# Identification of Odors by the Spatiotemporal Dynamics of the Olfactory Bulb

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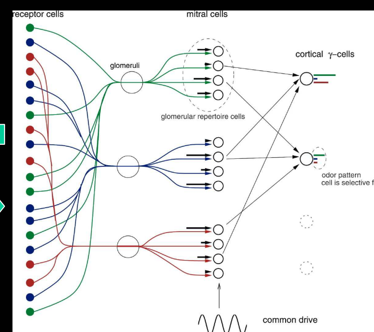


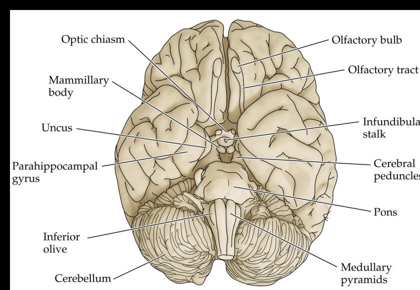

## Outline

- Why think about olfaction?
- Crash course on neurobiology.
- Some experimental insights about olfaction.
- Summary of some theoretical insights.
- Conclusions.

## Why Think About Olfaction?

- Brain is a spherically difficult problem.
- Oldest, most widespread of senses.
- Olfaction involves many of key mysteries.
- Experimentally accessible part of brain.

Mouse brain

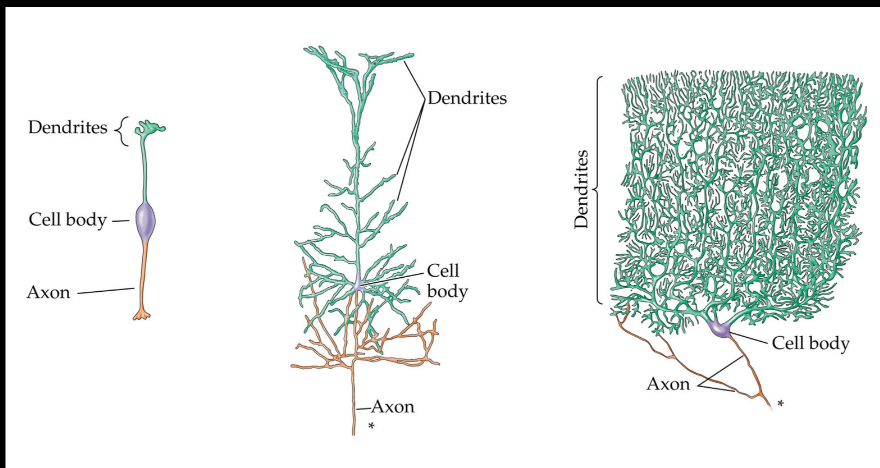



## Crash Course in Neurobiology: What Is the State?

What are the degrees of freedom that enter into any evolution equations?

Recall that for glass of water, there are quantum, molecular dynamic, and hydrodynamic descriptions depending on context.

## Crash Course: Neurons

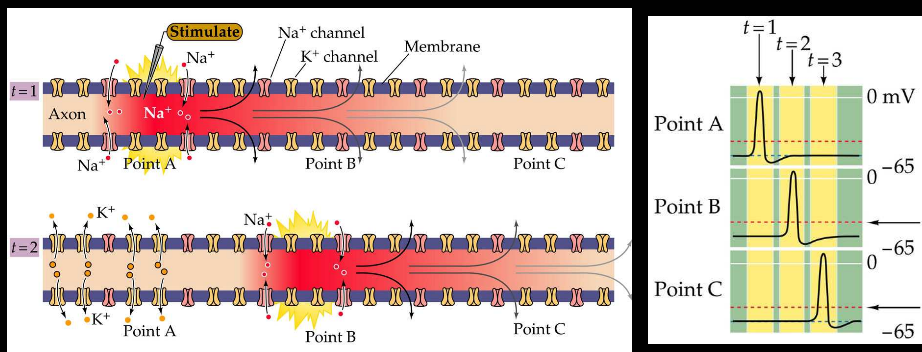



## Crash Course: Concentration Gradients

**Extracellular and Intracellular Ion Concentrations**

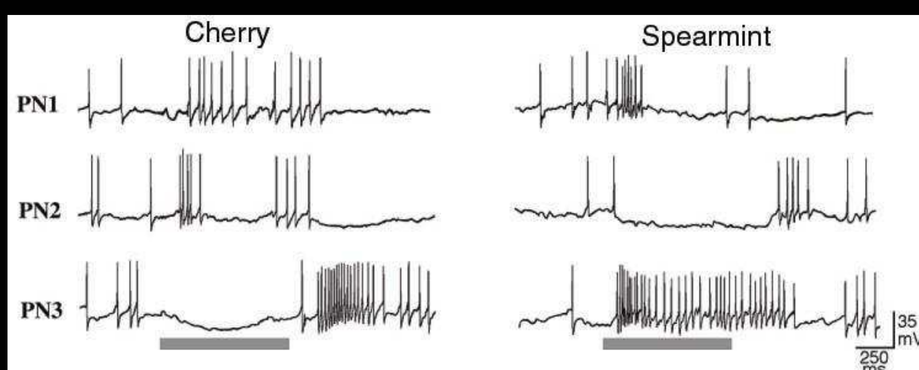
| *Ion* | *Concentration (mM)* *Intracellular* | *Extracellular* |
|---|---|---|
| **Mammalian neuron** | | |
| Potassium ($K^+$) | 140 | 5 |
| Sodium ($Na^+$) | 5–15 | 145 |
| Chloride ($Cl^-$) | 4–30 | 110 |
| Calcium ($Ca^{2+}$) | 0.0001 | 1–2 |

## Crash Course: Action Potential




Hodgkin-Huxley equations

## Intracellular Recordings of Projection Neurons in a Non-behaving Locust

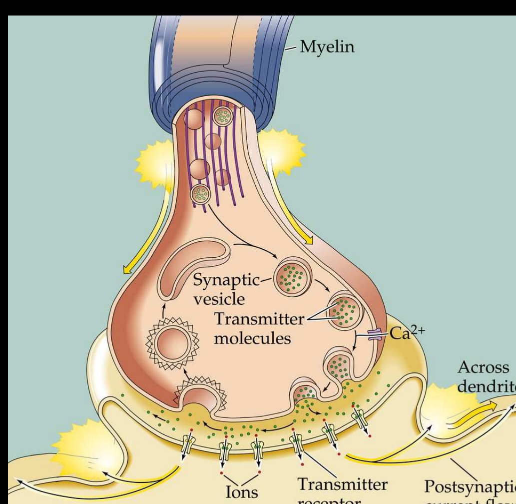


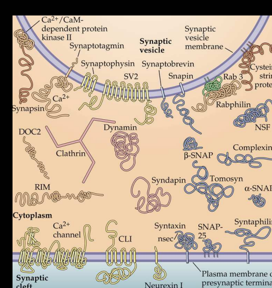

Bazhenov et al, Neuron **30**:569 (2001)

## Real-time Behavioral Observation

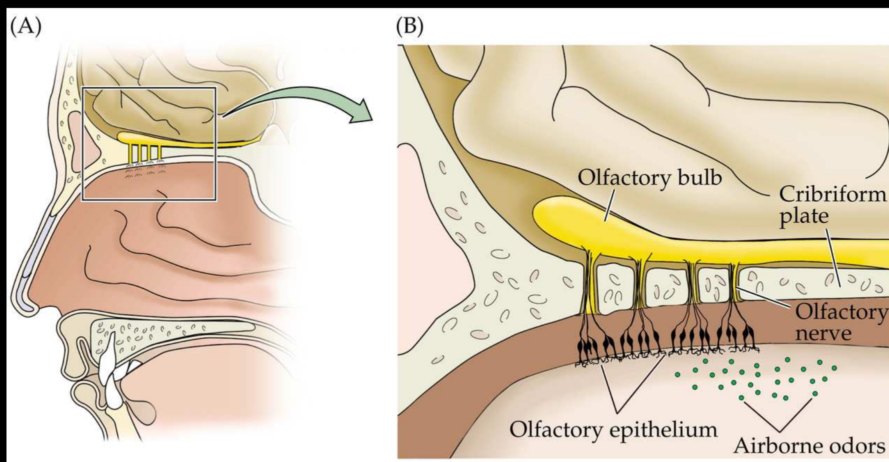

Minmin Luo et al, Science 299:1196-1201 (2003)

## Crash Course, Final Slide: The Synapse

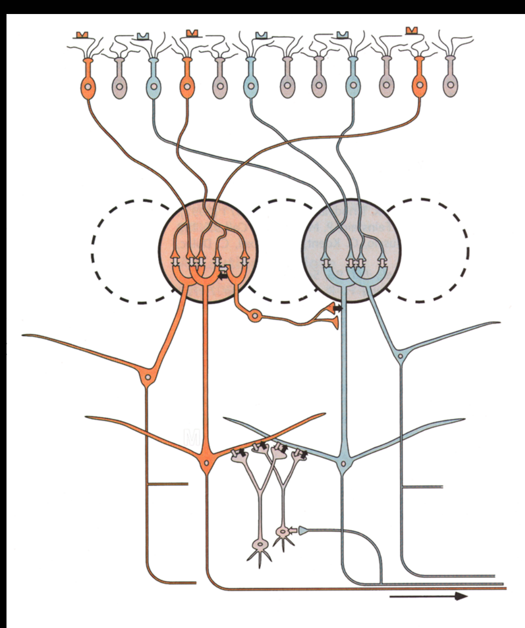


## Early Olfactory Processing




## Schematic of Early Olfactory Wiring

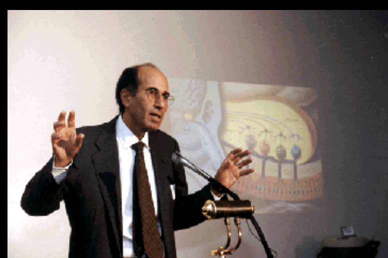


For each side of rat brain:

1. 1,700 glomeruli
2. 12,000 ORNs/glomeruli
3. 20-50 MT/glomeruli
4. 400-1000 PG/glomeruli
5. 50-100 GC/glomeruli
6. Many centrifugal fibers (not shown).

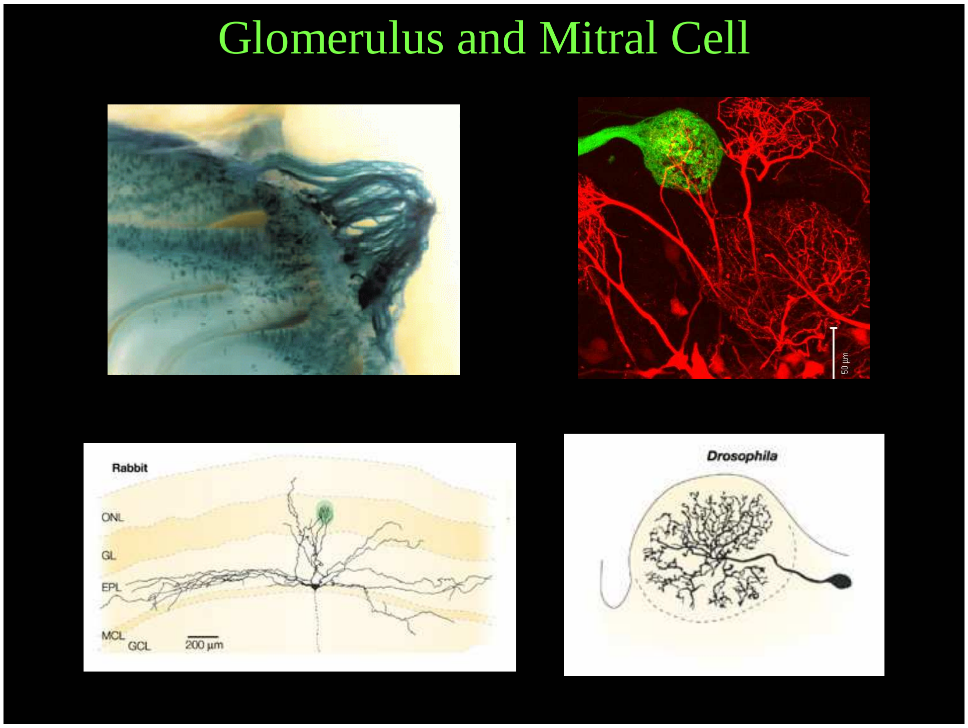
## The Breakthrough: Many Receptor Types

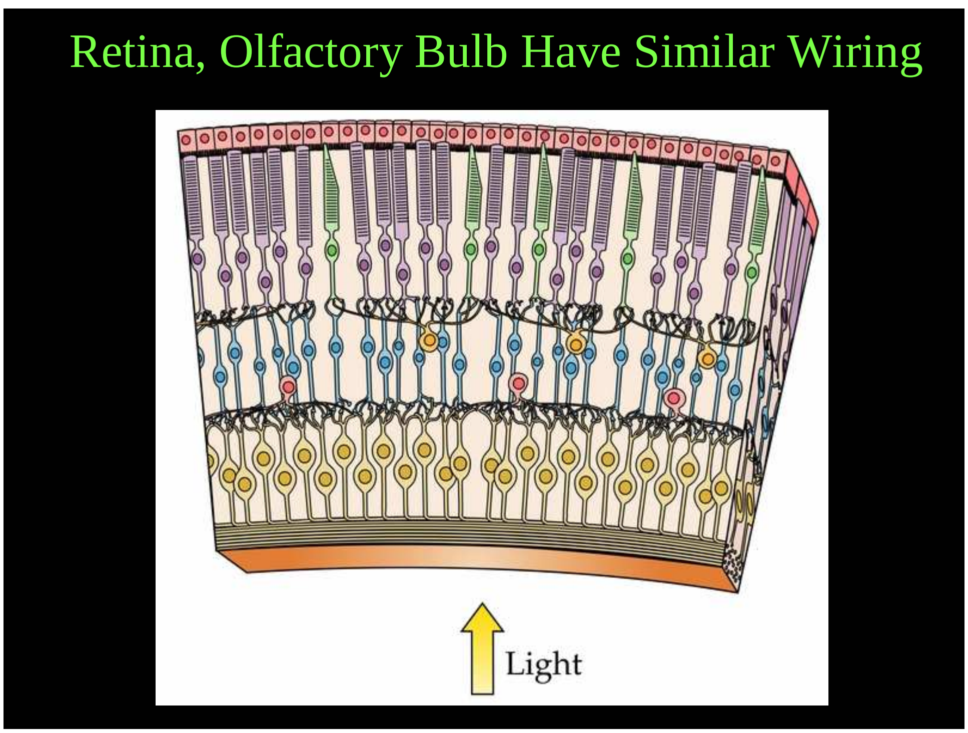
- “A novel multigene family may encode odorant receptors—a molecular basis for odor recognition”, Linda Buck and Richard Axel, Cell **65**:175-187 (1991).
- 1000 olfactory genes for mice, ~1% of its genome!



## Some Implications of Buck and Axel

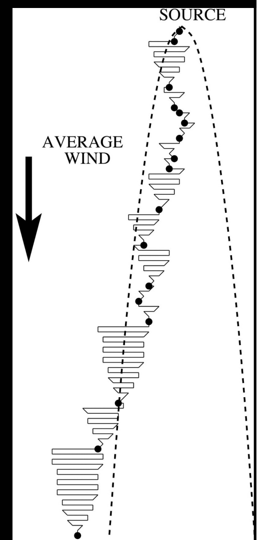
- Fundamental olfactory input is antenna array of 20,000,000 sensory cells of 1000 types.
- Each “sensor” reacts to many odorants, each odorant activates many sensors. (Pure molecules vs. mixtures: can’t be distinguished without fluctuations).
- More and different sensors activate with increasing odorant concentration: perception invariance?


Glomerulus and Mitral Cell
Rabbit
ONL
GL
EPL
MCL
GCL
200 µm
Drosophila

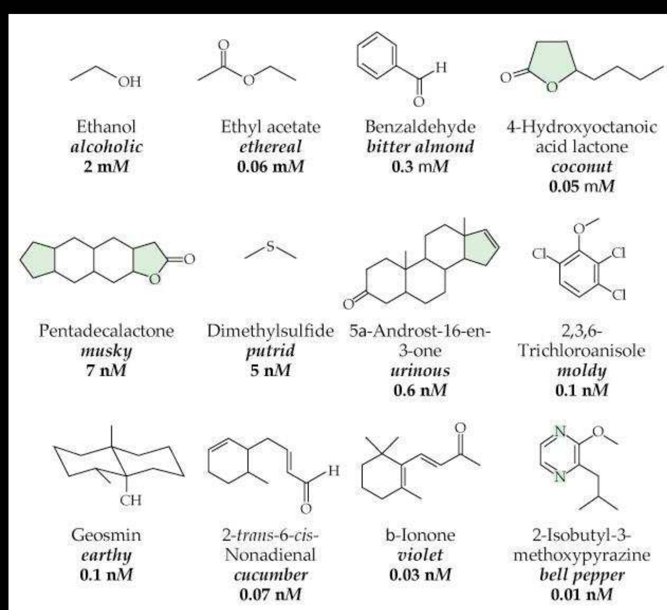

Retina, Olfactory Bulb Have Similar Wiring
Light

## What Has Evolution Selected the Nose For?

- What are typical or key odorants?
- What are typical mixtures?
- What are typical concentrations?
- What are typical fluctuations, e.g., of odor plumes from remote source or from sniffing?



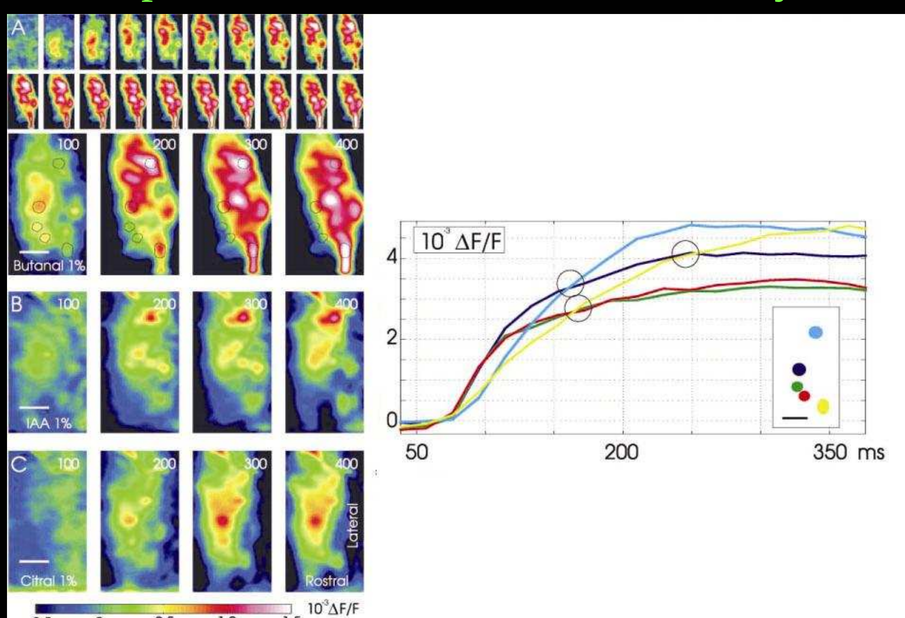

## Poorly Understood Discrete Odor Space



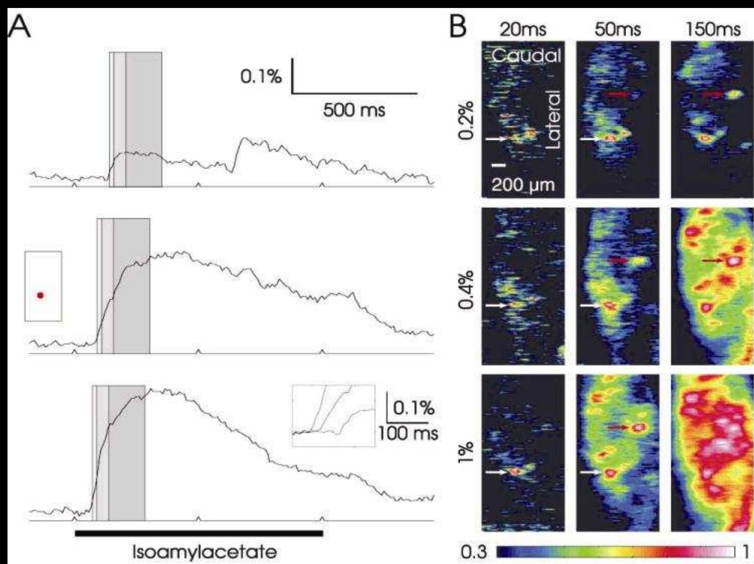
## A Theory of Olfaction

- Predict behavioral response.
- Predict *dynamics* of electrical activity as function of type, concentration, mixture, history.
- Explain *anatomy*: why glomeruli? Why the connections, numbers and ratios of ORNs, PGCs, M/Ts, GCs, etc.
- Principles, e.g. for robot design: segmentation, synthesis, recognition, location.

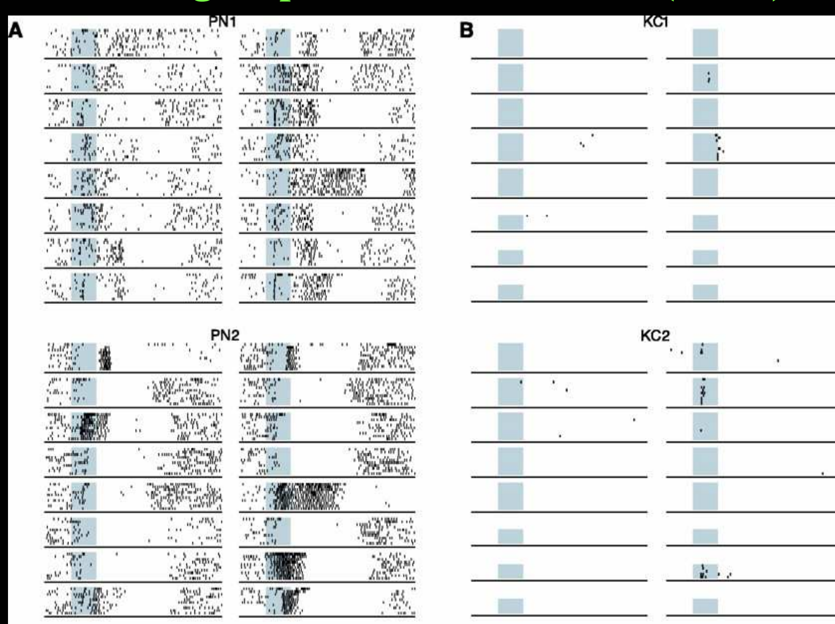
## Spors-Grinvald 2002: Odor Quality



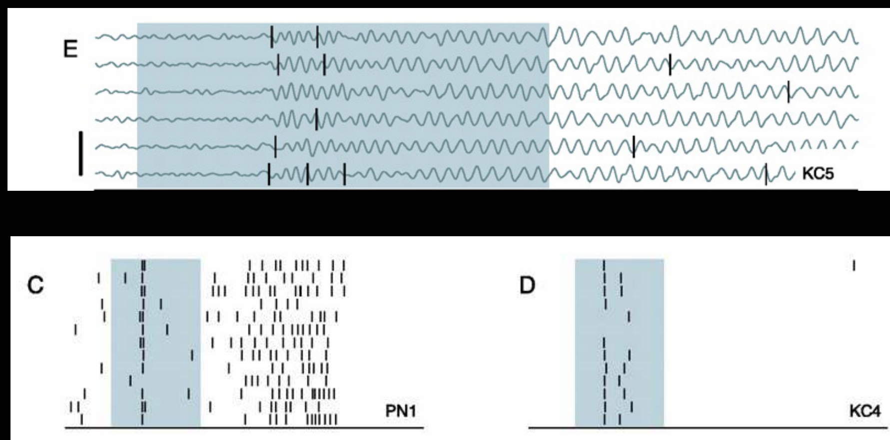
## Spors-Grinvald: Concentration Dependence




## Laurent group: Science 297:359 (2002)



## Laurent et al: Further Data




## Some Theory Achievements

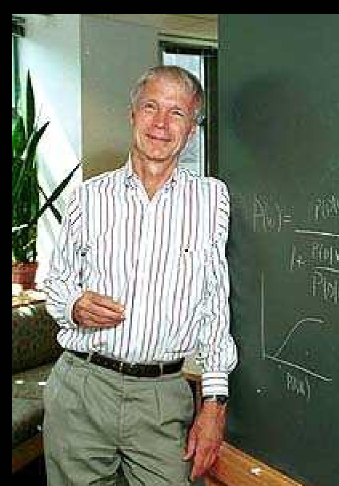
- Various mechanisms for generating oscillations, Bazhenov et al, Shepherd et al.
- Segmentation of odors.
- Concentration invariance over two decades.
- Associative memory out of excitatory, inhibitory network (Hopfield, many others).

## Some Theory Non-achievements

- Purpose of the oscillations and phase locking?
- Why the large number of receptor types?
- Purpose of the glomerulus?
- Purpose of the many inhibitory periglomerular and granule cells?
- Purpose of the many centrifugal fibers?

## Brody and Hopfield
## Neuron 37:83-852 (2003)

- Explanations for segmentation and odor concentration invariance.
- Consider only excitatory pathways.
- No experimental support but valuable.



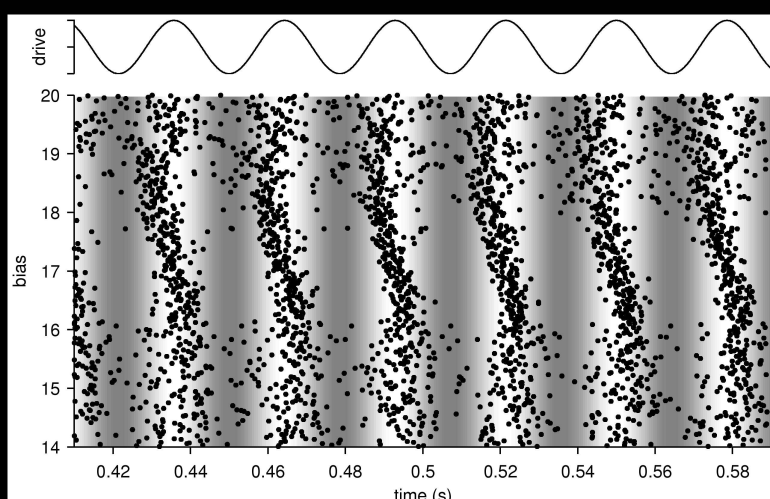
## Leaky Integrate and Fire Model of Neuron

$$\tau_m \frac{dV}{dt} = E_L - V - r_m g_s P_s (V - E_s) + R_m I_e$$

With additional rule:

1. If V > $V_{th}$ then generate instant spike.
2. Reset V = $V_{reset}$.

## Action Potential Rasters In Presence of Subthreshold Oscillatory Potential



## Empirical Distribution of Binding Constants

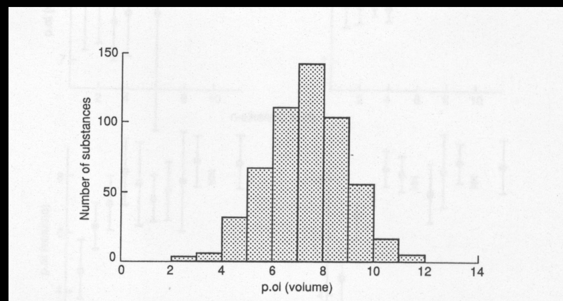
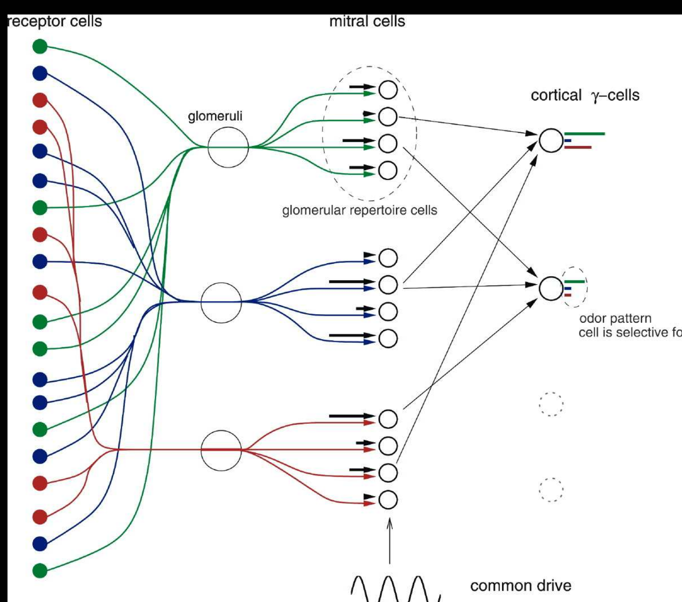



**Fig. 1.2** Distribution of standardized olfactory power p.ol(volume) for the 529 selected substances. The p.ol(volume) is defined as the negative decimal log of concentration expressed in volumic (or molar) fraction. A p.ol(volume) of 0, 6, 9 corresponds to odourlessness at normal atmospheric pressure, and to thresholds of 1 ppm and 1 ppb respectively.

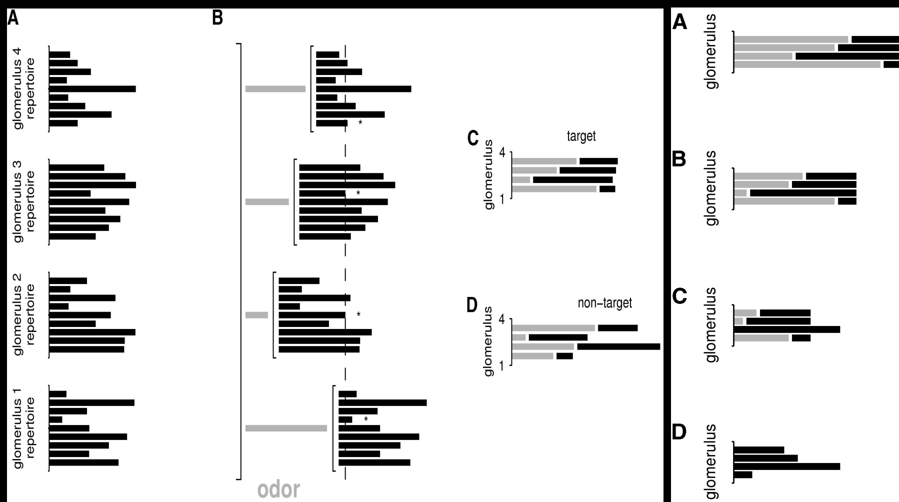
Deductions:

1. Threshold concentrations vary from $10^{-12}$ to $10^{-2}$ M.
2. If $cov_{min}$ is same for all odorants, horizontal axis is same as log of binding constants K=cov/[L], high affinity to right.
3. Range of about $10^{6}$ in strength of binding constants.

## Brody-Hopfield Model Olfactory System



## Many-Are-Equal Odor Recognition




## Conclusions

- Neurobiology is a surprisingly young field: anatomy, physiology, biochemistry, genetics nascent.
- Mechanism and function of spatiotemporal dynamics?
- What is a *population* of neurons doing? Expt + theory.
- Many years still before we will know why a rose smells like a rose!

## Lewis Thomas Olfaction Quote

"I should think we might fairly gauge the future of biological science, centuries ahead, by estimating the time it will take to reach a complete, comprehensive understanding of odor. It may not seem a profound enough problem to dominate all the life sciences, but it contains, piece by piece, all the mysteries."

From Lewis Thomas's essay "On Smell", in his book "Late Night Thoughts on Listening to Mahler's 9th Symphony" (New York, Viking, 1983)

## Mammalian Olfactory Pathways