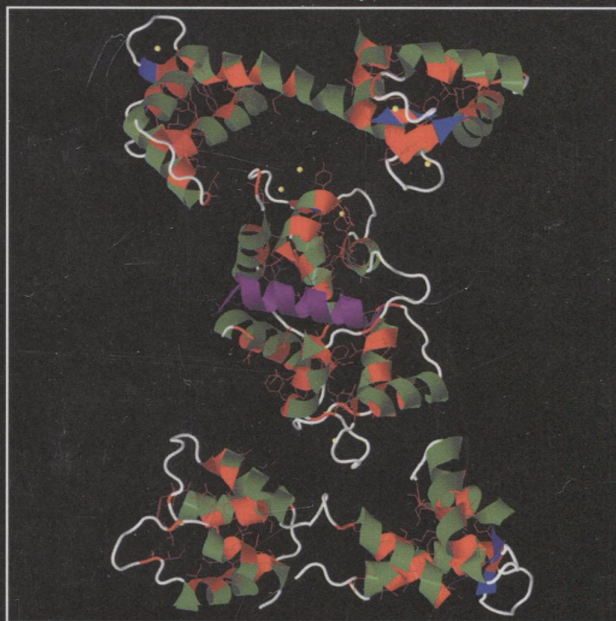


## About the Cover

The bottom structure on the cover shows the NMR structure of *apo-calmodulin*: a loosely folded, small flexible protein that modulates cellular calcium signaling. Alpha-helices are in green, beta sheet in blue, and hydrophobic amino acids (and their sidechains) in red.

When calmodulin binds four calcium ions (yellow), it undergoes a conformational change to the X-ray structure on top. The helices in the N-terminal (left) and C-terminal (right) domains are linked by a long flexible helix. The smaller helices within each domain move relative to each other to give two 'hands.' The 'palms' of both hands are lined with red hydrophobic residues. The left hand is turned toward us; the right hand away. The calcium ions bind to the 'knuckles.'

The calcium-activated calmodulin binds to an enzyme, shown in purple (middle). The long helix uncoils, allowing each 'hand' to grasp one side of the purple helix, activating the kinase enzyme. This enzyme makes up to 2% of the protein in the brain and is responsible for long-term memory.



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<b>Chapter 1</b>	Introduction	1
<b>Chapter 2</b>	The First Law: Energy Is Conserved	13
<b>Chapter 3</b>	The Second Law: The Entropy of the Universe Increases	55
<b>Chapter 4</b>	Free Energy and Chemical Equilibria	101
<b>Chapter 5</b>	The Statistical Foundations of Biophysical Chemistry	151
<b>Chapter 6</b>	Physical Equilibria	196
<b>Chapter 7</b>	Electrochemistry	238
<b>Chapter 8</b>	The Motions of Biological Molecules	264
<b>Chapter 9</b>	Kinetics: Rates of Chemical Reactions	305
<b>Chapter 10</b>	Enzyme Kinetics	378
<b>Chapter 11</b>	Molecular Structures and Interactions: Theory	408
<b>Chapter 12</b>	Molecular Structures and Interactions: Biomolecules	453
<b>Chapter 13</b>	Optical Spectroscopy	489
<b>Chapter 14</b>	Magnetic Resonance	539
<b>Chapter 15</b>	Macromolecular Structure and X-Ray Diffraction	574
<b>Appendix</b>	Mathematics	618
<b>Appendix</b>	Tables	628