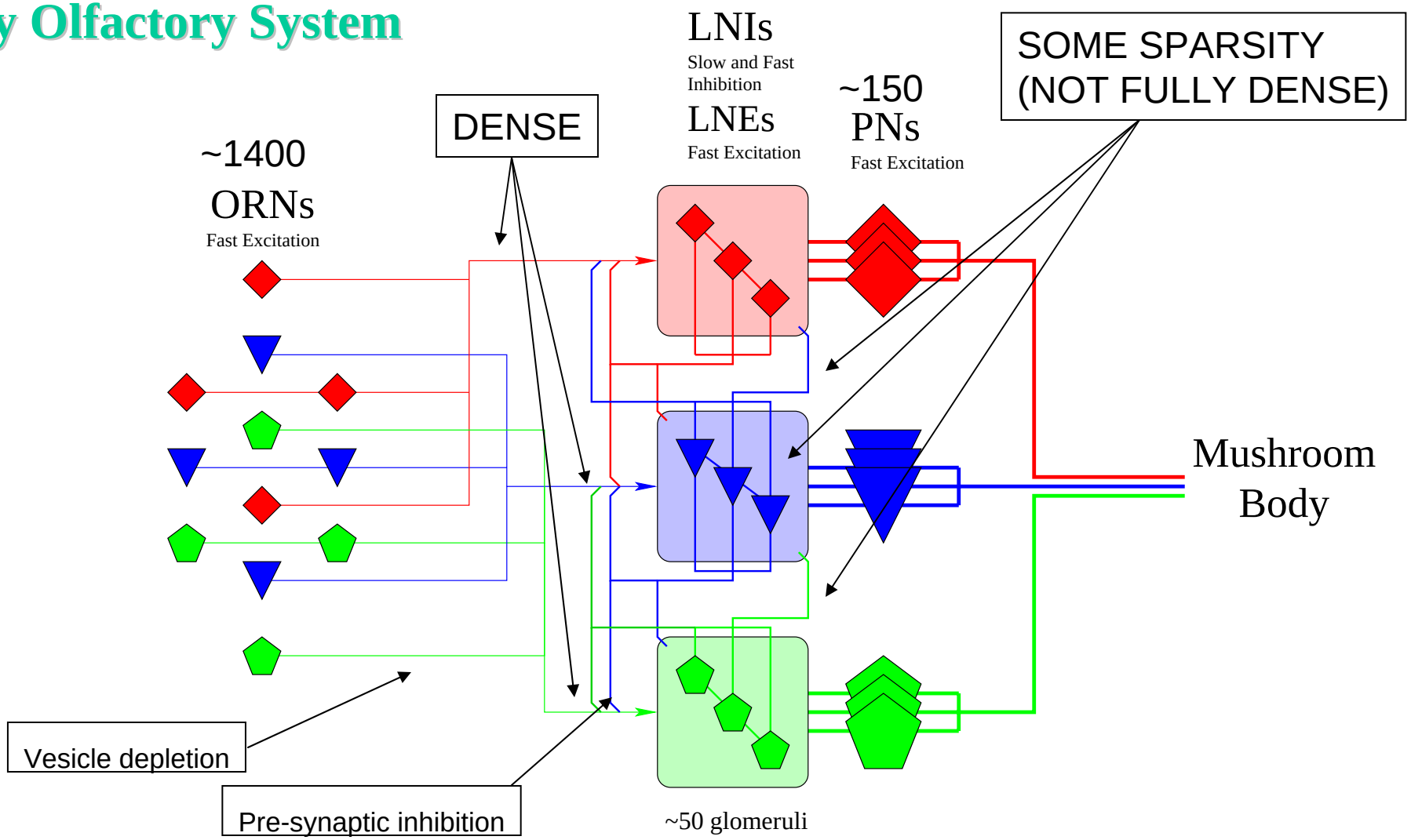
Coding and reliability within the Fly olfactory system



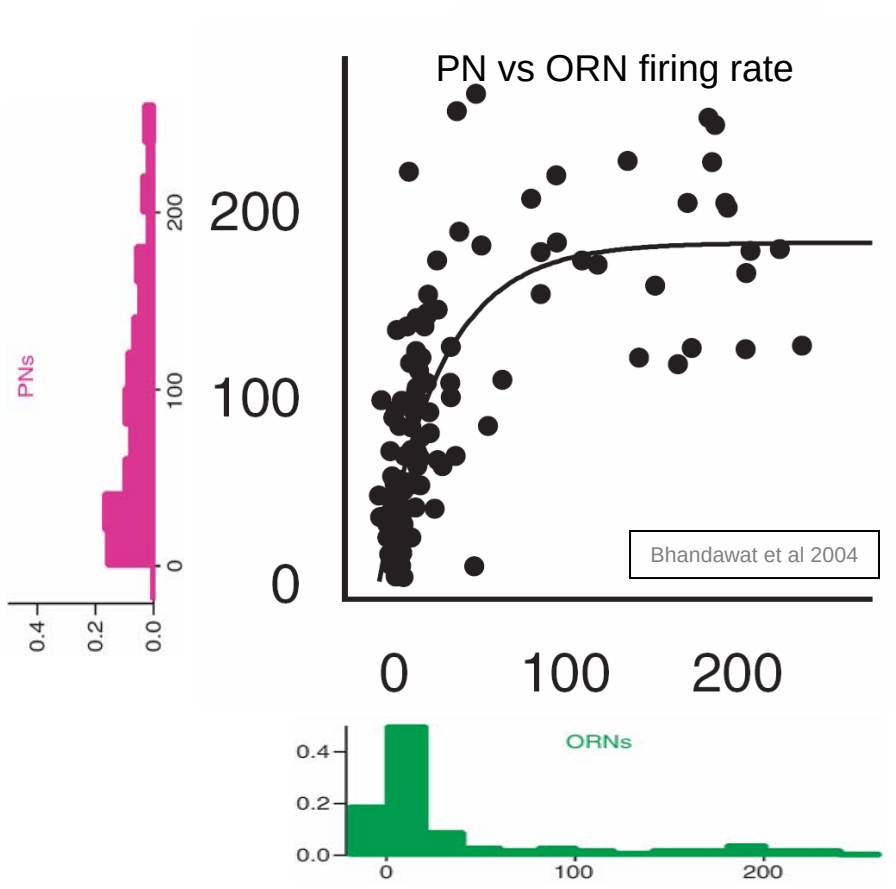
Aaditya Rangan
CIMS

Fly Olfactory System



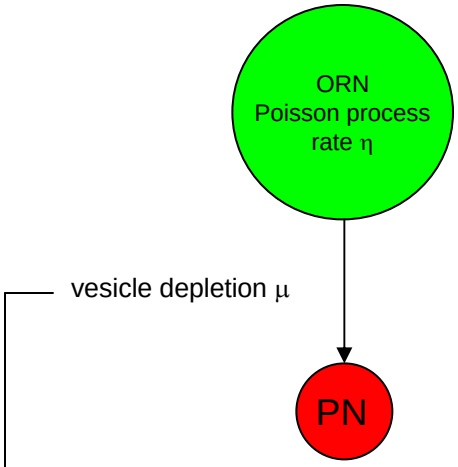
- Projections from ORNs onto glomerular targets are quite dense (PNs within a glomerulus are highly correlated).
- Substantial synaptic depression of ORN→PN synapses.
- Interconnectivity within the AL is relatively sparse.
- In contrast to locust and bee, the fly AL does not typically exhibit robust global oscillations when stimulated.
- Both Vesicle Depletion and Pre-synaptic inhibition of ORN→PN synapses.
- Synaptic depression serves as ‘gain control’.

Odor separation? AL serves to separate the firing-rate-vector representation of nearby odors



what happens at the plateau? Firing-rate-based discrimination no longer works.

Hypothesis 1: Variance coding



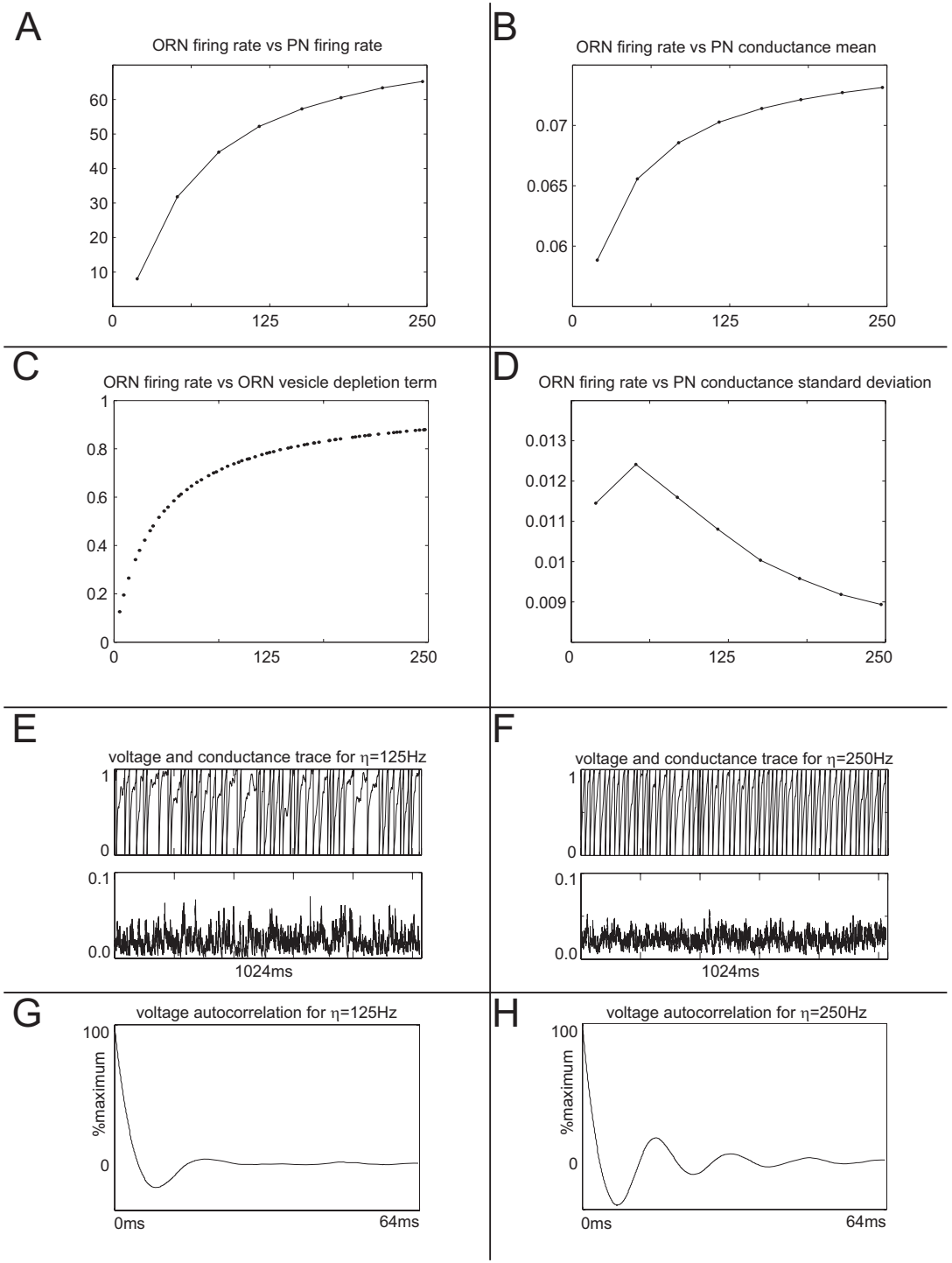
I&F neuron

$$\frac{dV}{dt} = -\frac{V}{\tau_V} - g \cdot (V - V_{EX})$$

$$\frac{dg}{dt} = -\frac{g}{\tau_g} + \sum_k [1-\mu] \cdot S\delta\left(t - T_k^{ORN}\right)$$

$$\boxed{\frac{d\mu}{dt}} = -\frac{\mu}{\tau_\mu} + \sum [1-\mu] \cdot \kappa\delta\left(t - T_k^{ORN}\right)$$

$$\kappa = 0.0075, \quad \tau_\mu = 400\text{ms}$$



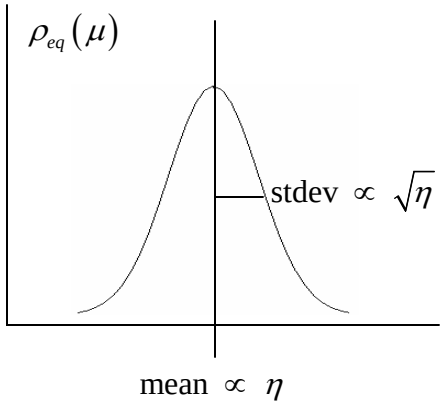
Simpler model of variance coding using 1-neuron FP-equations

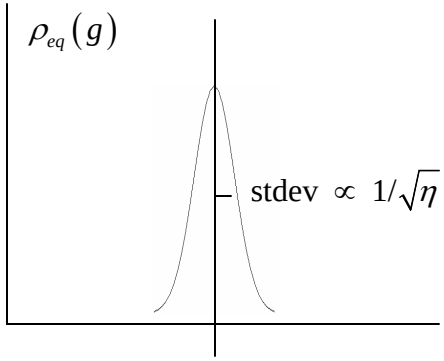
$$\frac{dV}{dt} = -\frac{V}{\tau_V} - g\left(V - V_{EX}\right)$$

$$\frac{dg}{dt} = -\frac{g}{\tau_g} + \sum_k \frac{1}{\mu}\delta\left(t - T_k^{ORN}\right)$$

$$\frac{d\mu}{dt} = -\frac{\mu}{\tau_\mu} + \sum_k \kappa\delta\left(t - T_k^{ORN}\right)$$

Poisson process input rate η





$$\rho_{eq}(\mu) \propto \exp\left(-\frac{(\mu-\bar{\mu})}{2\sigma_\mu^2}\right), \quad \bar{\mu} = \tau_\mu \kappa \eta, \quad \sigma_\mu^2 = \frac{\tau_\mu \kappa^2 \eta}{2}$$

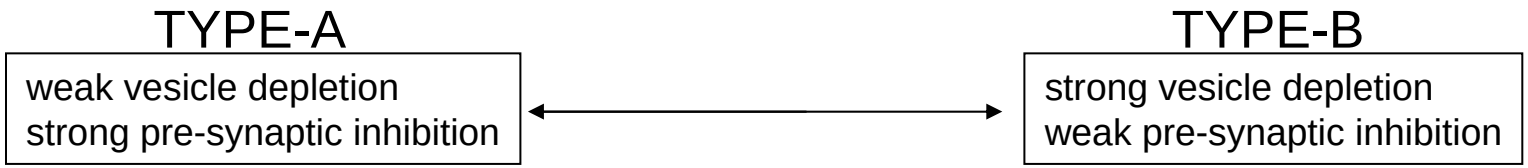
$$\rho_{eq}(g) \propto \exp\left(-\frac{(g-\bar{g})}{2\sigma_g^2}\right), \quad \bar{g} = \tau_g \frac{1}{\bar{\mu}}\eta = \frac{\tau_g}{\tau_\mu \kappa}, \quad \sigma_g^2 = \frac{\tau_g \eta}{2\bar{\mu}^2} = \frac{\tau_g}{2\tau_\mu^2 \kappa^2 \eta}$$

κ small, $\eta \to \infty \quad \Rightarrow \quad g$ constant and V current driven

Hypothesis 2: A tradeoff between reliability and coding capacity

• A given gain curve (i.e., a given amount of synaptic depression) can be achieved in many different ways.

• In general, there is a 1-parameter family of models which give rise to a given amount of synaptic depression.



- less reliable firing patterns
- more sensitive to changes in input

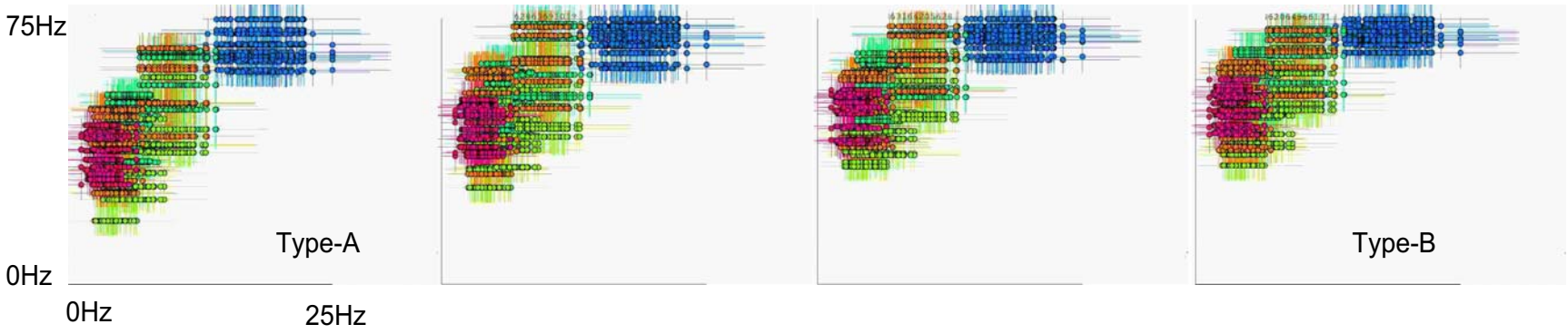
- more reliable firing patterns
- less sensitive to changes in input

HYPOTHESIS 2:
'Feedback' in TYPE-A networks allows for increased coding capacity…
but at the cost of reliability over short observation times.

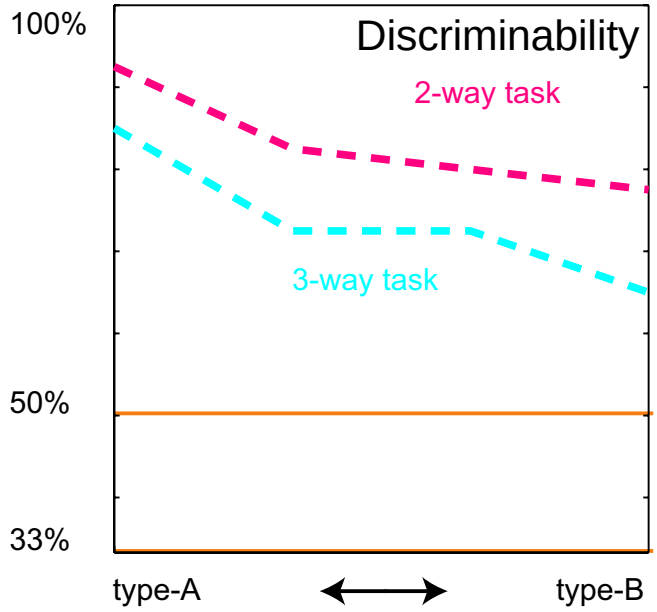
• In other words, vesicle depletion acts very reliably (given a high volume of ORN spikes, a large number of release sites per ORN, and a high original vesicle release probability)

• However, feedback through pre-synaptic inhibition 'amplifies' small changes in the input (given relatively few LNIs which receive odor-specific input and are sparsely coupled to ORNs)

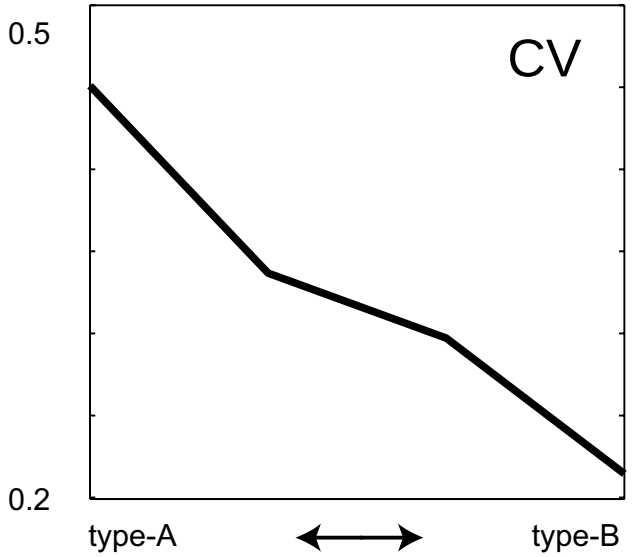
mPN(mORN) gain curve shown for 4 different networks ranging from type-A networks (left) to type-B networks (right)
Each dot is a PN, and the 5 different colors represent the 5 different glomeruli within each network



Discriminability of network based on firing rates measured over a 5120ms trial during which odor was presented for 512ms.
Discriminability results for a 2-way task and a 3-way task are plotted.
The 10th percentile (dashed) discriminability over multiple odors is plotted

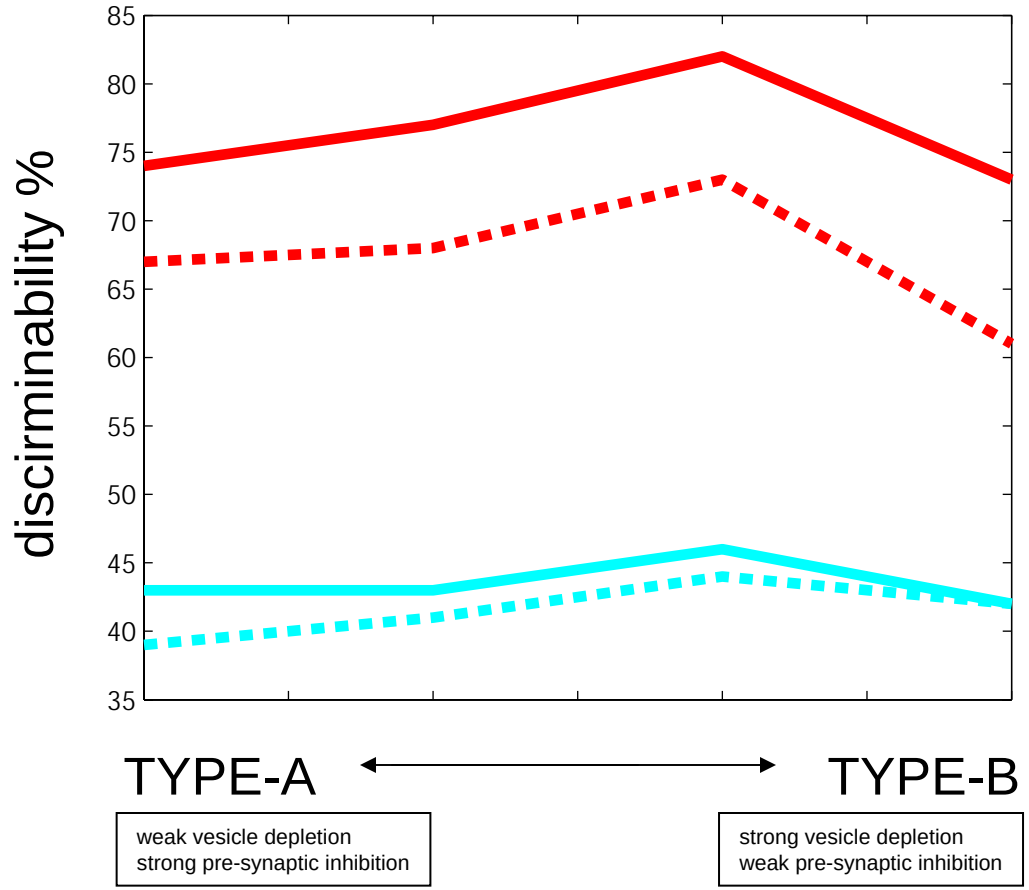


Average reliability of directly stimulated PNs
(averaged over 1024ms after odor onset)



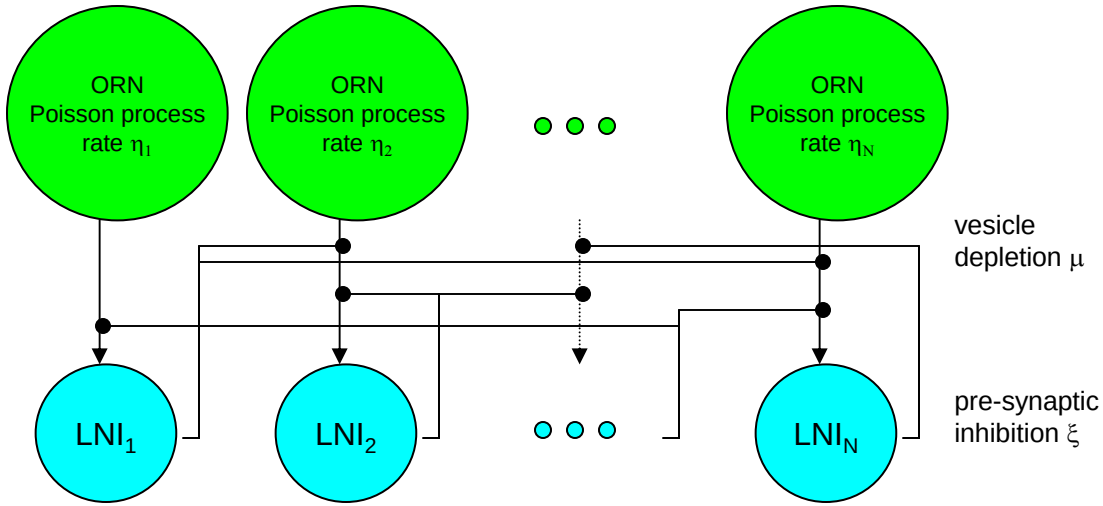
Sweet spot?

10th percentile of Discriminability of network based on firing rates (dashed) and 2-event-chains (solid) observed during only 256ms after odor presentation both 2-way and 3-way discriminability are shown



Possibly relevant for understanding evolution?

Simpler ‘current based I&F’ model to analyze the coding/reliability tradeoff



LNIs are I&F neurons

- Only a single ORN per LNI
- LNIs are sparsely coupled to ORNs
- Coupling between LNIs and ORNs is pre-synaptic in nature

$$\frac{dV^{LNI_i}}{dt} = -\frac{V^{LNI_i}}{\tau_V} + \sum_k S^{LNI \leftarrow ORN}\left[1-\mu_i\right]\left[1-\xi_i\right]\delta\left(t - T_k^{ORN_i}\right)$$

$$\frac{d\mu_i}{dt} = -\frac{\mu_i}{\tau_\mu} + \sum_k \kappa_\mu \cdot \left[1-\mu_i\right] \cdot \delta\left(t - T_k^{ORN_i}\right)$$

$$\frac{d\xi_i}{dt} = -\frac{\xi_i}{\tau_\xi} + \sum_{j \in LNIs} \sum_k \Delta_{i,j}^{ORN \leftarrow LNI} \cdot \kappa_\xi \cdot \left[1-\xi_i\right] \cdot \delta\left(t - T_k^{LNI_j}\right)$$

$$\tau_\mu = \tau_\xi$$

- Given a network (Δ), what are the dynamics?

- Coding Capacity = differential shift in firing rates of LNI_1 and LNI_2 when η_1 increases and η_2 decreases

- Reliability = variance of isi distribution associated with any given LNI

- Solve for the multi-neuron equilibrium distribution associated with this network: $\rho\ (V_1, \mu_1, \xi_1, \ldots, V_N, \mu_N, \xi_N)$

- Impossible to solve for ρ, so instead we can approximate ρ via a weak coupling expansion (expand in terms of $\kappa\xi$ and $\kappa\mu$)

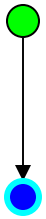
- The approximation to ρ involves a sum of direct products of single-neuron distributions, each term corresponds to a subnetwork of the original network (i.e., a subgraph of Δ)

- Once ρ (as well as the state-transition operator) for the system are sufficiently well approximated, the coding capacity and isi-distribution associated with any neuron in a given network can be calculated

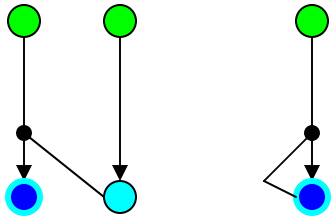
- Importantly, the contributions (to any given dynamic observable) associated with each subnetwork can be disentangled

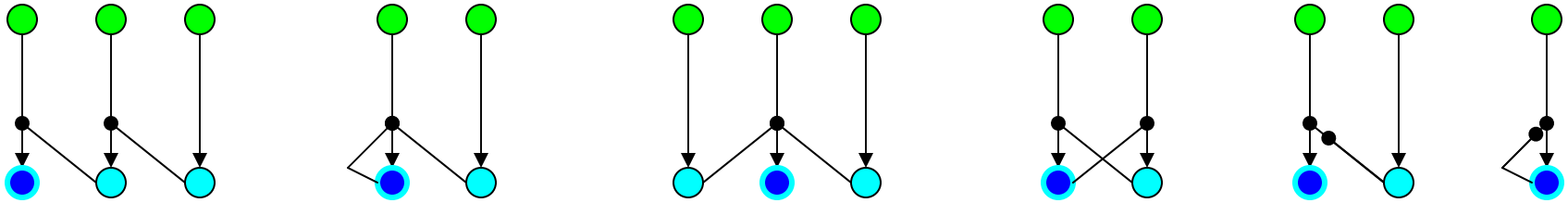
Simpler ‘current based I&F’ model to analyze the coding/reliability tradeoff

(zeroth order subnetworks in terms of $\kappa\xi$)



(first order subnetworks in terms of $\kappa\xi$)

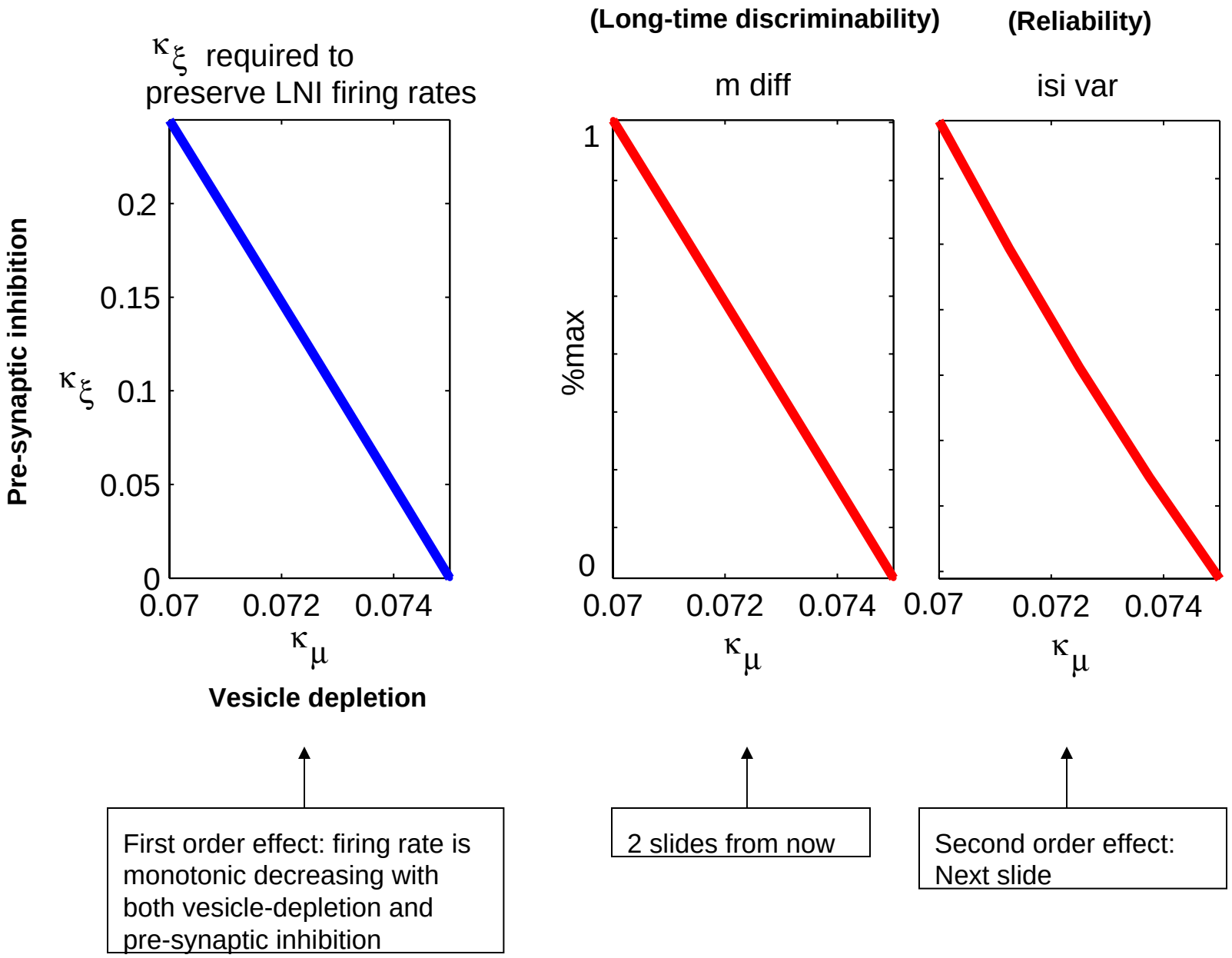


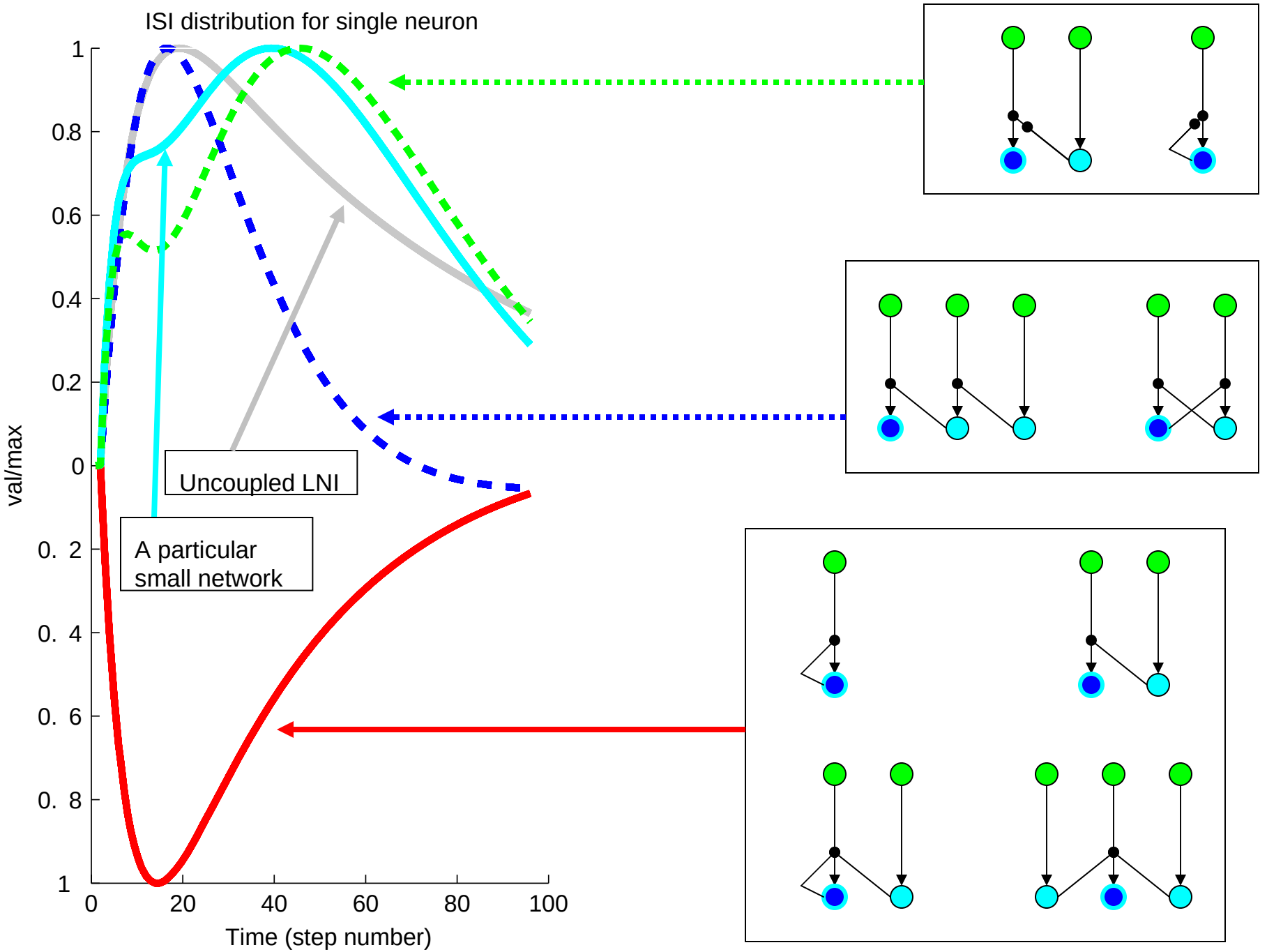


(second order subnetworks in terms of $\kappa\xi$ only, fourth order in terms of $\kappa\xi$ and $\kappa\mu$).

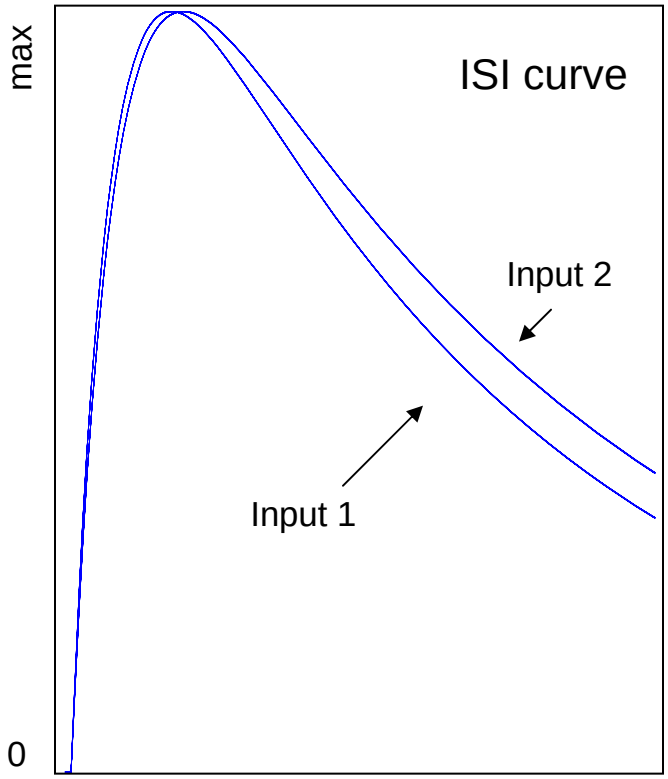
To fourth order in $\kappa\xi,\kappa\mu$, the LNI firing rate is a polynomial, with linear terms (coming from first order subnetworks) dominating. These linear terms imply that there is (locally) a 1-parameter family of variations in $\kappa\xi,\kappa\mu$ that preserve LNI firing rate, ranging from TYPE-A networks (with high $\kappa\xi$) to TYPE-B networks (with high $\kappa\mu$).

(results for a typical sparse network, not valid when connectivity is too dense --- see later)



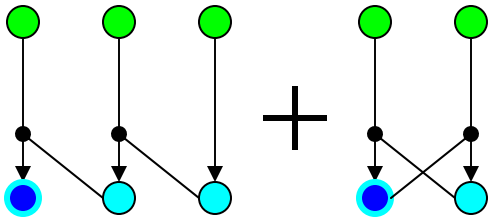

ISI distribution for single neuron
val/max
Time (step number)
Uncoupled LNI
A particular
small network

As input η shifts, firing statistics change
(i.e., mean m and variance v of ISI distribution)



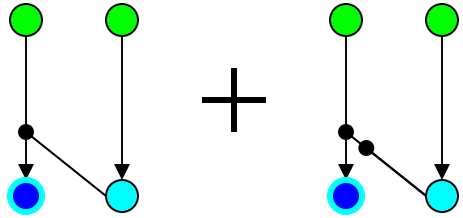
How do $dm/d\eta$ and $dv/d\eta$ depend on subnetworks?

$dm/d\eta$ and $dv/d\eta$ BOTH increase as functions of $\kappa\xi$ for most typical sparse networks



Subtracts from $dm/d\eta$
Subtracts from $dv/d\eta$

Contribution to dm/dI from each of the above subnetworks is only about $50/\kappa\xi$ times smaller than the contribution of the below 2 subnetworks:

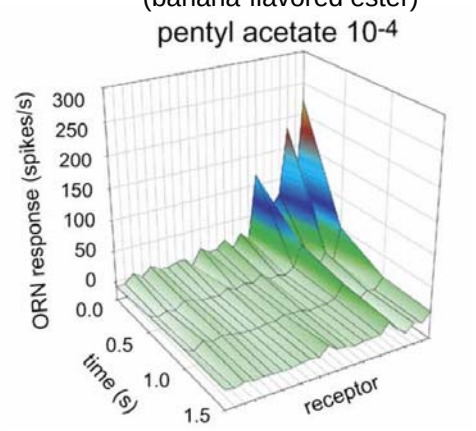


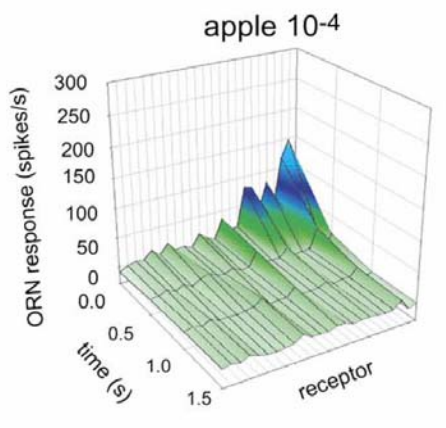
Adds to $dm/d\eta$
Adds to $dv/d\eta$

Thus, Type-A networks have higher long-time-discriminability, and worse short-time-discriminability (for small changes in input) provided that the network is sufficiently sparse (i.e., fewer than $50/\kappa\xi$ pre-synaptic LNIs)

ORNs

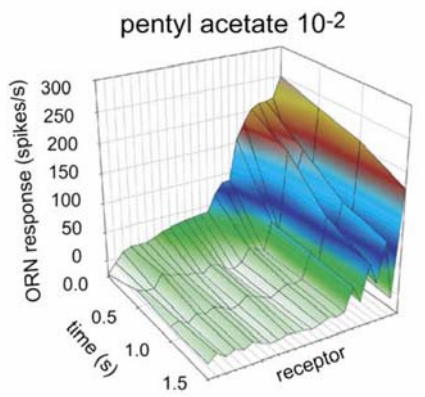
(banana-flavored ester)

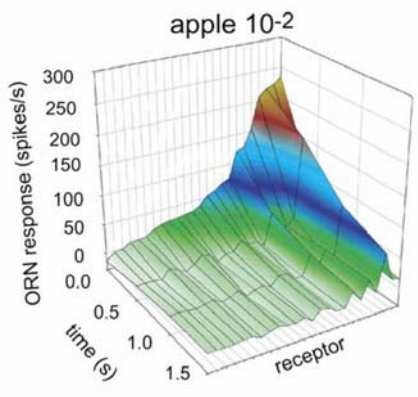




Increased concentration

Increased concentration

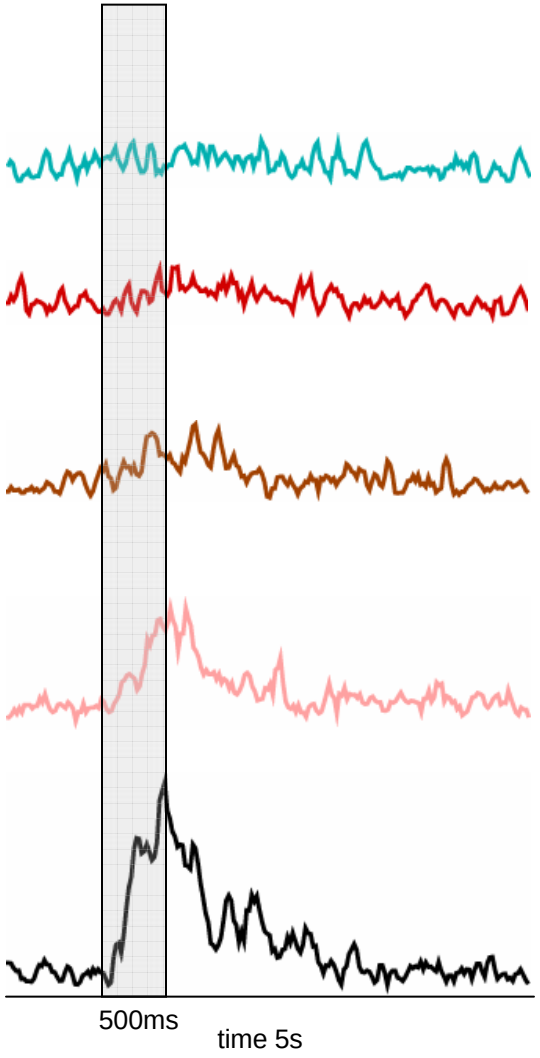




Hallem and Carlson 2006

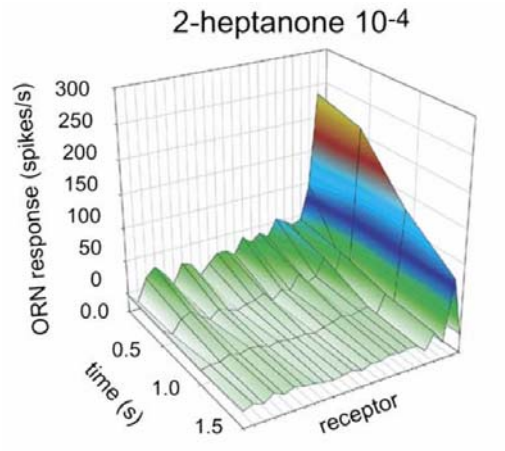
model ORN response

Increased concentration

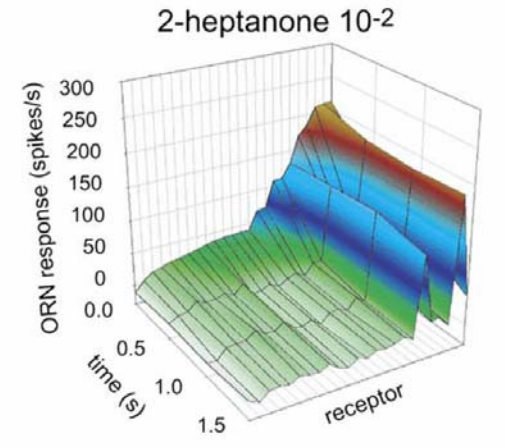


ORNs

(banana-flavored ketone, found in potato chips and wonderbread)



Increased concentration



Hallem and Carlson 2006

- Typically ORN activity increases with concentration
- Exceptions, such as 2-heptanone.

- Decay time-scales range from 100ms to 2s.

- Some biologically critical odors lead to more recruitment than others (i.e., CO^2 or pheremones).

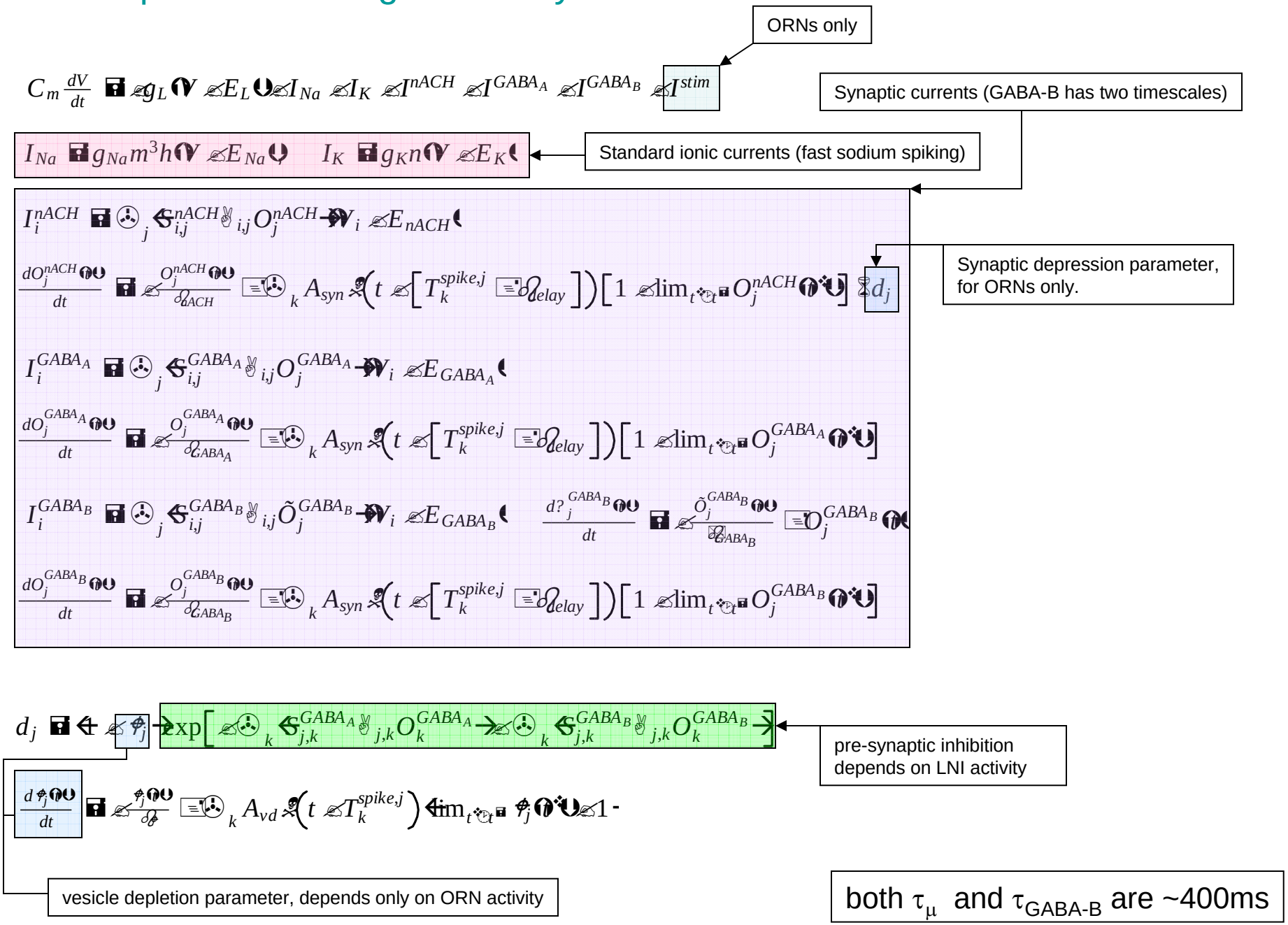
- By appealing to complicated ORN activity, it is possible to justify just about anything you see in the AL.

- ORN diversity may be important for some odors… but the AL may still have relevant functional properties for more typical odors

- To address functional role of AL architecture, we use only one simple class of ORNs – excitatory response with 1s decay.

- Simulated model odors will involve stimulation of some subset of ORN classes. Increasing concentration will correspond to an increase in ORN stimulus

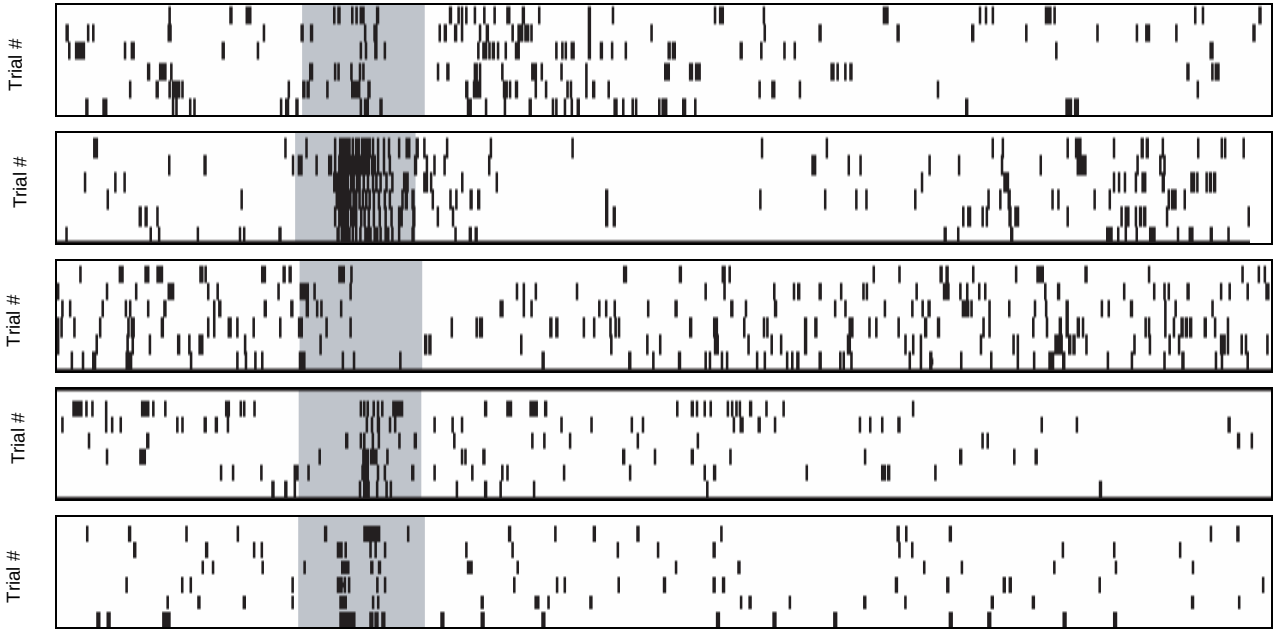
Model equations – Hodgkin-Huxley



PNs

Wilson Turner Laurent 2004

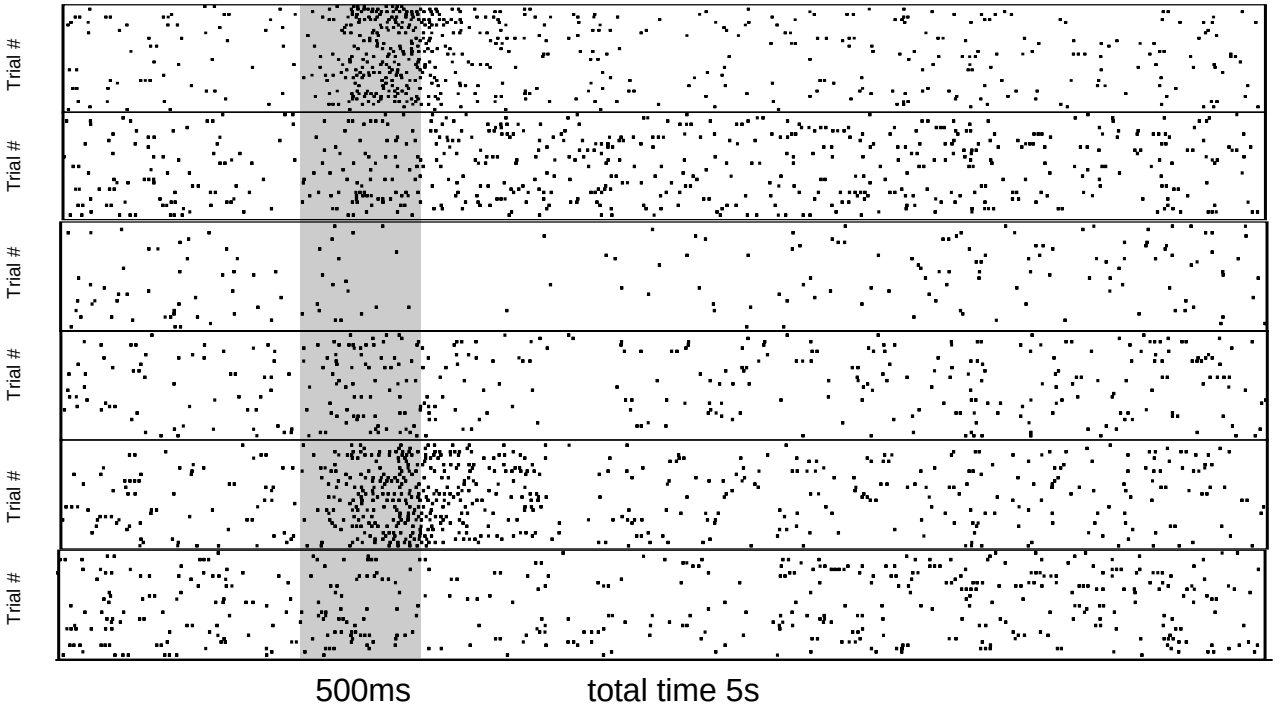
variability in PN responses
not well predicted by that PN's
respective ORN-class



model PNs

- PNs exhibit excitatory and inhibitory responses.
  (inhibition must control PN activity, but
  inhibition cannot be too strong).

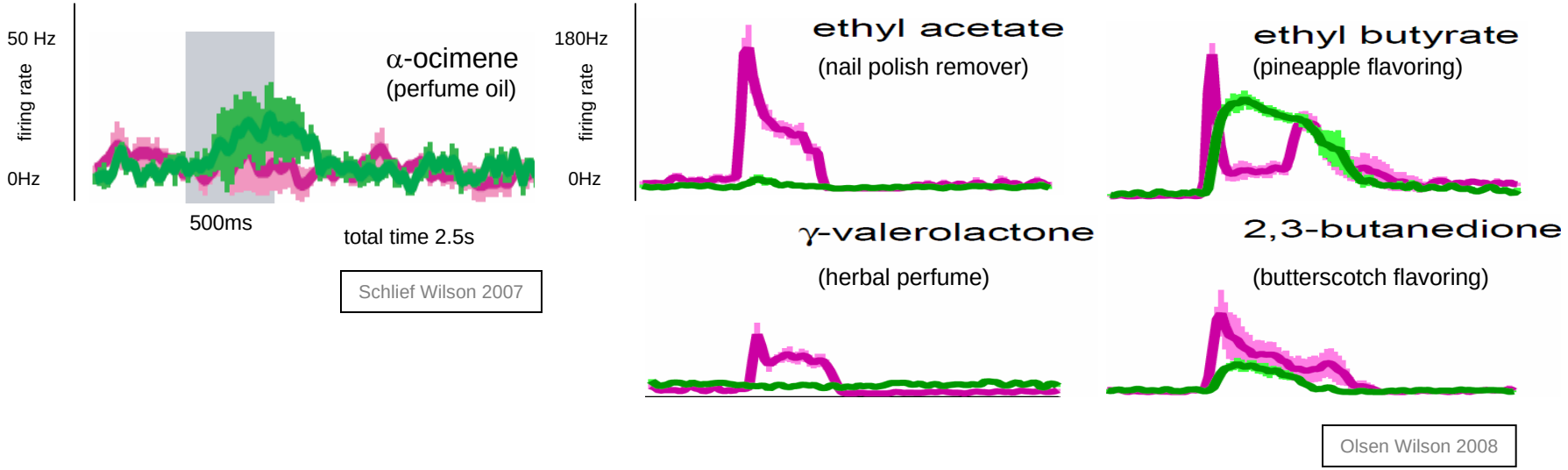
- PNs respond even when parent ORNs removed.
  (lateral excitation sufficiently strong).



Variability in PN responses not well predicted by respective ORN activity

Some PNs do not respond when ORNs do. Other PNs respond when ORNs do not. (LNs show similar variability)
Thus, there must be sufficiently strong lateral excitation and inhibition within the AL

ORNs and PNs



Schlief Wilson 2007

Olsen Wilson 2008

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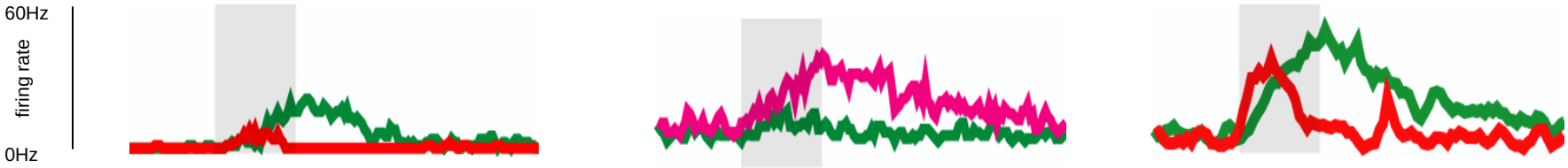
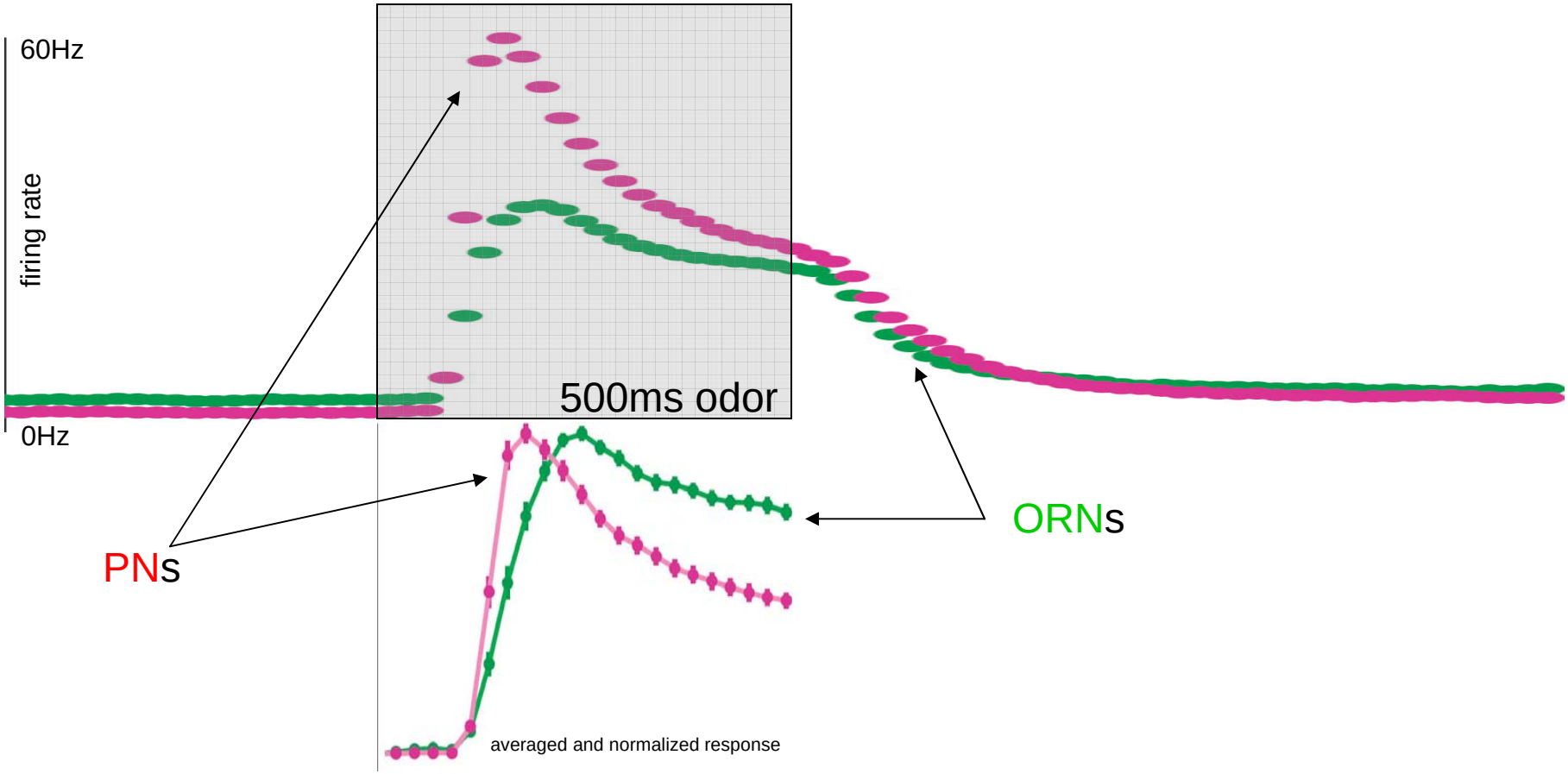
model ORNs and PNs



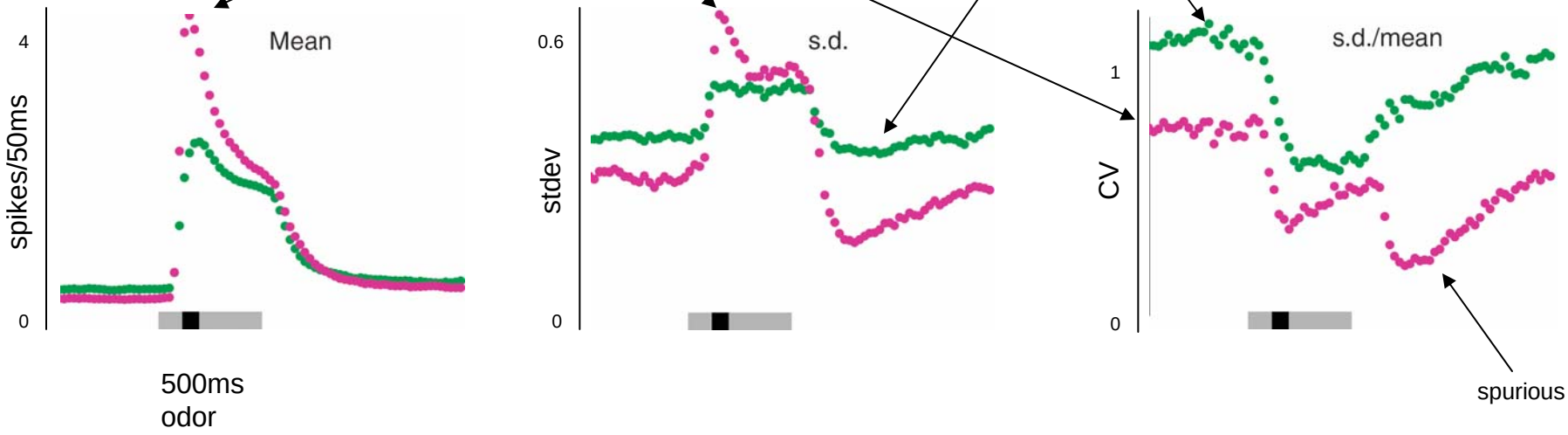
PN's exhibit rapid response, often firing very quickly after odor onset
PN response often peaks within 100-200ms (before ORN response peaks)
Synaptic Depression at ORN→PN synapses instrumental

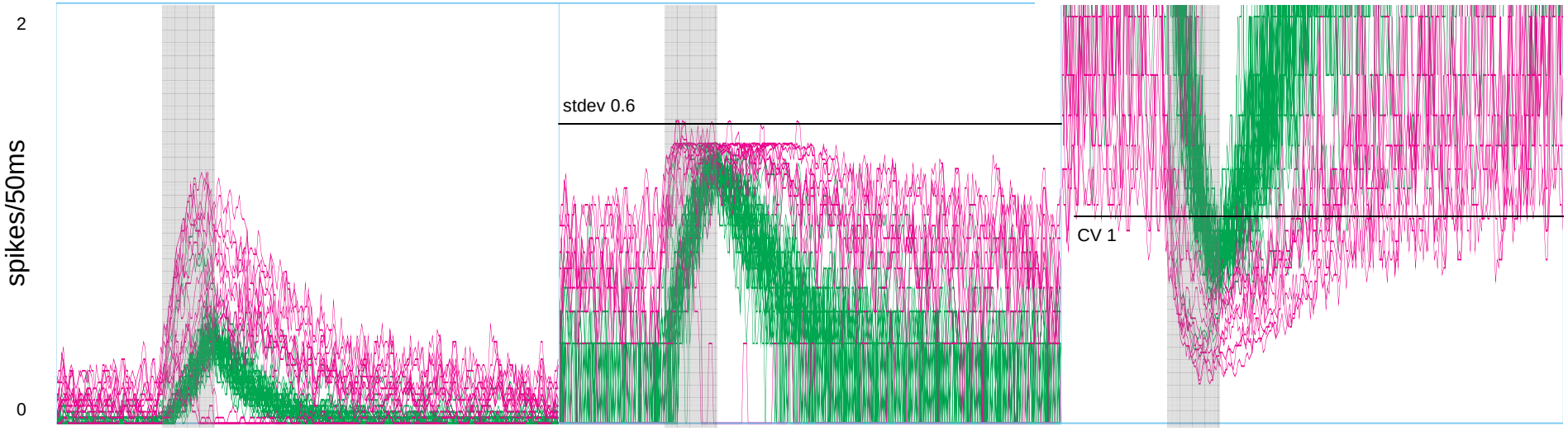


Bhandawat et al 2004

Bhandawat et al 2004

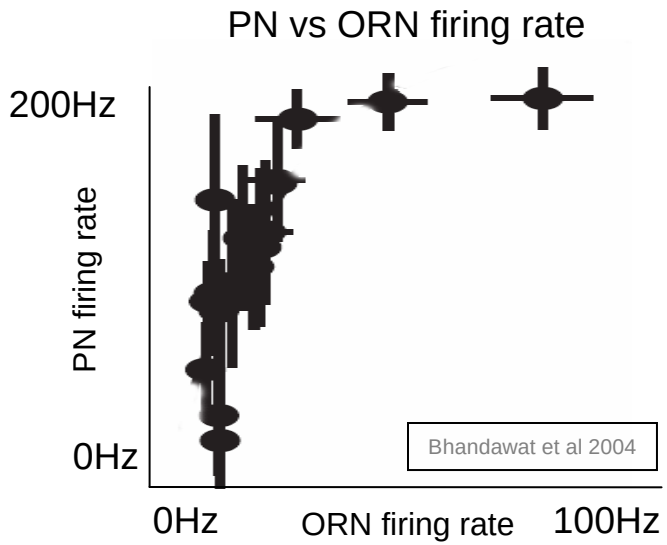
PNs are more reliable than ORNs



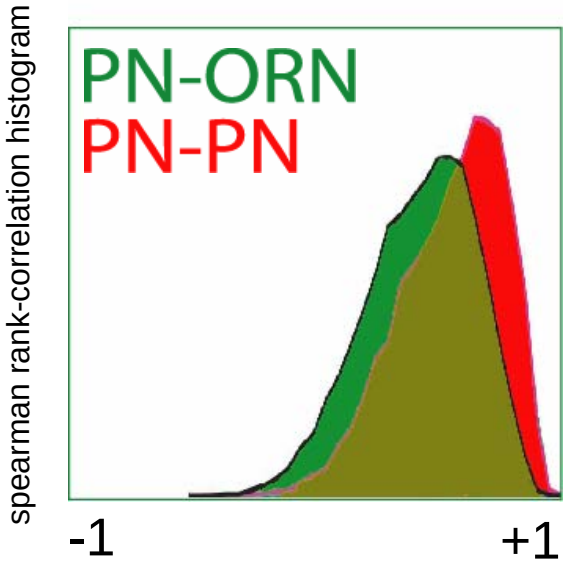


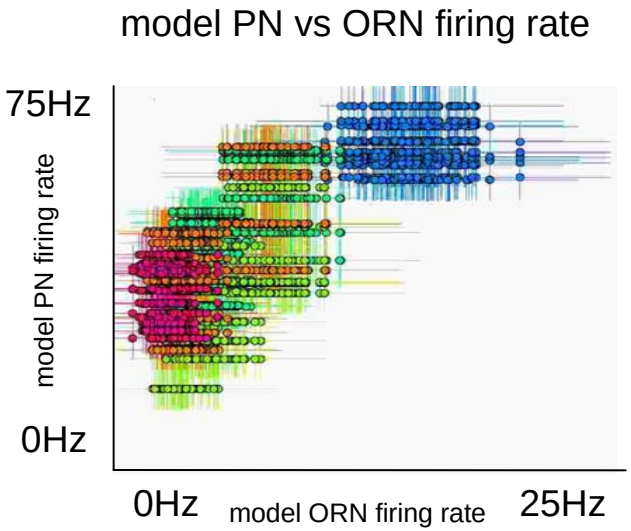
model PNs and ORNs

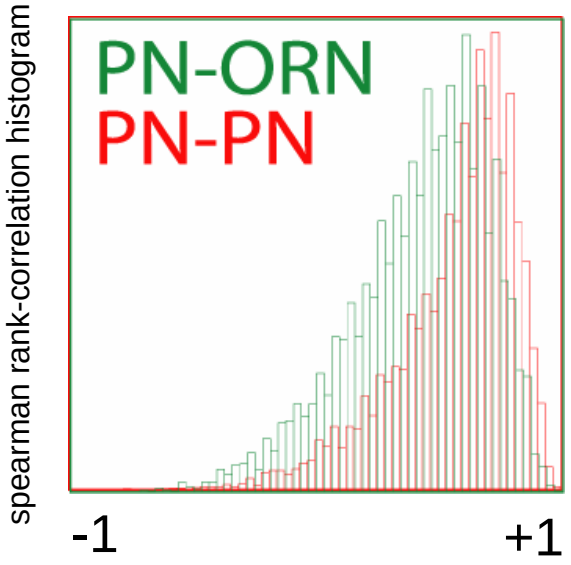
PNs are very sensitive
– high gain and saturation



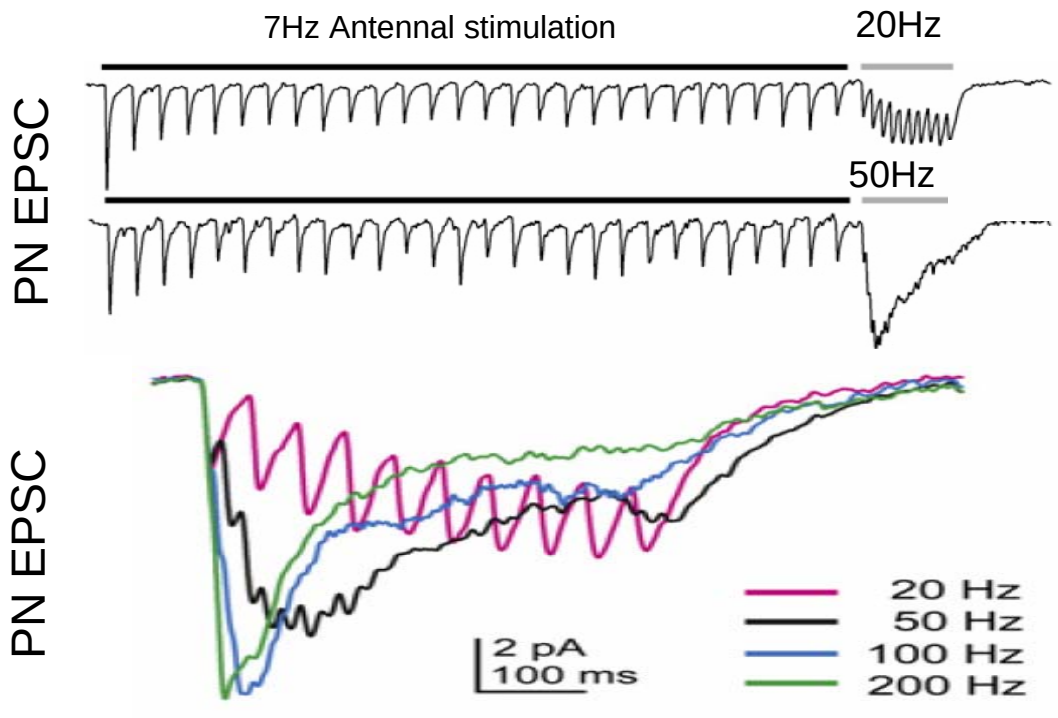
Odor representation is more distributed
at PN level than at ORN level





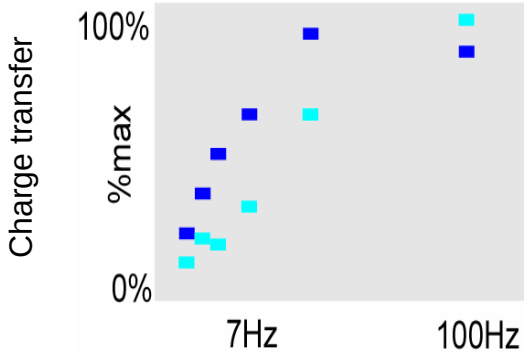


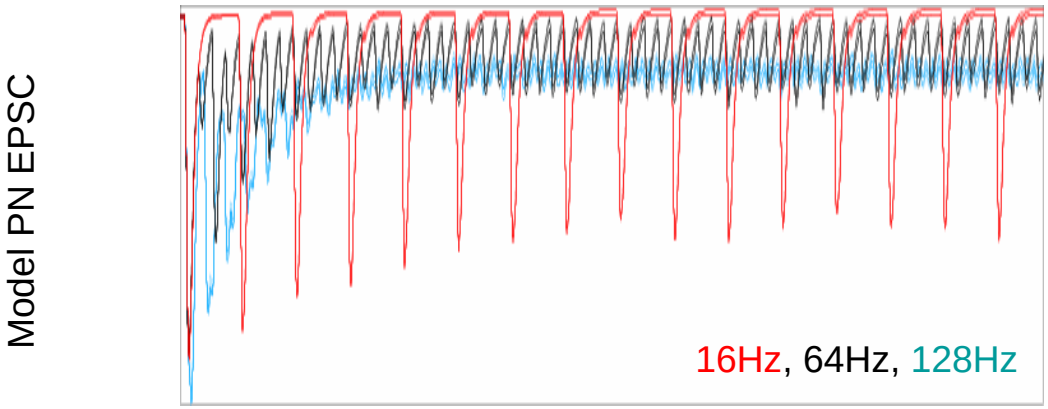
Physiological benchmark for synaptic depression

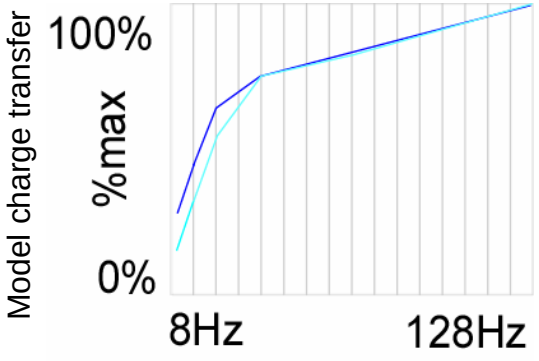


Kazama and Wilson 2008

accumulated charge transfer
over first 100ms or first 500ms

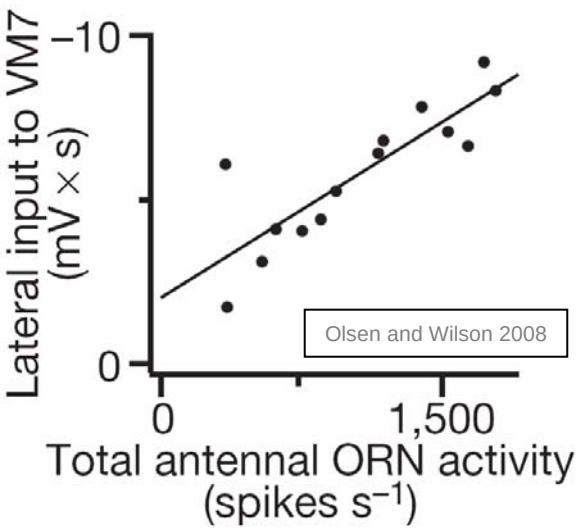




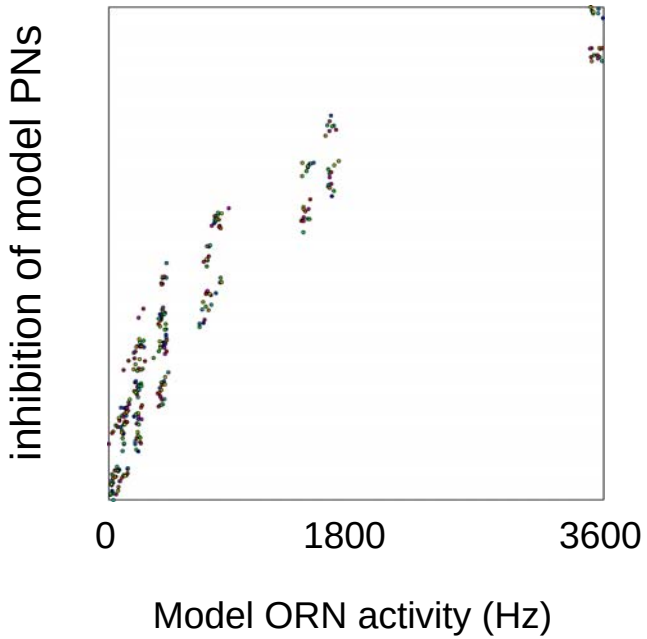


Physiological benchmark for pre-synaptic inhibition

PN measured while respective ORN is ‘shielded’



Some pre-synaptic inhibition must contribute to ORN→PN synaptic depression



Takeaway from tuning/benchmarking model:

- In order to achieve high PN gain and reliability, ORN→PN connectivity must be dense.
- In order to achieve a wide variety of PN responses, PN→LN→PN connectivity must be sparse.
- Given dense ORN→PN connectivity, PN→LNI→ORN and PN→LNI→PN interconnectivity must be sparse, otherwise oscillations form.
- Given variety of LNI and LNE responses (similar to PN variety), LN→LN connectivity cannot be too dense
- Given linear correlation between total ORN activity and PN suppression (olsen et al 2008), pre-synaptic inhibition must be responsible for some of the synaptic depression at ORN→PN synapses.
- One essential ‘degree-of-freedom’ left unconstrained by experiments – the nature of synaptic depression.

Questions:

- How does this model represent different odors?
- Are there any general underlying network mechanisms?

Manifestation within model: 16 odors tested, varied concentrations that saturate PN firing rates