INTERNATIONAL ATOMIC ENERGY AGENCY
UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION

INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
34100 TRIESTE (ITALY) - P.O.B. 586 - MIRAMARE - STRADA COSTIERA 11 - TELEPHONE: 2240-1
CABLE: CENTRATOM - TELEX 460392 - I

SMR/302-50

COLLEGE ON NEUROPHYSICS:
"DEVELOPMENT AND ORGANIZATION OF THE BRAIN"
7 November - 2 December 1988

"The Chemical Senses: Olfaction"

Obaid SIDDIQI
Tata Institute of Fundamental Research
Molecular Biology Unit
Bombay, India

THE CHEMICAL SENSES (OLFACTION)

Gen. Reading: 1. Moncrief; The Chemical Sense
2. National Geographic. 1986 September, The intimate sense of smell.
3. Handbook of Sensory Physiol Vol IV. Olfaction

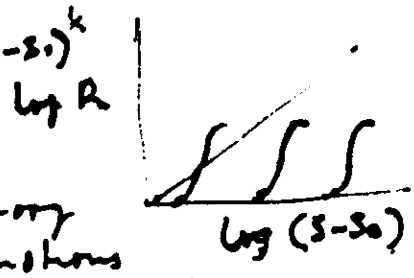
REMARKS:

Why is the chemical sense neglected?
The dying sense?
Connection to emotions & memory
Difficult to study

PSYCHOPHYSICS:

T. Engen, Handbk. sens. Physiol. 4, 216 (1971)

Sensitivity
Dose-response curve $R = a(S-S_0)^k$
Odour quality
Adaptation
Other features { Memory, Emotions, Hallucinations



RECEPTION:

What is detected?

Vibrational energy?
Lipid solubility?
Stereochemical features — Shape, Size, Charge; Functional groups

How many receptors?

100,000 or '10-20'

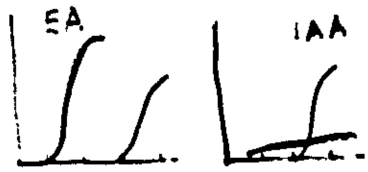
T1
T2

Is there an elementary set of odour receptors?
Amoore's programme. (Genetic anosmias)
Olfactory mutations in Drosophila

Is there a special genetic mechanism for churning out odour receptors. (a la antibodies)? (Identity odours)

Specificity of sensory neurons:

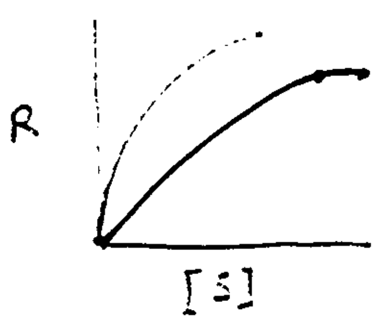
Specialised neurons
Neurons with subsets of receptors < Vertebrates / Insects

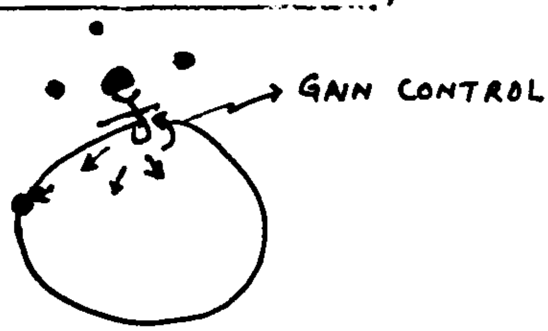


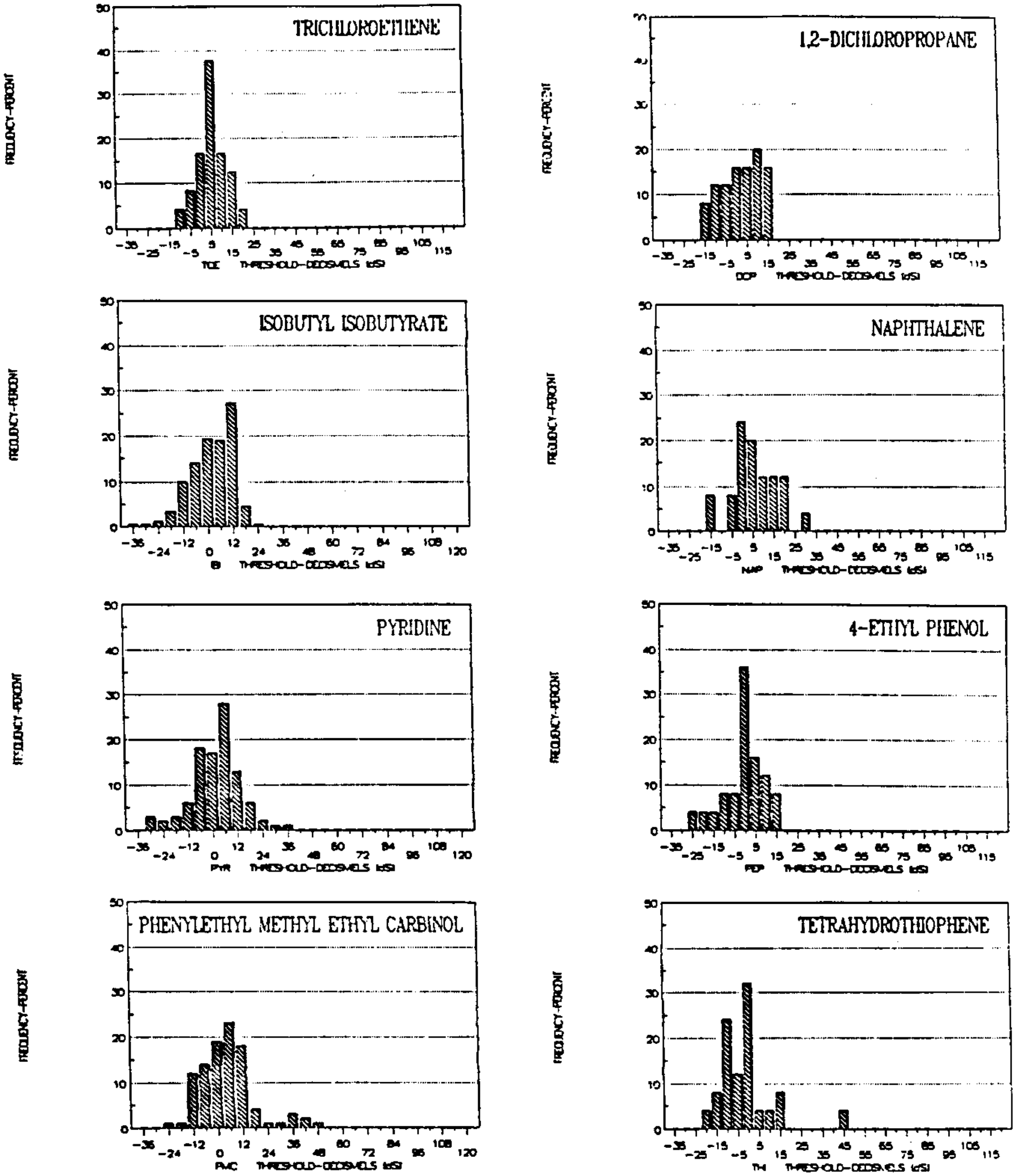
Are odour receptors regulated?
Neurons turn-over
Receptors turn-over

P. Graziadei,
M. Graziadei
Brain Res. 262, 303
J. Comp. Neurol. 217, 17

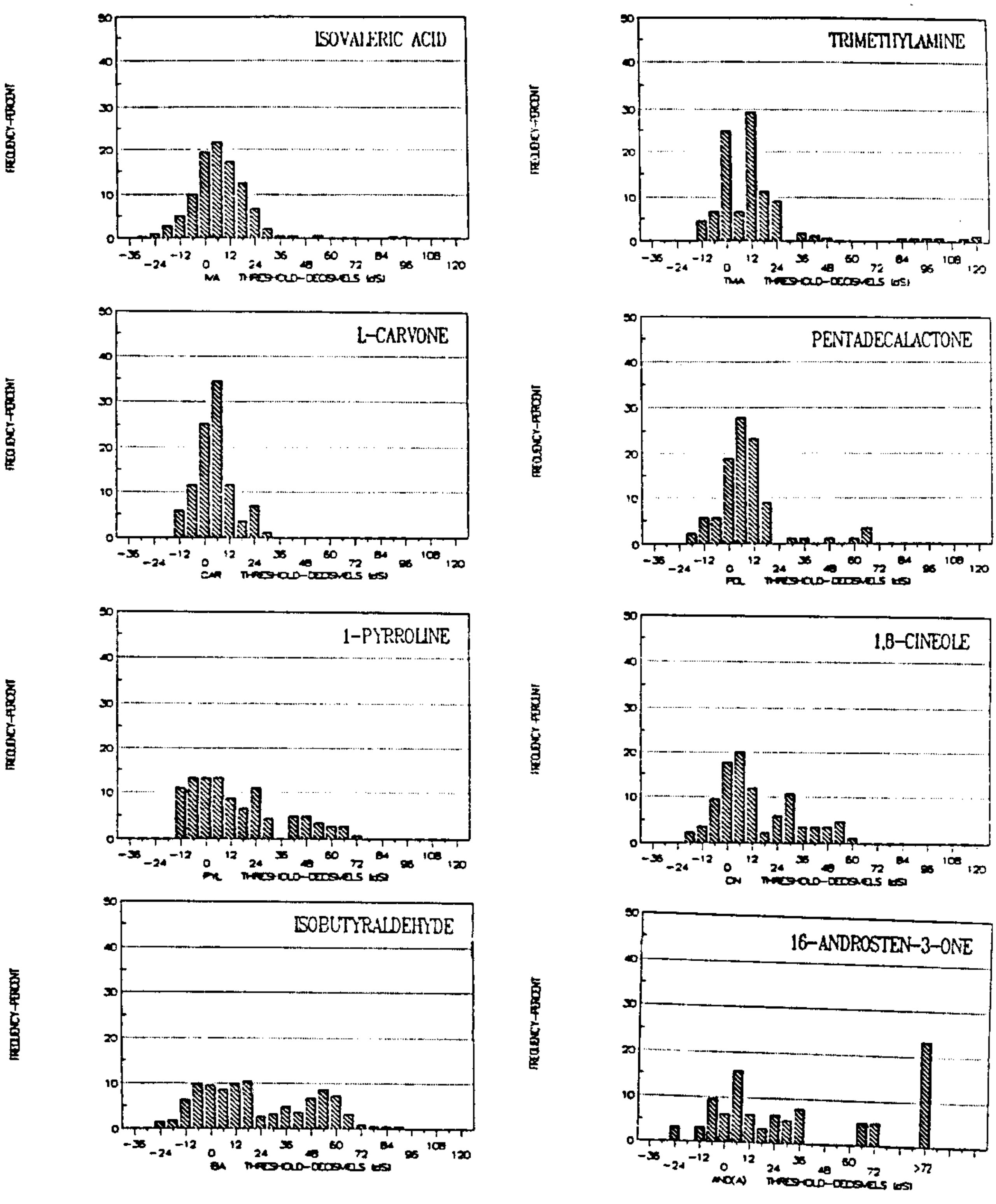
AMPLIFICATION & CELLULAR SIGNALLING:







Distributions of olfactory detection thresholds for eight odorants that show little or no signs of hyposmia. These are re-calculated for samples of 100 subjects. Odor thresholds expressed on the "decismel scale"

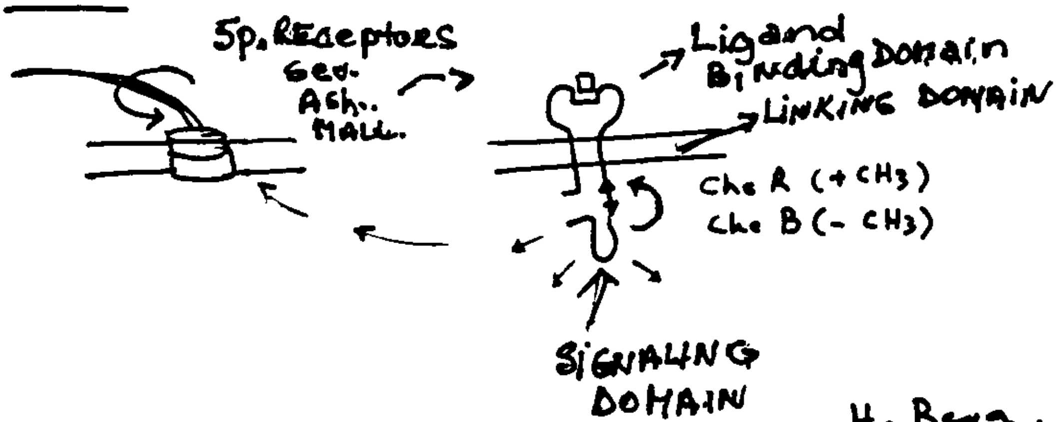


Olfactory thresholds for eight "primary odorants" that exhibit, from top to bottom, increasing proportions of specific anosmics in the population samples. Original data were in binary steps, recalculated as decismels.

Chemoreceptors in *E. coli*

J. Adler
Koshland

MCPs



H. Berg. (Caltech)
J.S. Parkinson (Utah)
M. Simon. (Caltech)

Two conformational states determined by level of methylation determine rotation CCW or CW

Mutations in certain residues lead to locked CCW or CW state - or biased swim

Mutations in binding domain lead to loss of affinity.

Signalling system is a phosphorylation cascade

Olfactory transducers are very likely somewhat like this but.

<u>How many 'Golf' proteins?</u>
<u>What second messengers?</u>

<u>CENTRAL PROJECTIONS OF OLFACTORY SIGNALS:</u>

<u>Glomerular circuits</u>

T3
T4 Connections, bidirectional synapses.

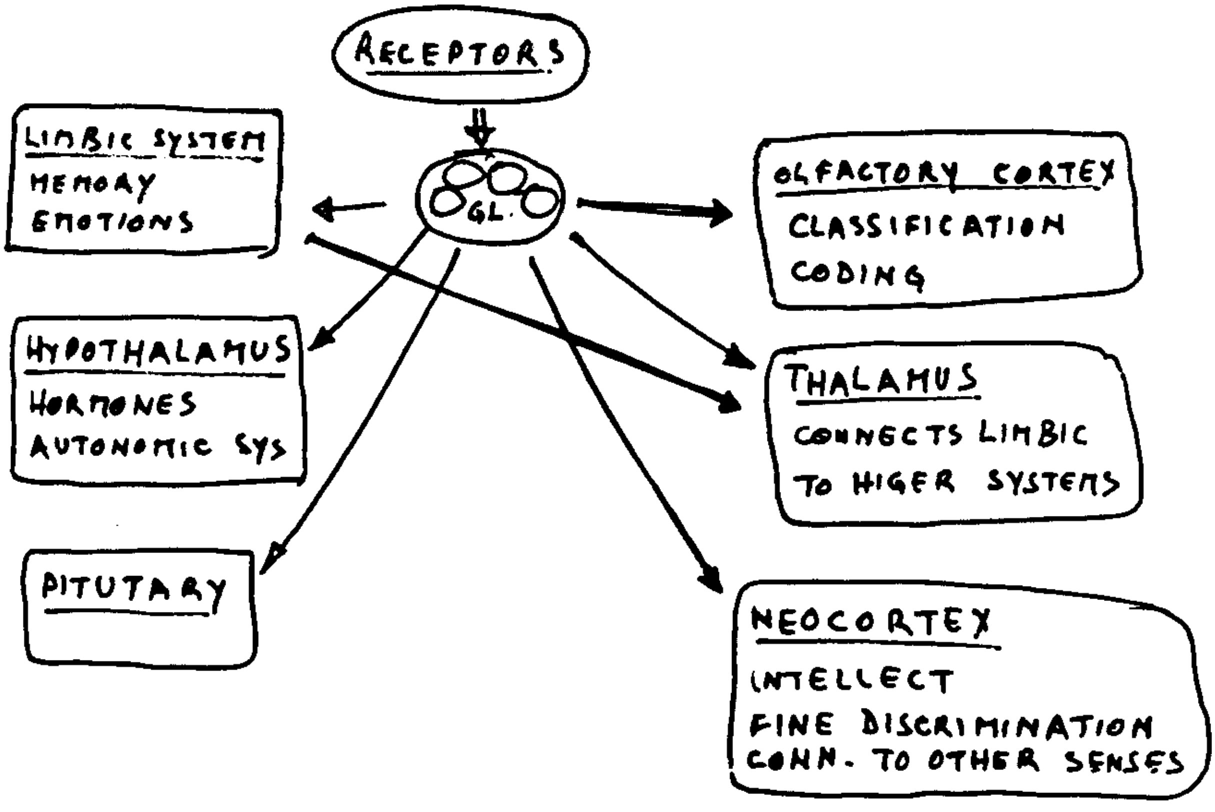
T5 Firing patterns

T6
S1
S2 Theoretical model

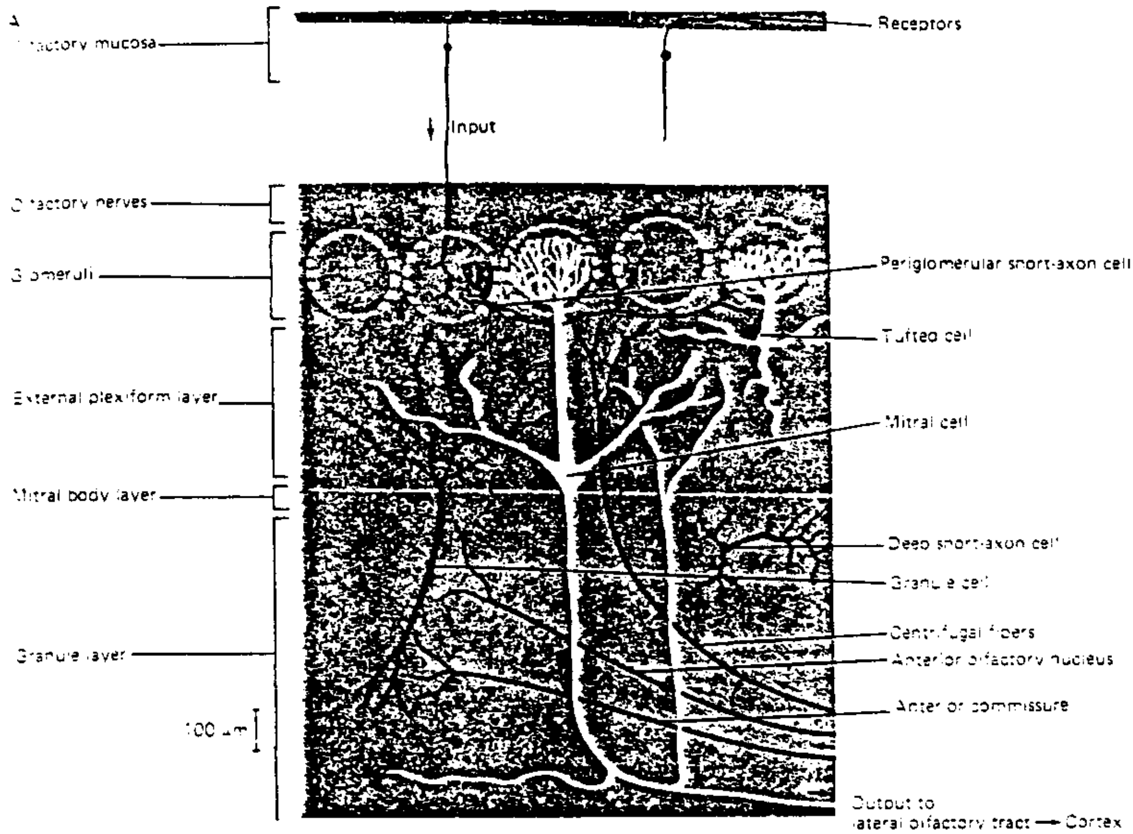
<u>Spatial representation of odours</u>

DOG maps (Vertebrates)
<u>Drosophila</u>

<u>HIGHER CORTICAL PROJECTIONS</u>



A



B

9–15 Mammalian olfactory bulb. A. Neuronal elements. Inputs: afferent fibers (from above) from olfactory receptors; and central fibers (from below) from three sources—centrifugal fibers from the nucleus of the horizontal limb of the diagonal band, ipsilateral fibers from the anterior olfactory nucleus, and contralateral fibers from the anterior commissure. Principal neurons: mitral cell (1) and tufted cell. Intrinsic neurons: periglomerular short-axon cell, deep short-axon cell, and granule cell. (Adapted from Shepherd, 1974.) B. Organization of functional units. Dotted lines enclose "functional units," each defined as the morphological substrate for a specific function. The units differ in size and complexity: single synapse with its pre- and postsynaptic terminals; reciprocal synapses and other patterns involving dendritic terminals and axonal inputs; parts of dendritic trees with their associated input–output ensembles of processes; and long-distance "loop units" through neighboring structures (anterior olfactory nucleus). Arrows indicate functional polarity of synapses. (Adapted from Rakic, 1975.)

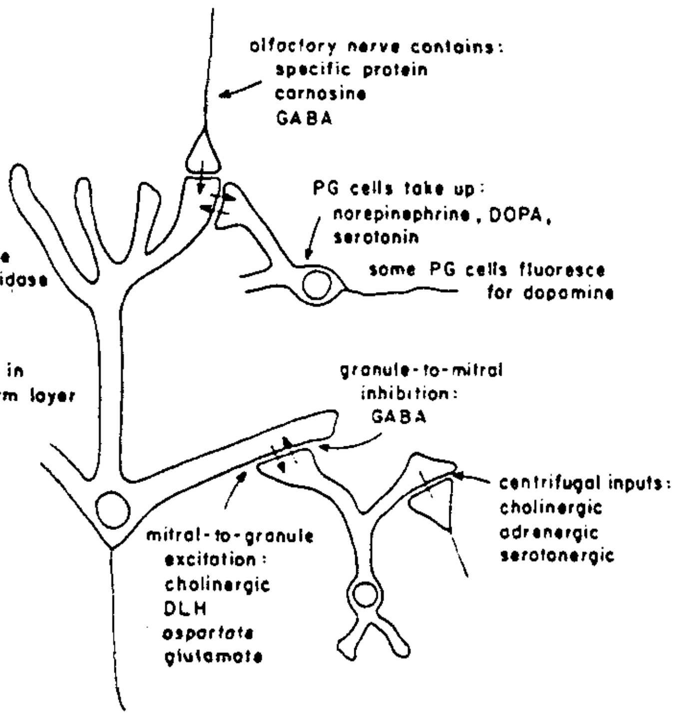


FIGURE 11 Summary of evidence for neurotransmitter substances in the olfactory bulb. For details see text. (Modified from Shepherd, 1977.)

T4

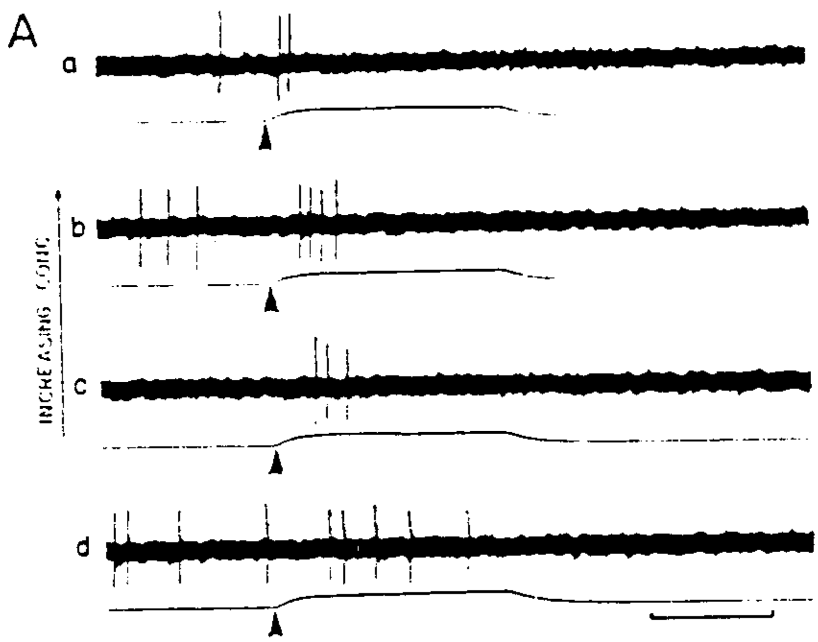


FIGURE 9. Extracellular unit responses in salamander olfactory bulb to odor pulse stimuli delivered to the olfactory mucosa. Lower traces are pulse monitors, with onsets indicated by arrows. Successive trials at increasing concentration as shown; test odor was amyl acetate. Time, 1 msec. (From Kauer and Shepherd, 1977.)

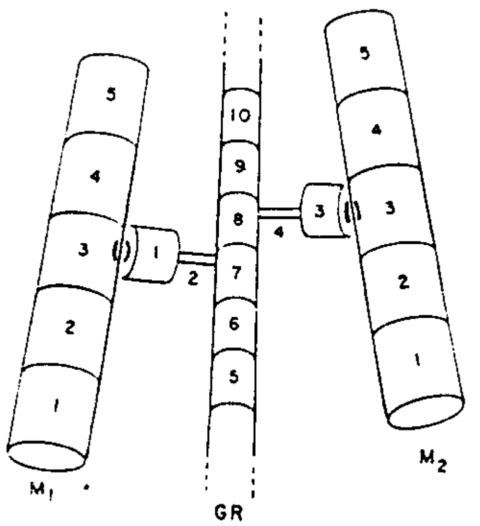


Figure 5 Compartmental model of dendrodendritic synaptic circuit, comprised of two mitral secondary dendrites (M_1 and M_2) and a branch of a granule-cell dendrite (GR) with two spines. Reciprocal synapses connect the spines to the mitral cells. The mitral dendrites are 4 μm in diameter; each compartment is 100 μm in length, with specific membrane resistance of 2,000 Ω-cm^2 and specific cytoplasmic resistance of 80 Ω-cm. For the granule-cell dendrite, the corresponding values are 4,000 Ω-cm^2 and 80 Ω-cm; compartments 5–10 are 1 μm in diameter and 50 μm in length; the spine necks (2 and 4) are 0.2 μm in diameter and 3 μm in length; the spine heads (1 and 3) are 1 μm in diameter and 3 μm in length.

T 6

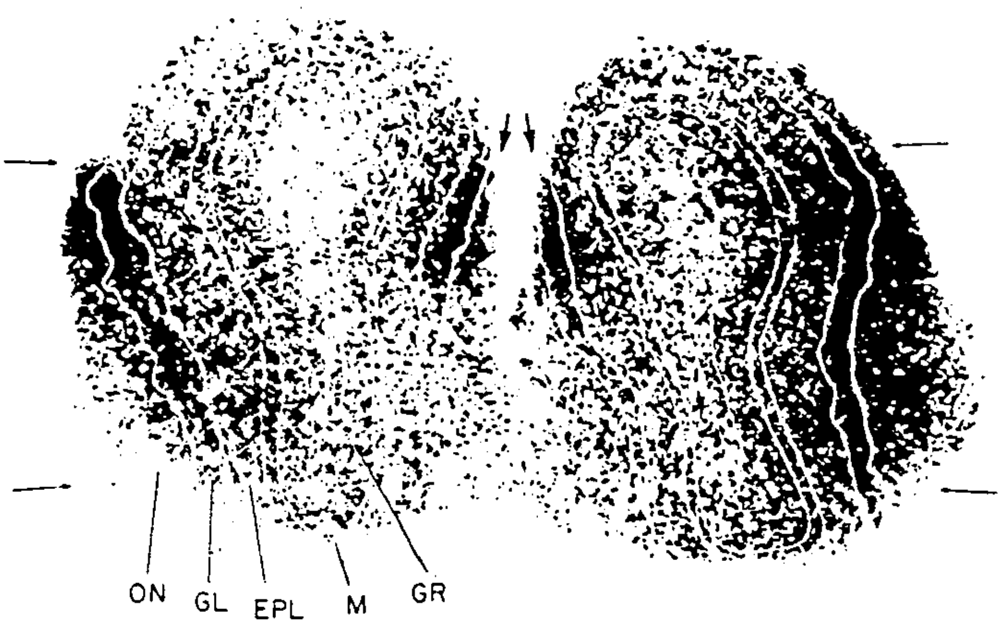


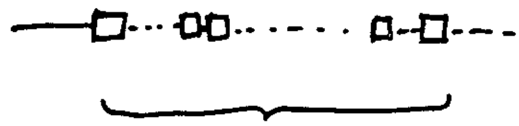
FIGURE 10 Autoradiograph of frontal sections of olfactory bulbs of a rat exposed to strong odor of amyl acetate. The outlines of the histological layers of the olfactory bulb, as determined from the subsequently stained sections, are shown superimposed on the autoradiographs. Small arrows indicate extent of lateral active regions; large arrows indicate medial active regions. Scale bar is 500 μm. (From Sharp, Kauer, and Shepherd, 1977.)

How do glomeruli project to cortex?
Spatial pattern? Distributed?

If glomerular connections are plastic, how about cortical connections?

IDENTITY ODOURS

Female mice distinguish the identity
T7 of individual mates by their odours.
T8 Pregnancy blocking
T9 Maze - learning
The individuality odour depends upon
the MHC region



over 50 MHC loci

- Tissue Transplants & Graft rejection
- Immune response
- olfactory indiv.

Congenic Strains

Is MHC product the individuality signal?
The microbial flora?

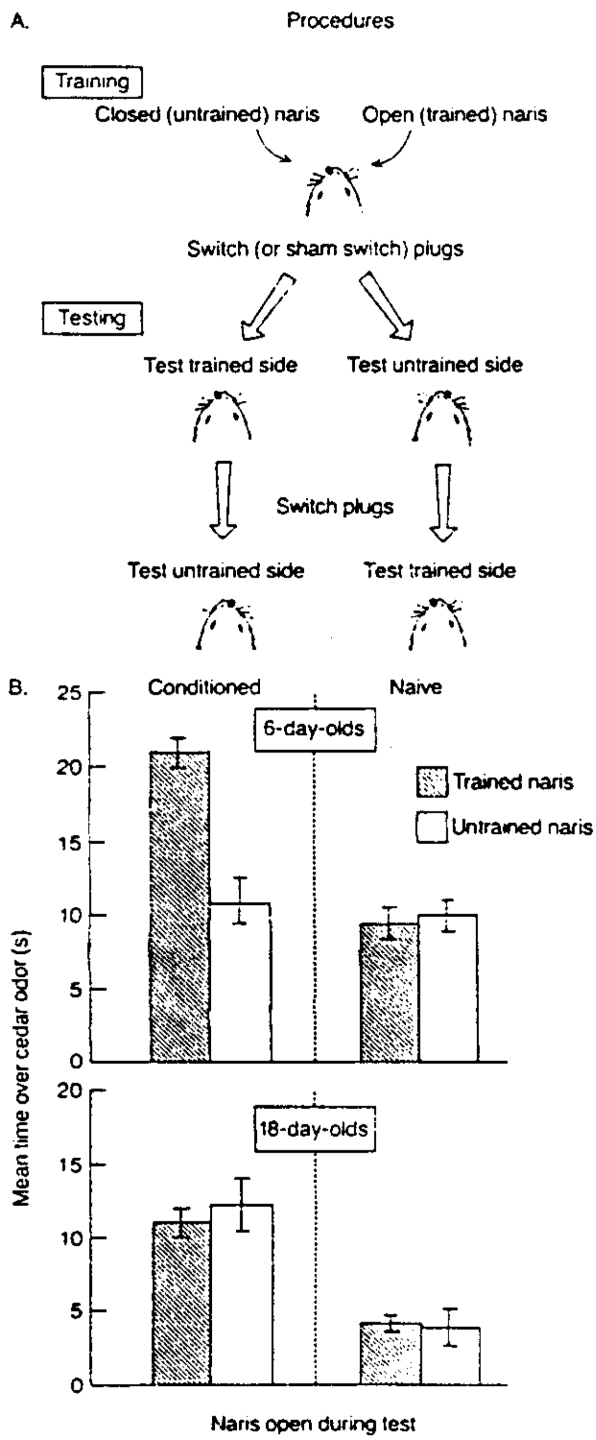
B. Roser, unpublished (Cambridge)
Beauchamp et al. Sci. Amer. 253-86
Yamazaki et al. Proc. Nat. Acad 83: 740

ODOUR IMPRINTING + PLASTICITY

T7 Imprinting of nipple odours
T8 Scent training and the critical period
T9
Glomerular changes?

M. Leon, (U.C. Irvine)
Trends in Neuroscience
10: 434-438

Fig. 1. **(A)** *Paradigm for unilateral early olfactory preference training.* **(B)** *Time over cedar odor for learning and control pups with their naris open during preference trials (trained or untrained) for 6-day-old (top) and 18-day-old pups (bottom).* (Taken, with permission, from Ref. 10.)



T8

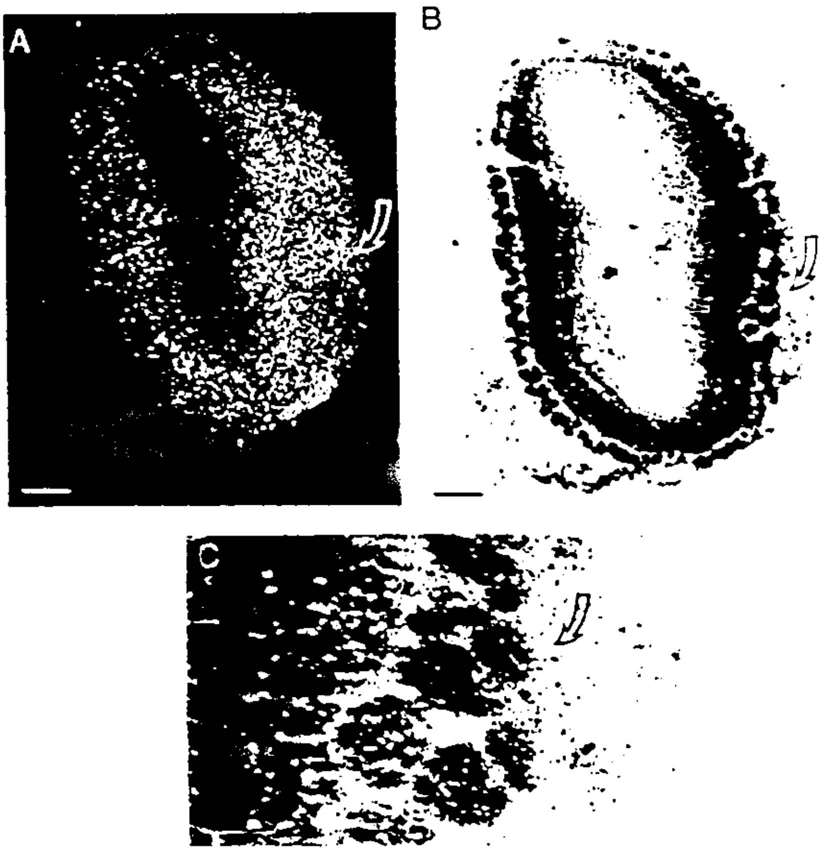


Fig. 2. (A) *Sample autoradiograph and* **(B)** *adjacent section stained for succinic dehydrogenase (SDH) from a pup that has acquired a preference for peppermint odor. Arrow in (A) points to a focus of 2-DG uptake, arrow in (B) points to corresponding glomerular cluster, determined by the alignment of adjacent sections. The enlarged glomerular cluster can be seen at higher magnification in* **(C)**. *Scale bar in (A) and (B) is 400 μm; in (C), 100 μm.* (Taken, with permission, from Ref. 18.)

Fig. 3.
(**A**) *Olfactory bulbs of pups that have been given preference training for peppermint odor just after being exposed to peppermint odor. The tissue has been stained for glycogen phosphorylase-a activity. Small arrows in (A) point to patches of staining in the internal plexiform layer, deep to the enlarged glomerular clusters.* (**B**) *Comparable areas in untrained pups exposed to peppermint odor. Scale bar is 100 µm.* (Taken, with permission, from Ref. 23.)