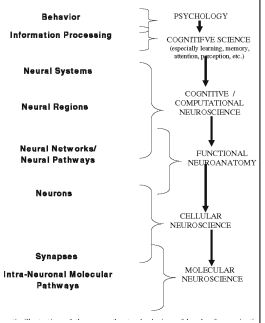
Reduction II: Ruthless and Mechanistic Reductionism

The Multiple Bridge View

- Bickle sets up as an alternative to his ruthless reductionism a perspective in which reduction must proceed step-by-step from each level to the one immediately below it
- Defenders of the theory-reduction view often focus on reduction to some basic level, but this is accomplished via a sequence of step-wise reductions
  - An important components of each step in the reduction is the role of boundary conditions which limit the context in which the lower-level laws give rise to the higher-level regularities
  - What happens to these on the ruthless account?



Clicker Question

What is Bickle's ruthless reduction alternative to the multiple bridge view?

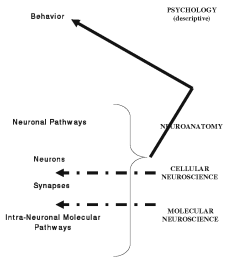
- Intervene behaviorally and track at the cellular/molecular level
- Intervene at the cellular/molecular level and track behaviorally
- Defend the claim that the behavioral level is autonomous from the cellular/molecular level
- Reduce theories at the behavioral level directly to theories at the cellular/behavioral level

Skipping the Intermediaries

- Bickle's ruthless reductionism cuts right through the intermediary levels to that of cell and molecular processes
- Strategy: Intervene at the molecular or cell level, detect effects at the behavioral level
  - "intervene causally at the level of cellular activity or molecular pathways within specific neurons (e.g., via genetically engineered mutant animals);
  - "then track the effects of these interventions under controlled experimental conditions using behavioral protocols well accepted within experimental psychology."
- "One only claims a successful explanation, a successful search for a cellular or molecular mechanism, or a successful reduction, of a psychological kind when one successfully intervenes at the lower level and then measures a statistically significant behavioral difference."

Skipping the Intermediaries

- "When this strategy is successful, the cellular or molecular events in specific neurons into which experimenters have intervened, ***in conjunction with the neuronal circuits in which the affected neurons are embedded***, leading ultimately to the neuromuscular junctions bridging nervous and muscle tissue, directly explain the behavioral data."



What Role for Higher Levels in the Brain?

- Servants of the cell and molecular level research. Useful to answer questions such as:
  - What are good experimental protocols for tracking behavioral outcomes for the psychological phenomenon we seek the cellular and molecular mechanisms of?
  - Where shall we begin making our cellular and molecular interventions? (The possibility space in both brains and intra-neuron molecular pathways is enormous!)
  - What kinds of neural activities seem to be involved? (Spiking frequency? Spiking pattern? Field potentials? Synaptic plasticity? This list only scratches the surface of possibilities, and each entry involves quite different molecular mechanisms.)
- These questions are (only) heuristic: they serve "the search for underlying cellular and ultimately molecular mechanisms."

Discussion Question

What motivates Bickle's contention that when one has successfully intervened at the cellular/molecular level and changed behavior, one has explained that behavior?

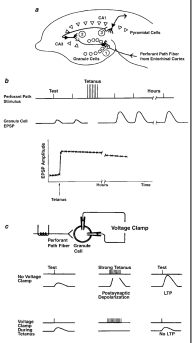
- If manipulations at the molecular level succeed in altering behavior, they must have affected something causally relevant
- Explanation should focus on the lowest level at which one can find causally relevant factors
- Higher-levels don't identify factors that can independently alter the phenomenon—they do so only by altering cellular and molecular factors
- Other

Contrast with the Theory Reduction Account

- On the theory reduction account, the goal was to recover the higher-level theory from the lower-level one
  - "On successful 'intervene molecularly and track behaviorally' reductions, explanations of behavior no longer appeal to features of higher levels (besides those of the functional neuroanatomy of the organism under investigation).
- The theory reduction view appealed to laws, generalizations, or model-theoretic components
  - But ruthless reductionism does not
    - Neither does cell and molecular neuroscience
- Theory reduction accounts aim at reducing to more general theories
  - Ruthless reduction only appeals to regularities in very restricted contexts

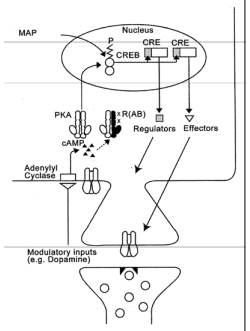
Case I: LTP

- Memory consolidation: When acquiring new information, organisms can retain it briefly in short-term/working memory, but for it to be maintained for longer periods it must be *consolidated* into long-term memory
- The discovery of long-term potentiation in cells in the hippocampus provided a candidate mechanism
  - Electric stimulation of neurons results in increase lasting for hours/days/weeks in excitatory post-synaptic potentials (EPSPs) to inputs on axons that synapse there
  - Ongoing theta (5-7 Hz) oscillations linked to LTP
    - They involve inputs on interneurons that project to the same synapse as the excitatory projection representing the stimulus and together provide the equivalent of the tetanus



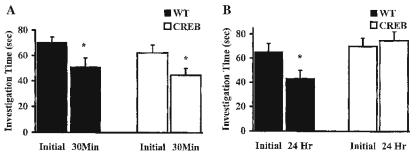
What Explains LTP?

- LTP itself is a cellular phenomenon involving changes in synapses
- Molecular processes in LTP have been identified
  - Dopamine from the interneurons primes Adenylyl Cyclase, which catalyzes reaction from ATP to cAMP
  - cAMP binds to regulatory subunits of protein kinase A (PKA)
  - PKA turns off inhibition of phosophorylated calcium-calmodulin kinase II (CaMKII), allowing it both
    - to bind to AMPA receptors so as to move them to the synapse and
    - to bind with cyclic AMP response element binding protein (CREB), which turns on gene expression needed to build new synapses



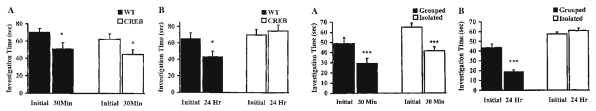
Case 2: Linking LTP to Memory

- Silva and colleagues have intervened in part of the LTP mechanism
  - Created knock outs of two isoforms of CREB by inserting a targeting vector into embryonic mouse stem cells which are transferred into blastocytes where they disrupt CREBαδ expression
- The interventions produce memory deficits
  - Long-term amnesia for social recognition without affecting initial learning or sort-term recognition memory involving associating a context with a shock
  - Recognizing a previous encountered individual after 24 hours--measured in reduction of time investigating that individual compared to a novel individual



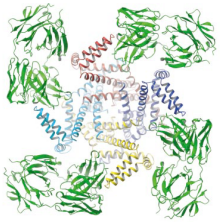
Comparison with Behaviorally-induced Deficit

- Rearing mice in socially isolated environments for three weeks prior to experiment produced the same result
  - "This raises the intriguing possibility that CREB α and δ isoform availability in various neurons is a molecular mechanism through which a cause as "high level" and "external" as a mammal's environmental interactions with conspecifics affects a central kind of cognition and behavior (social recognition memory).
- Note: the fact that two interventions have comparable effects does not show that they are produced in the same way



How Far Down Should the Reductionist Go?

- As far down as researchers can intervene directly and produce changes in the phenomenon to be explained
- We are already in the early days of "intervene biophysically and track behaviorally"
  - Tools such as nuclear magnetic resonance imaging is making it possible to image the structure of proteins
  - Proteins have "active sites" at which they mind substrates and catalyze reactions
  - The overall structure of proteins is continuously changing, and this often affects the ability of molecules to bind to the active sites
  - In many areas of biology, one can identify structural changes that affect the phenomenon of interest



Voltage-dependent potassium ion (K^+) channel

Clicker Question

What is the major point on which mechanistic reduction differs from ruthless reduction?

Mechanistic reduction rejects the value of investigations at the cellular/molecular level

Mechanistic reduction emphasizes the importance of identifying the full mechanism responsible for the phenomenon

Mechanistic reduction doesn't appeal to the behavioral level to track the effects of lower-level interventions

Mechanistic reduction does not focus on theories as the units to be reduced

Mechanistic Explanation: A Review

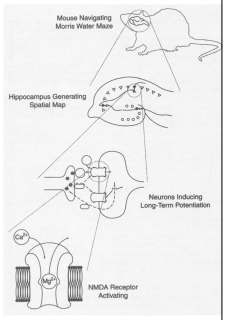
- A mechanism is "a structure performing a function in virtue of its components parts, component operations, and their organization"
- An important part of mechanistic research is decomposing the mechanism--identifying its parts and determining what operations they perform
  - The emphasis on taking a mechanism apart into its parts and operations is reductionistic
    - Moreover, it is a process that can be iterated by decomposing the parts themselves to explain how they perform their operations
- But equally important to mechanistic research are
  - Recomposition--figuring out how the parts fit together so that the operations can work together to generate the phenomenon
  - Situating--relating the mechanism to the various factors in its environment that impact on its functioning

Similarities with Ruthless Reduction

- Like ruthless reduction, mechanism does not focus on laws but on parts of the system that are responsible for operations involved in generating the phenomenon
  - They are both therefore contrasted with theory-reduction accounts
- Both maintain that testing hypotheses often involves manipulating a part within the mechanism and observing an effect on the behavior of the whole
- Mechanistic reduction agrees with ruthless reduction that there are times when pursuing the explanatory process down to the molecular (or even the biophysical) level is appropriate
  - For mechanism the goal is not to go to the lowest level for its own sake but because it can answer questions about how the phenomena are produced

Differences Between Mechanistic and Ruthless Reduction

- On the mechanistic account, explanation of a given phenomenon aims at identifying all the parts and operations that interact to produce the phenomenon
  - This requires identifying productive continuity between the operations of the different parts
- In many cases the entities identified by ruthless reduction in explaining cognitive activities such as learning are multiple levels below the parts and operations of the initial mechanism
  - They are not directly the parts of the mechanism that are, when properly organized, produce the phenomenon
  - Rather, they are parts of another mechanism that is responsible for one of the component operations of the first mechanism (or of some mechanism further down)
- On the mechanistic account, one can iterate the process of decomposition, but then one is treating the operation of the part as the phenomenon to be explained



The Importance of Recomposition on the Mechanist's Account

- To understand the phenomenon, mechanistic explanation requires showing how the operations of the various parts can actually realize the function
  - Researchers need to show that carrying out the different operations suffices to realize the phenomenon
    - They often do this in computational models that specify each of the operations and their relations to others
  - Researchers aim for an with an account that exhibits productive continuity
- Ruthless reduction only seeks to show that the part in question does affect the phenomenon
  - It neither seeks to recompose the mechanism nor to identify the productive continuity between the operations of the parts
    - Accordingly, it can easily lead to over stating what the components identified actually contribute to the phenomenon

Discussion Question

What would researchers find it valuable to recompose a mechanism?

They wouldn't. Ruthless reduction is all they need

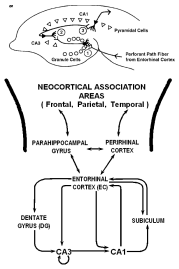
Only if they can recompose a mechanism that is productively continuous can they have confidence they have accounted for the phenomenon

If one can recompose a mechanism, then one is in position to build a system that produces the same phenomenon

By recomposing the mechanism one may learn of many other parts through which one can productively intervene on the mechanism (or treat broken mechanisms)

From LTP Back to the Whole Hippocampus

- To learn new memories, it is essential
  - To recognize when a stimulus is another instance of one that has already been learned
    - Requires recurrent connections so as to have a network with attractors
  - To learn to respond differently to a different stimulus, one must differentiate the new inputs from the previous ones
    - Requires sparse coding that separates the inputs
- Different parts of the hippocampus appear suited for these different tasks
  - The Dentate Gyrus provides sparse coding
  - The CA3 fields have large number of recurrent projections that generate attractors
- Rolls recomposed this network in a computational simulation and showed it would exhibit the desired behavior
  - This moves up from the molecules to the organized network in the hippocampus



The Hippocampus Is Just Part of the Higher-Level Mechanism

- McGaugh showed that other structures, such as the amygdala are important for memory consolidation
  - Agonists to the β-Adrenergic receptor on the amygdala can enhance memory
  - Antagonists to the receptor block the ability of dexamethasone to enhance memory
- McGaugh concludes "It is clear from these findings that memory consolidation involves interactions among neural systems, as well as cellular changes within specific systems, and that amygdala is critical for modulating consolidation in other brain regions"

Extended Consolidation

- Hippocampal lesions produce both anterograde and extended retrograde amnesia extending back months to years before the lesion
- Most researchers assume that long-term memories are eventually encoded in a distributed fashion in the cortex
  - Extended training of cortex may contribute to development of memories that are not readily overwritten with the next event
- During parts of sleep without rapid eye movements (hence, non-REM sleep), new LTP is blocked but previous LTP is maintained
  - May figure in the gradual training of cortex
    - McNaughton and collaborators have shown synchronous firing during maze-learning and during non-REM sleep and suggest that the latter may be important for memory consolidation

Memory Must Be Reconsolidated

- When a memory is recollected, it must be reconsolidated or it will be forgotten
- This phenomenon was discovered in the 1960s in the heyday of electroshock therapy
  - Electroshock administered in conjunction with a second foot shock 6 or 24 hours after an initial one eradicated the learning associated with the first shock
  - Similar effects produced by a protein synthesis inhibitor
- Also possible to enhance memory after recall with electrical stimulation of the mesencephalic reticular formation (same as effect if applied during learning episodes)
- Research on molecular mechanisms led to neglect of these findings but in the last decade they have again become the focus of research
  - Memories may be surprisingly labile after recall
- Mechanism of reconsolidation appears to be similar to that of consolidation, but to involve different brain regions--further expanding the network of brain regions involved in memory

The Scope of the Memory Consolidation Mechanism

- Much more is involved in memory consolidation than synthesis of new receptors in regions of the hippocampus
  - Network of neurons with different patterns of connectivity
  - Structures such as the amygdala, cortex, and whatever is required for reconsolidation
- Mechanistic research, which emphasizes recomposition of the mechanism, is geared towards finding these additional components whereas ruthless reduction is not