Making Your Mind: Molecules, Motion, and Memory
2008 Holiday Lectures on Science
Chapter List

Lecture One
Mapping Memory in the Brain
Eric R. Kandel, M.D.

1. Start of Lecture 1
2. Welcome by HHMI President Dr. Thomas Cech
3. Profile of Dr. Eric Kandel
4. The brain: Learning and memory
5. The devastation of learning and memory disorders
6. Video: Clive Wearing, a man without memory
7. The systems problem of memory: Where is memory stored?
8. Gall's insights into the brain
9. An overview of brain structure
10. Gall localizes brain functions based on skull shape
11. Demonstration: Phrenology
12. Broca challenges Gall's theory by studying brain function
13. Broca studies aphasia to localize language in the brain
14. Localizing brain areas that control motor functions
15. Wernicke: Complex brain functions are not in a single area
16. Location of language areas suggests a model of language
17. Wernicke's language model predicts a conduction aphasia
18. Video: A patient with conduction aphasia
19. Left brain and right brain language functions
20. MRI identifies brain areas for recognizing faces
21. Q&A: Do basic brain functions reside deeper in the brain?
22. Q&A: Is there a correlation between brain size and intelligence?
23. Q&A: How is the brain organized in bilingual people?
24. Lashley's experiments cast doubt on memory localization
25. Penfield finds memories are localized in human brains
26. The patient H.M. loses memory after brain surgery
27. Brenda Milner finds H.M. retains some memory functions
28. H.M. unable to convert short-term to long-term memory
29. Mirror tracing: H.M. can unconsciously learn new tasks
30. Student results of mirror tracing activity
31. Different mechanisms for explicit vs. implicit memory
32. Video: Clive Wearing plays piano despite memory deficit
33. Summary
34. Q&A: Did H.M. show any capability of emotional response?
35. Q&A: Are stem cells involved in implicit memory storage?
36. Q&A: Can brains compensate for a lesion?
37. Closing remarks by HHMI President Dr. Thomas Cech

Lecture Two
Building Brains: The Molecular Logic of Neural Circuits
Thomas M. Jessell, Ph.D.

1. Start of Lecture 2
2. Welcome by HHMI Vice President Dr. Peter Bruns
3. Profile of Dr. Thomas Jessell
4. Assembly of neural circuits and behavior
5. Human development from egg to adult
6. Comparing the brain to a cell phone
7. Zooming in on circuits and single neurons
8. Synapses are the points of communication between neurons
9. Animation: Molecular mechanism of synaptic function
10. How do neurons differentiate during development?
11. Animation: Development of the human embryonic brain
12. Specific genes control early patterns of brain development
13. A young neuron's location determines its ultimate identity
14. Animation: Signal molecules trigger transcription factors
15. Studying simple motor circuits in the spinal cord.
16. Motor neuron type derives from position in the neural tube
17. Sonic hedgehog (SHH): an important signaling molecule
18. Eye position depends on SHH signaling
19. Demonstration: SHH concentration and eye position
20. Blocking SHH signaling can create a cyclops
21. Q&A: Do signal molecules have to be present throughout cell life?
22. Q&A: Can cell type be changed after initial signaling?
23. Q&A: How do cells secrete the correct amount of signal?
24. Demonstration: The electrical activity of Dr. Jessell's arm
25. Neurons use growth cones to find partner cells
26. Video: Growth cones in action
27. Neuronal pathways are like a subway system
28. Video: Long-distance neuronal path-finding
29. Neuronal path-finding by attraction and repulsion
30. Video: Contact repulsion of a growth cone
31. Repellant cues and motor neuron path-finding
32. Animation: Repellant ephrin signals guide limb innervation
33. Finding the right partner in a very crowded brain
34. Binary choices produce specific neuronal connections
35. Gene knock-outs reveal importance of repulsive signals
36. Some synapses are stabilized and others eliminated
37. Synaptic stabilization proteins implicated in autism
38. Summary
39. Q&A: What causes synaptic elimination?
40. Q&A: Connection between synapse activity and intelligence?
41. Q&A: When does most axon formation occur in development?
42. Closing remarks by HHMI Vice President Dr. Peter Bruns

Lecture Three
Making Your Mind: Molecules, Movement, and Memory
Thomas M. Jessell, Ph.D.

1. Start of Lecture 3
2. Welcome by HHMI President Dr. Thomas Cech
3. Profile of Dr. Thomas Jessell
4. Neural circuits: Controlling behavior, particularly movement
5. Video: Computer analysis of human movement
6. Damage to motor systems by disease and injury
7. Motor neurons get input from multiple sources
8. The proprioceptive sensory feedback system
9. Demonstration: Testing a student's proprioceptive reflex
10. Diagram showing the knee-jerk reflex circuit in action
11. Proprioception is a subtle "sixth sense"
12. Demonstration: Proprioception makes raising a mug easy
13. Video: Without proprioception, standing or raising a mug is hard
14. Genetically killing proprioceptive neurons in mice
15. Video: Behavior of mice that lack proprioception
16. Mice lacking proprioception have irregular muscle activity
17. The role of interneurons in controlling motor patterns
18. Video: Walking versus hopping
19. Video: Dr. Jessell's muscle activity when he hops or walks
20. The role of inhibition from the opposite side for walking
21. Video: Mutant mice lacking crossed inhibition hop
22. Reactivating damaged interneurons using sensory stimulation
23. Q&A: Do organisms that change gait have multiple interneurons?
24. Q&A: How do muscle spindles sense contraction?
25. Q&A: How does polio cause paralysis?
26. Q&A: Are proprioceptive signals also sent to the brain?
27. Hearing and vision also control motor behavior
28. Video: Ian Waterman—vision compensates for proprioceptive loss
29. Demonstration: Touching thumb to fingers using proprioception
30. Video: Waterman touching thumb/finger without visual feedback
31. Functional MRI localizes brain activity during touching task
32. Demonstration: Using spatial memory to clear an obstacle
33. Analyzing a cat's ability to remember obstacle location
34. Video: Cat remembers obstacle location for many minutes
35. Animation: Neurons in parietal cortex are active during straddling
36. Quantifying neuronal activity in Area 5 parietal cortex
37. Inputs to motor neurons can compensate for one another
38. Compensating for loss of motor neurons due to ALS
39. Using stem cells to create new motor neurons in mice
40. Using skin cells to make patient-specific stem cells
41. Summary
42. Q&A: Does proprioception compensate for vision in blind people?
43. Q&A: Is all neuroscience research targeted to diseases?
44. Q&A: Is ALS inherited?
45. Q&A: What is the mechanism behind phantom limb pain?
46. Q&A: Are motor neurons responsible for muscle atrophy in space?
47. Closing remarks by HHMI President Dr. Thomas Cech

Lecture Four
Memories Are Made of This
Eric R. Kandel, M.D.

1. Start of Lecture 4
2. Welcome by Grants Program Director Dr. Dennis Liu
3. Profile of Dr. Eric Kandel
4. Review of the systems problem of memory
5. Comparing implicit and explicit memory for molecular analysis
6. Selecting a model to study the molecular basis of memory
7. Demonstration: Meet a live *Aplysia californica*
8. *Aplysia*'s simple nervous system makes experiments easier
9. *Aplysia*'s gill-withdrawal reflex shows learning
10. *Sensitization*: A form of learned fear
11. Video: *Aplysia*'s gill-withdrawal reflex and sensitization
12. *Aplysia* long-term memory depends on protein synthesis
13. The neural circuit controlling gill withdrawal
14. Temporary changes to the circuit vs. anatomical changes
15. Simplifying the learning circuit in a culture dish
16. Animation: Molecular activity in *Aplysia* short-term memory
17. Animation: Molecular activity in *Aplysia* long-term memory
18. Gene expression, long-term memory, and autism
19. Synaptic growth from learning in *Aplysia* and humans
20. Q&A: Are new connections added only to existing partners?
21. Q&A: Do neurons vary in the ability to create new connections?
22. Spatial learning and explicit memory storage in mice
23. Video: Mice navigate a Barnes maze to test spatial learning
24. Hippocampal circuits involved with explicit memory
25. Long-Term Potentiation (LTP): a form of hippocampal memory
26. Animation: Molecular basis of early LTP (short-term memory)
27. Animation: Molecular details of late LTP (long-term memory)
28. PKA-deficient mutant mice have a reduction in late LTP
29. The PKA-mutant mice perform poorly in the Barnes maze
30. Summary of the contribution of molecular analysis to memory
31. Aging, memory loss, and Alzheimer disease
32. The Alzheimer associated Aβ peptide is toxic to neurons
33. Aβ protein shuts down PKA activation
34. Lowering cAMP breakdown activates PKA, reverses synapse loss
35. Alzheimer mice increase synaptic connections after Rolipram
36. Summary
37. Q&A: Is serotonin being used to enhance memory?
38. Q&A: How does Aβ spread throughout the brain?
39. Q&A: What accounts for varying memory abilities?
40. Q&A: Can repetition improve social interactions in autism?
41. Closing remarks by HHMI President Dr. Thomas Cech