# WAM-BAMM '05

## Large-Scale Neural* Network Models

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* the real kind

# Outline

- Introductory remarks
- Goals of network modeling
- Problems with network modeling
- Some implementation issues
- Example: piriform cortex model
  - construction of the model
  - results/insights from the model
- Conclusions and future directions

# Non-outline

- This is not a hands-on tutorial on how to write GENESIS scripts to simulate your favorite neural network
- We will concentrate on "big picture" issues
  - without which, detailed tutorial is useless
- We will talk about the network modeling *process* as a whole
- But implementation issues will come up too

# What is a network model?

- Network models consist of
  - single neuron models (several kinds)
  - connections between them
  - inputs to a subset of the single neuron models from outside the network
  - some measurable outputs of the network model

# Goals of network modeling

- We want to figure out how the brain works
- The brain consists of a network of neurons
  - actually, a network of networks of neurons
    - or a network of network of network of neurons
      - ad nauseum
  - but let's not get carried away just yet
- Many people feel that networks are where *computations* really happen
  - and computation is what we're interested in

# Goals of realistic network modeling

- Lots of "high level" computational "neural network" models out there
  - most with only superficial relationship to biology
  - but many do interesting things nevertheless
- Realistic network models provide a reality check on such models
- Help to disprove bad theories
- And hopefully to suggest better ones

# Goals of realistic network modeling

- Some theorists are fond of saying "the details don't matter"
  - and point to *e.g.* thermodynamics as "proof"
- Network models offer a great way of showing them that the details often *do* matter
  - not that this will convince them

# Caveat

- Network modeling is a young field
- Only a handful of people have made large-scale network models with any claim to validity
- I've done one such model...
- ...which is approximately 1 more than most modelers
- ...but that doesn't make me an "expert"

# Problems with network modeling

- From The Hitchhiker's Guide to the Galaxy:

Space is big. Really big. You just won't believe how vastly hugely mind-bogglingly big it is. I mean, you may think it's a long way down the road to the chemist, but that's just peanuts to space.

# From our perspective...

- Network modeling is hard. Really hard. You just won't believe how vastly hugely mind-bogglingly hard it is. I mean, you may think it's a lot of work to get your 20-compartment pyramidal neuron model working, but that's just peanuts to network models.

# Why so hard?

- Why are good realistic *single neuron* models so hard to make?
  - need extensive data set
    - input data
    - morphology
    - passive dendritic response
    - details of dozens of active channels
    - Ca dynamics

# Why so hard?

- Why are good realistic *single neuron* models so hard to make?
  - need to build model
    - GENESIS, neuron, other simulator
  - need to parameterize neuron
    - not all parameters known from data
  - need to ask interesting questions of model

# For networks...

- All this is multiplied *at least* by the number of distinct kinds of neurons
- Plus some neurons are far less well characterized than others
  - pyramidal neurons (good)
  - aspiny inhibitory interneurons (bad)
- Not all neuron types for a given region are characterized at all or even known
  - Is the model doomed before even beginning?

# Connections

- And as if this wasn't bad enough...
- Need to accurately specify connections between neurons
  - connection densities
    - between different neuron types
    - between same type in different regions
  - connection strengths
  - delays (axonal and dendritic)

# Computational limitations

- Level of detail possible for single neurons simply infeasible for 1000 neuron network
  - not to say 1000000 neuron network
- Approximations *must* be made
- Do approximations throw baby out with bathwater?
  - probably
  - but maybe will put you on an interesting track

# Our approach

- Make as reasonable approximations as we can
- Don't expect model to be as true a representation of real situation as a good single neuron model
- Instead, use to explore space of possibilities in a *more* realistic context than abstract models

# Implementation issues (1)

- Good news: nearly any simulator can support construction of network models
- Just need pre- and postsynaptic mechanisms
  - *e.g.* spike generation and synapses
  - nearly always provided for you

# Implementation issues (2)

- GENESIS contains many commands designed to help you set up network models
  - volumeconnect, volumeweights, volumedelays
- I encourage you *not* to use them
  - even though I wrote most of them
- Instead, use power of script language to write equivalents yourself
  - far more flexible and almost as fast

# Implementation issues (3)

- Sometimes need to create custom objects
  - special inputs to network
    - see example later
  - special kinds of synapses
    - LTP
    - facilitation

# Example: Piriform cortex model

- GENESIS originally designed to enable construction of Matt Wilson's piriform cortex model
- Original model realistic for its time
  - but hopelessly abstract now
  - Much more data available now
    - at neuron and network levels
- New model is "second-generation" model

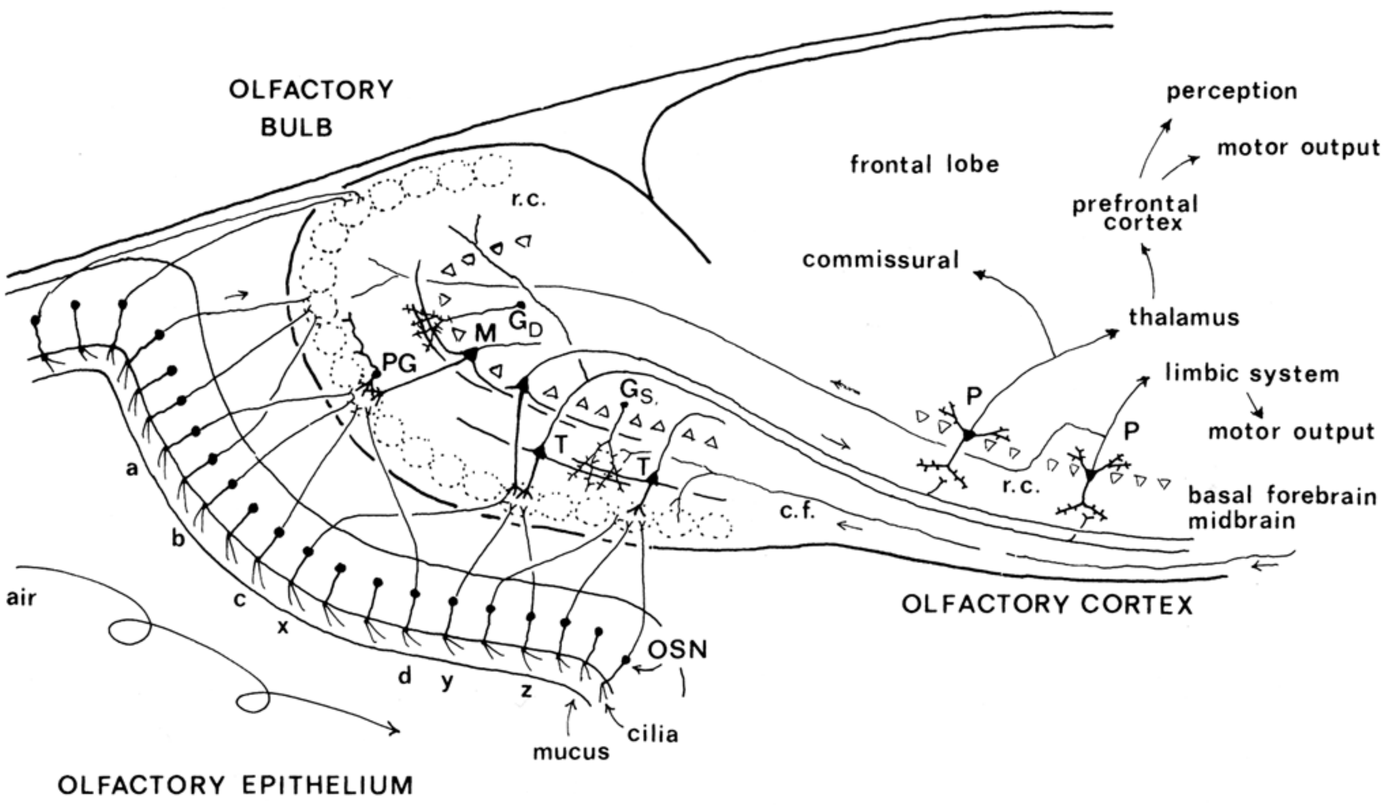
# Example: Piriform cortex model

- Piriform cortex = primary olfactory cortex
  - receives direct input from olfactory bulb
  - which receives direct input from olfactory sensory neurons
  - which receive direct input from odors
- We're already in trouble – can you guess why?
- Let's introduce the players first

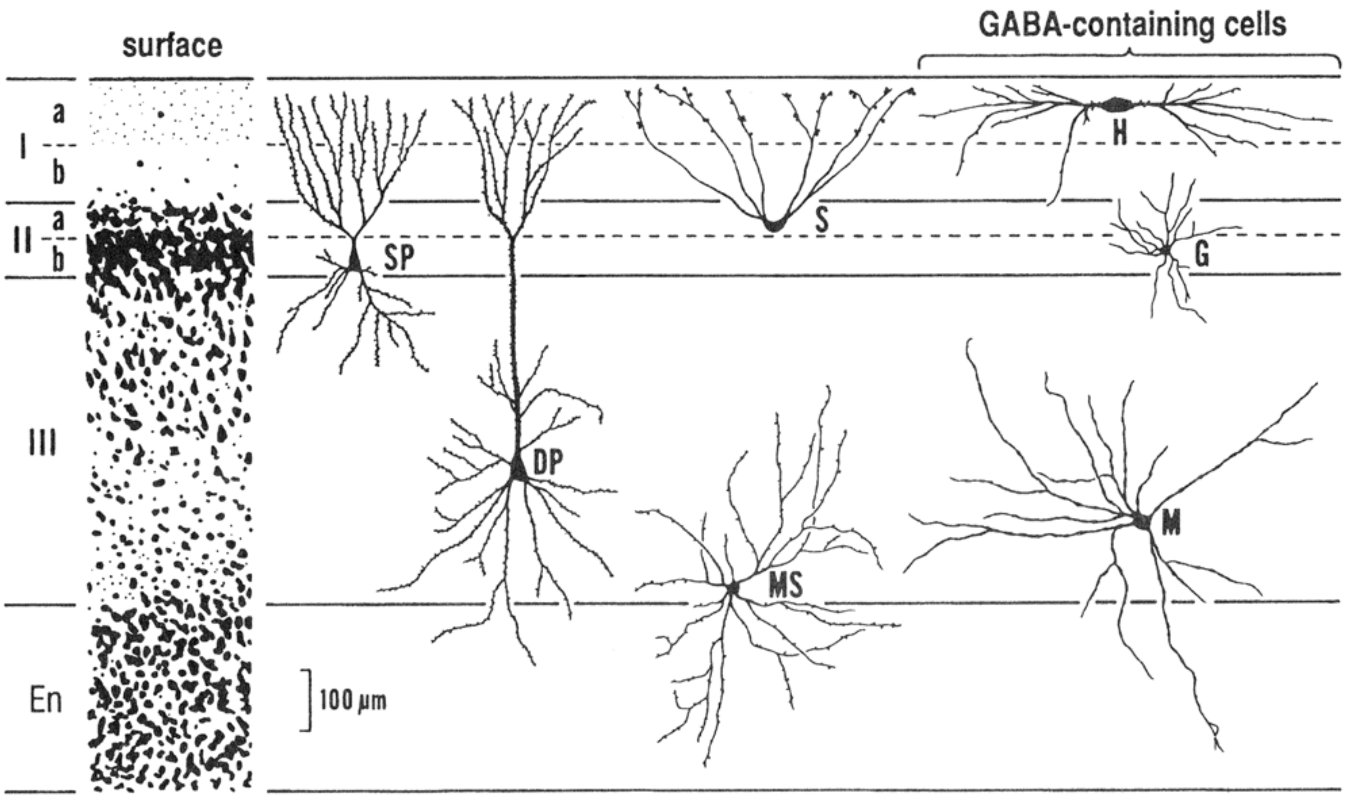
# Good news about piriform cortex

- Lewis Haberly has spent his life collecting amazingly detailed data about piriform cortex
  - anatomy of all major neuron types
  - connectivity studies
  - current-source density (CSD) studies
  - some single neuron physiology
- Without this, model would be pure guesswork

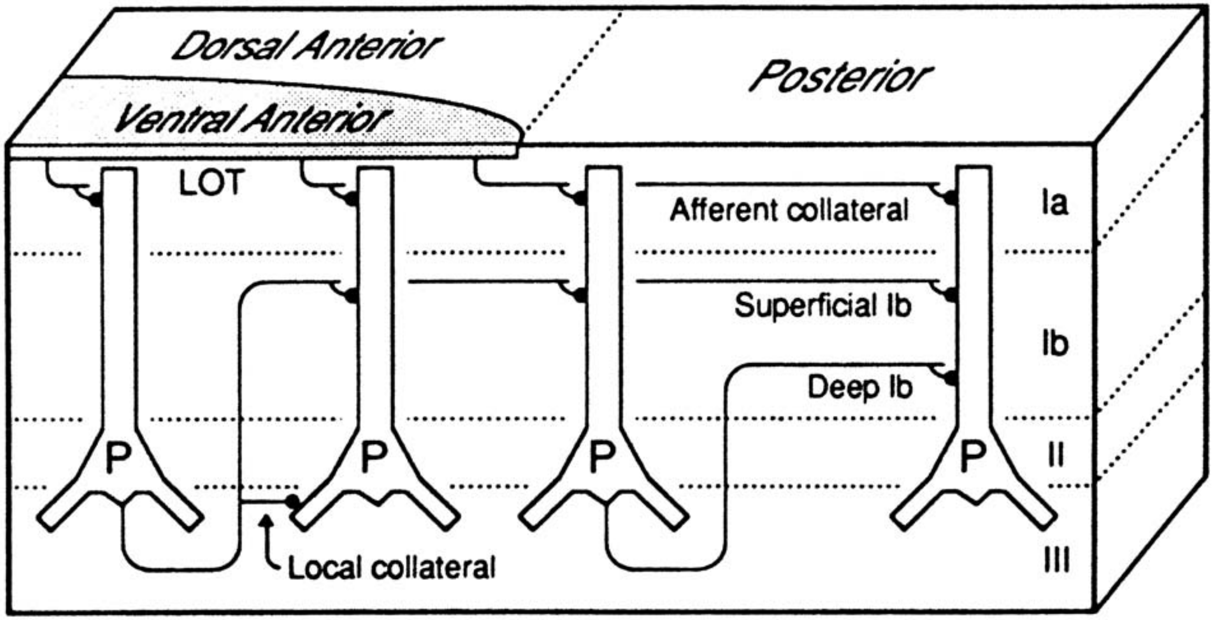
# Mammalian olfactory system



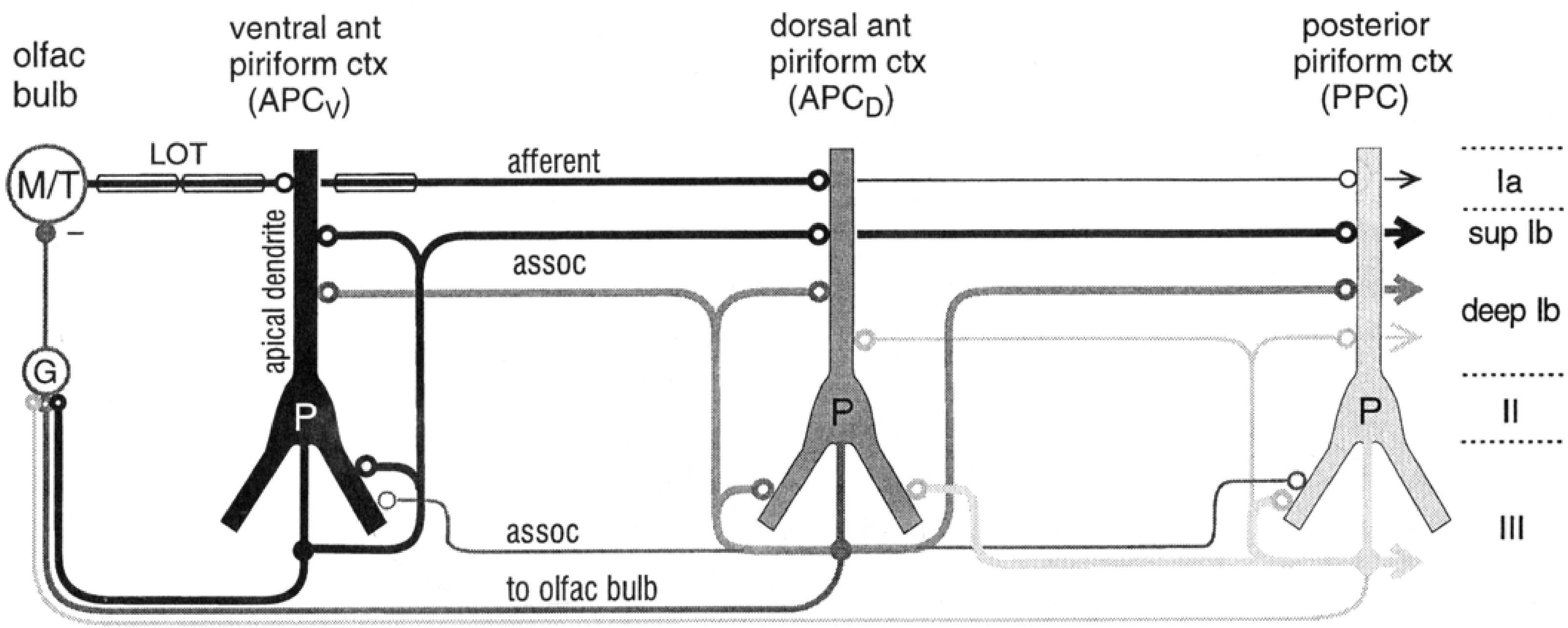
# Piriform cortex: neuron types



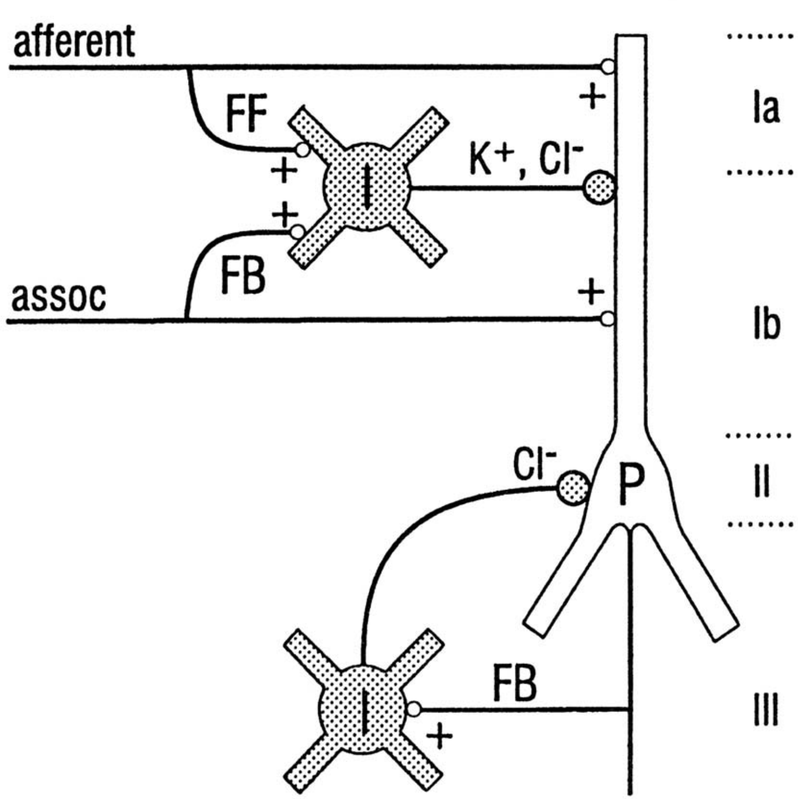
# Piriform cortex: subdivisions



# Piriform cortex: wiring



# Piriform cortex: wiring



# Inputs to piriform cortex

- Output of olfactory bulb is through *mitral cells*
- Their firing patterns in response to odors are a subject of huge debate
  - every experimenter seems to get different results
  - no obvious conclusions on what bulb does
- What to do?

# Inputs to piriform cortex model

- Two useful things:
  - 1) Response of piriform cortex to strong and weak electrical shocks to input fibers (LOT) is well known
  - 2) We had some recordings of mitral cells in awake behaving rats in response to odors
- Need to synthesize these to generate useful inputs
  - that don't depend on specifics of OB code

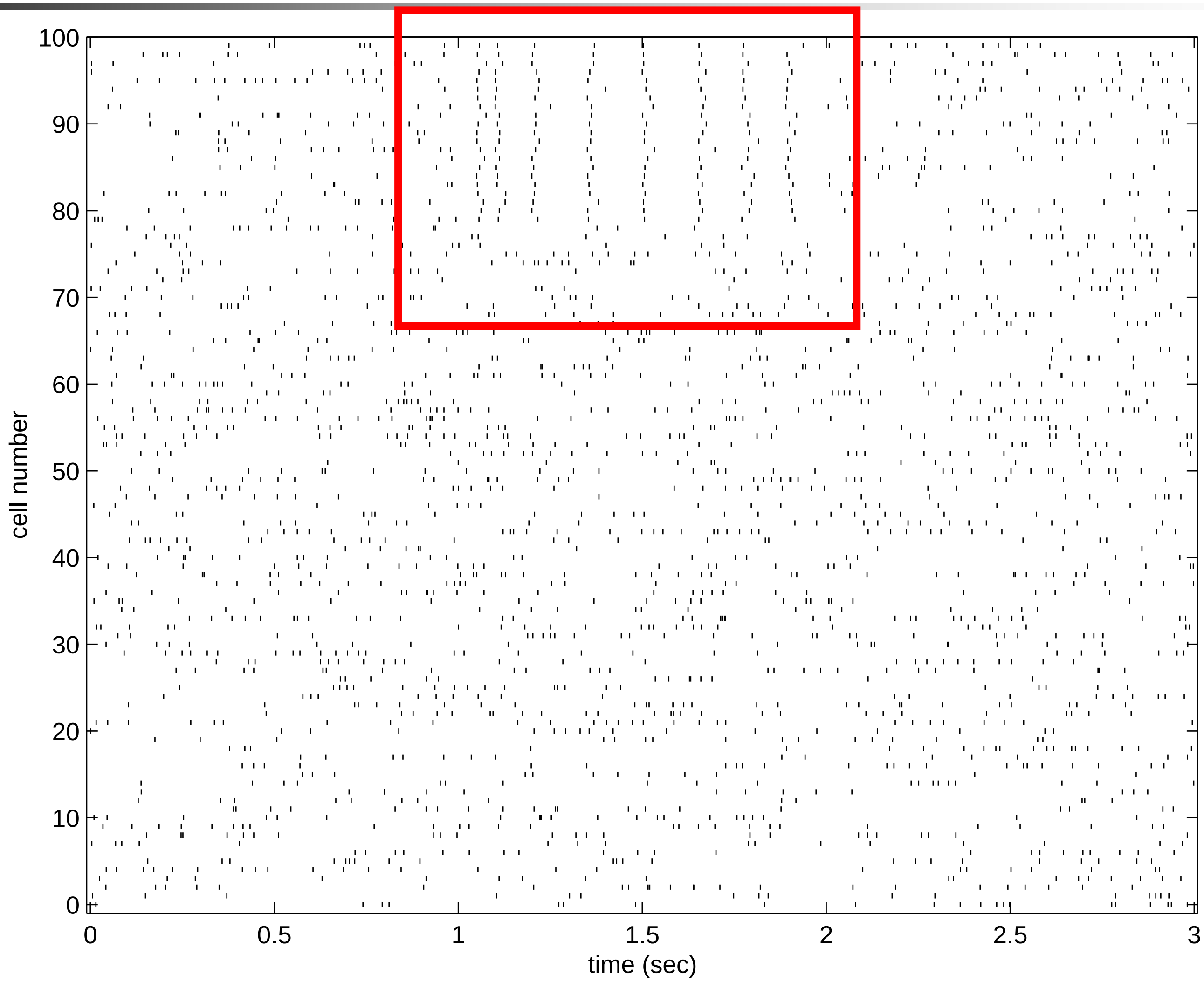
# Inputs to piriform cortex model

- Odor response of mitral cells is not obvious
- But background response is easily modeled by spike generating objects (Poisson process)
- And superimposing shock stimuli is easy
  - just make large number of mitral cells fire nearly simultaneously

# Inputs to piriform cortex model

- Therefore, I built a spike generating object
  - called `olfactory_bulb`
  - specific to this model only
  - can generate background firing patterns
  - can generate shocks with varying number of neurons involved
  - can do other things too (e.g. repetitive shocks)

# Inputs to piriform cortex model



# Outputs from piriform cortex model

- Assuming we have model, how do we validate it?
- Need some way of comparing its responses to the response of the real network
- For single neuron models, can compare
  - spike timings, interspike waveforms in response to current clamp inputs
  - responses to voltage clamp inputs
- What can we use for network models?

# Outputs from piriform cortex model

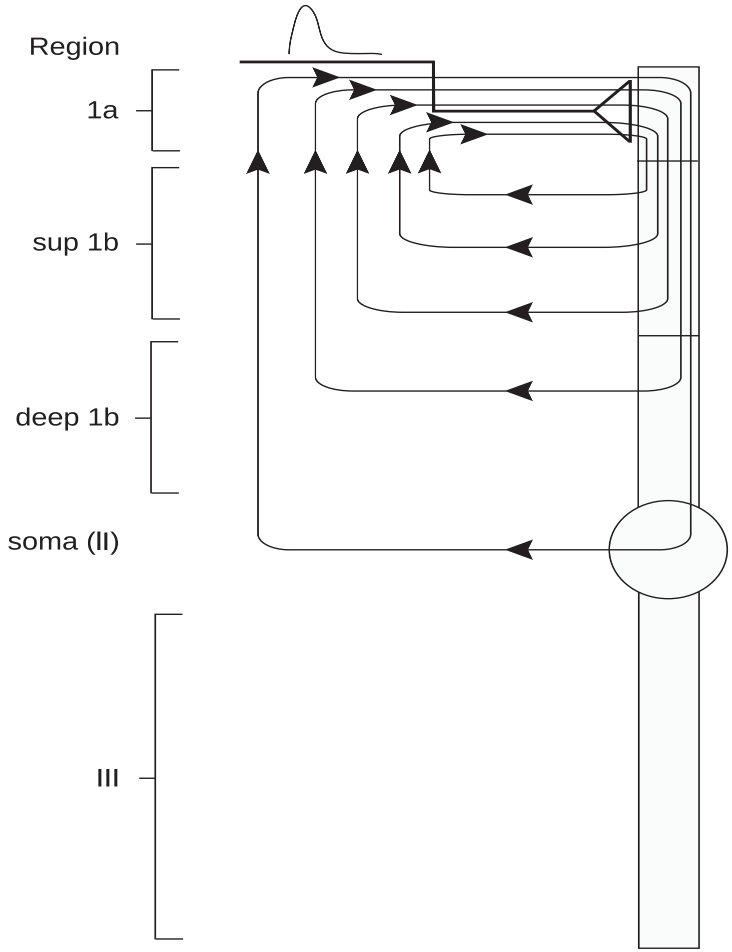
- Experimental network outputs may include:
  - single neuron recordings in awake behaving animals
  - single neuron recordings *in vitro*
  - EEGs
  - Current-source density (CSD) data
- For piriform cortex, have EEG and CSD
- CSD subsumes EEG, so just use that
- Very few awake/behaving single neuron recordings
  - (when this model was made)

# CSDs

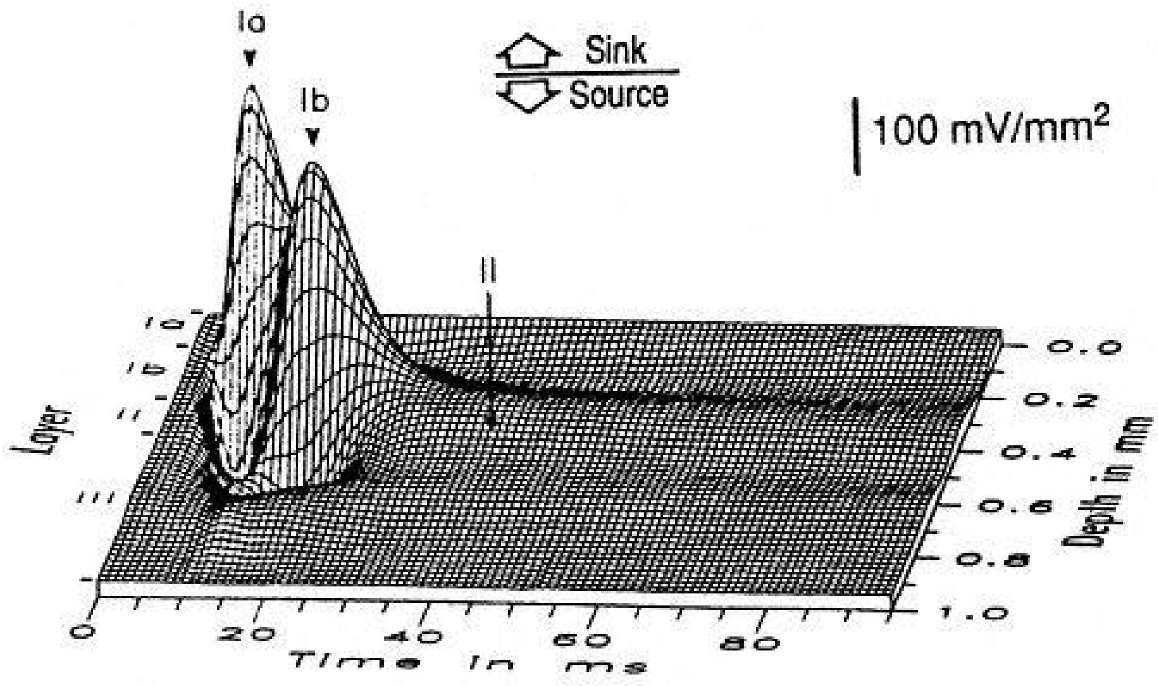
- Current-source density plots are like EEGs on steroids
- Monitor extracellular potentials in varying locations in brain during stimulus
  - Usually vary Z axis, fix X and Y
  - Here, stimulus is strong or weak shock
- Compute $d^2V/dz^2$ to get current sources over time at each Z location

# Outputs from piriform cortex model

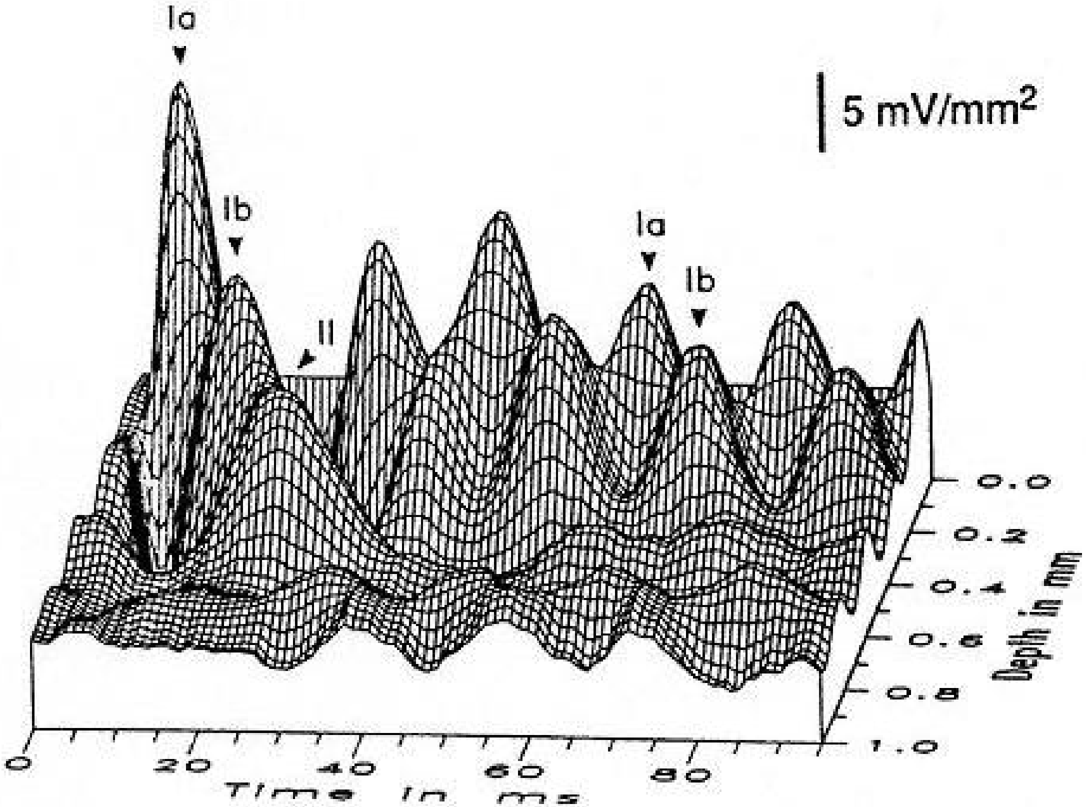
- Synaptic input in 1a causes
- current sink in layer 1a, leading to
- current sources elsewhere
- Similarly with synaptic input elsewhere in model



# Strong shock CSD response



# Weak shock CSD response



# Goals of modeling effort

- To reproduce intracellular responses to current injections
  - where available
- To reproduce these CSD responses
- To see if this tells us anything about computation

# Making the model: phase 1

- First need to build neuron models
  - pyramidal neurons: lots of data
  - inhibitory interneurons: very little data
  - other neurons: no data at all
- Approximations:
  - only 4 types of neurons
  - pyramidal + 3 inhibitory interneuron types
    - pyramidal: 15 compartments
    - interneurons: 1 compartment!

# Making the model: phase 1

- 15 compt pyramidal neuron model replicates current clamp data pretty well
- interneuron responses are fairly simple
  - so 1 compt model gives phenomenologically correct results
  - some experimental data used to constrain them
- Also a variety of synaptic data used to constrain model

# Making the model: phase 2

- Once neurons are there, wire them up
- Here Haberly data is invaluable
  - qualitative connection densities
  - axonal delay data from CSDs
- Still a LARGE number of parameters
  - hundreds

# Making the model: phase 2

- Have different scales of model
- 100 pyramidal neurons
  - + comparable # of inhibitory neurons
  - good for parameter explorations
  - too coarse for "realistic" behavior
- Could scale up to 1000 neuron model
  - beyond that, computers were too slow

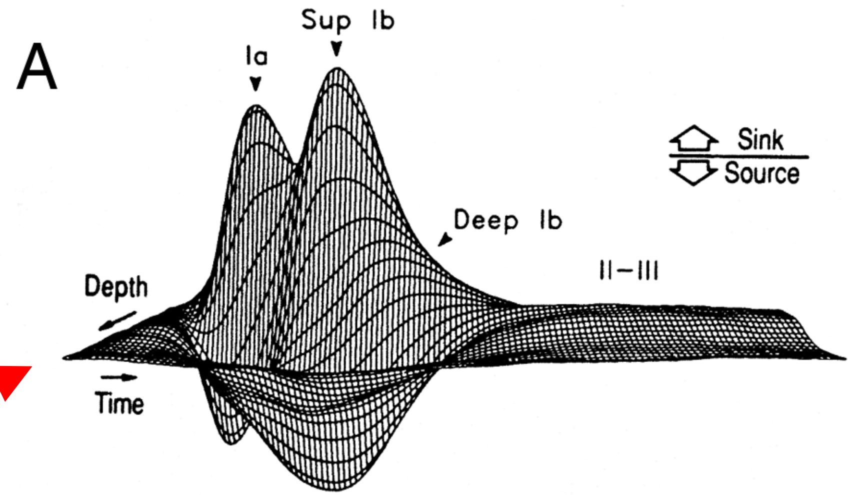
# Making the model: phase 3

- Add olfactory bulb inputs
  - background firing rates
  - + strong or weak shock
- Sometimes used repetitive shocks
  - one per sniff cycle

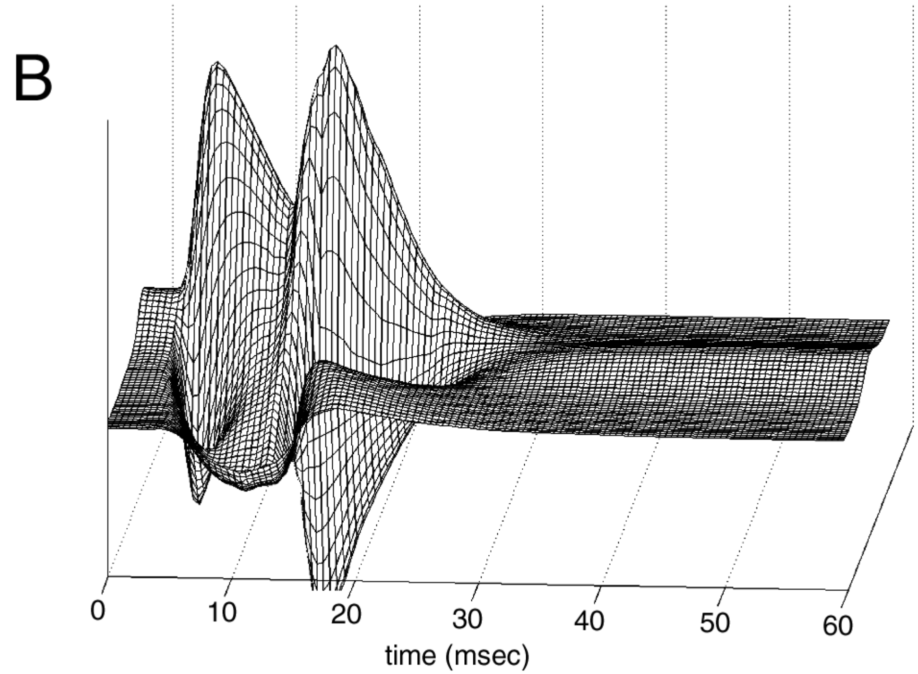
# Results of model

- Strong shock CSDs were not too hard to reproduce with reasonable accuracy
- Weak shock CSDs were found to be much harder to reproduce accurately
  - Was there something fundamentally wrong with model?
  - If so, what to do about it?

experiment



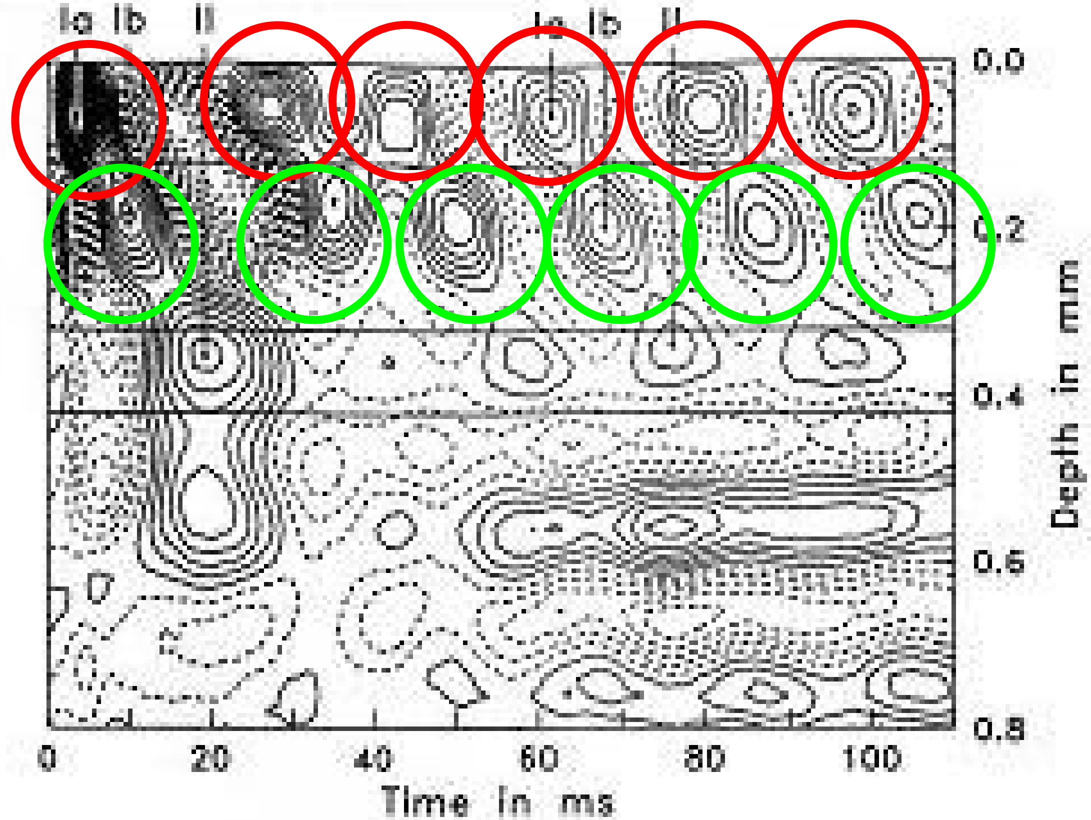

model



# Problems with weak shock results

- Assumptions:
  - 1) neurons wired together randomly
  - 2) oscillations in weak shock due to internal dynamics of cortex
- Leads to CSD results which cannot match data

# Problems with weak shock results



# Problems with weak shock results

- With random connectivity and high feedback
  - model originally had just one large peak in 1a
  - still get multiple peaks in 1b
- Multiple 1a peaks suggest OB is sending waves of input tied to sniff cycle
- Easy to model with OB spike generator
  - so I tried that

# Problems with weak shock results

- Still no good!
- Feedback from dorsal PC to ventral PC disrupts ordered pattern
- CSD data suggests that model is mainly feedforward
- OK, easy to turn down strength of feedback

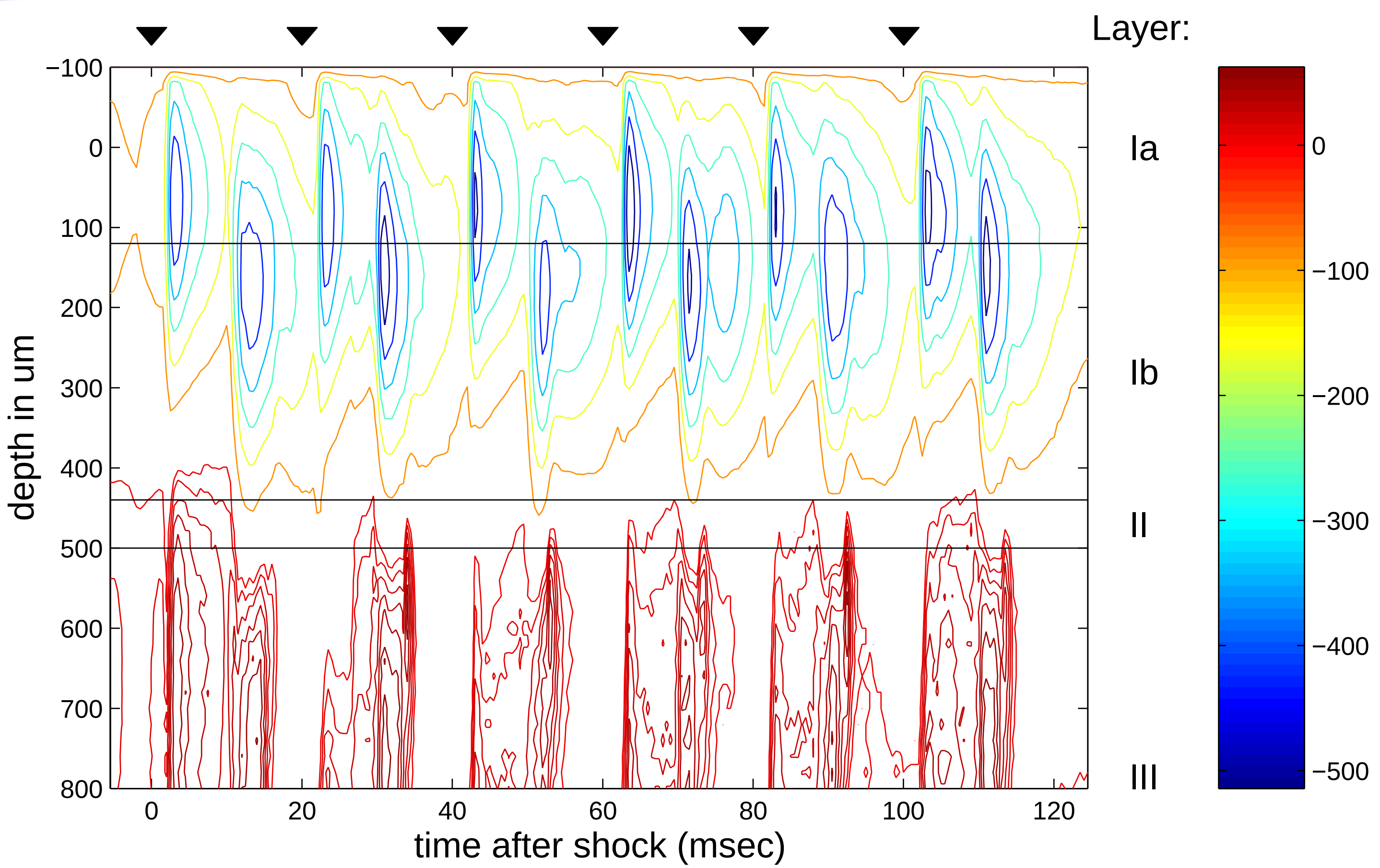
# Problems with weak shock results

- *Still* no good!
- Even small feedback disrupts pattern eventually
- But feedback known to exist
- Needed to question assumptions

# Resolution of weak shock problem

- I postulated a moderately radical concept
  - 1) Multiple semi-independent subnetworks in PC whose connectivities don't overlap
  - 2) Different subnetwork activated each sniff cycle
- Some anatomy supports this notion
  - but far from a mainstream idea!
- With this, get qualitatively correct weak shock CSDs
  - and new insight into possible function of PC

# Resolution of weak shock problem



# Conclusions

- Is my theory right?
  - probably not
  - but old theory probably wrong too
- Most important: model suggests ideas/experiments that would not have occured without model
  - and helps to discredit overly simplistic ideas

# Take home message 1

YOU DO NOT NEED A THEORY!

- "If you built it, [insights] will come."

# Take home message 2

- Don't expect a network model to be remotely definitive
- Expect it to be *suggestive*
- Aspire to "as accurate as possible"
- Don't throw away accuracy unless you have to

# Other take home messages

- Expect a lot of work and frustration
- Puts heavy demands on data set
  - boon for bored experimentalists!
- Puts heavy demands on computer power
- Requires lots of work on software
- Parameter searching problem is hard!
- But network modeling much more rewarding than single neuron modeling