1 Enzymes: Their Place in Biology

One marvels at the intricate design of living systems, and we cannot but wonder how life originated on this planet. Whether first biological structures emerged as the self-reproducing genetic templates (genetics-first origin of life) or the metabolic universality preceded the genome and eventually integrated it (metabolism-first origin of life) is still a matter of hot scientific debate. There is growing acceptance that the RNA world came first – as RNA molecules can perform both the functions of information storage and catalysis. Regardless of which view eventually gains acceptance, emergence of catalytic phenomena is at the core of biology. The last century has seen an explosive growth in our understanding of biological systems. The progression has involved successive emphasis on taxonomy → physiology → biochemistry → molecular biology → genetic engineering and finally the large-scale study of genomes. The field of molecular biology became largely synonymous with the study of DNA – the genetic material. Molecular biology however had its beginnings in the understanding of biomolecular structure and function. Appreciation of proteins, catalytic phenomena, and the function of enzymes had a large role to play in the progress of modern biology.

Enzymes and catalytic phenomena occupy a central position in biology. Life as we know it is not possible without enzyme catalysts. Greater than 99% of reactions relevant to biological systems are catalyzed by protein catalysts. A few RNA-catalyzed reactions along with all the uncatalyzed steps of metabolism occupy the rest 1%. While it may do to explain living beings as open systems that exchange matter and energy with their environment – thermodynamic feasibility alone is insufficient to be living! Kinetic barriers have to be overcome. Reactions with relatively fast uncatalyzed rates, like removal of hydrogen peroxide or hydration of carbon dioxide, also need to be accelerated. Enzymes are thus a fundamental necessity for life to exist and progress. The key to knowledge of enzymes is the study of reaction velocities, not of equilibria. After all living beings are systems away from equilibrium.

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Enzymology – the study of enzymes – has been an autocatalytic intellectual activity. Apart from knowledge gained on their structure and function, the study of enzymes is a driving force in advancing our understanding of biological phenomena as diverse as intermediary metabolism and physiology, molecular biology and genetics, cellular signaling and regulation, and differentiation and development. The confidence in our experience with enzymes is so strong that they have found applications in a variety of industries including food, pharmaceuticals, textiles, and the environment.

We encounter enzymes in every facet of biology and are forced to admire their exquisite roles. Enzymes were excellent models and earliest examples to understand protein structure-function. These include enzymes like hen egg white lysozyme, bovine pancreatic ribonuclease A (RNase A), trypsin, and chymotrypsin. A few of these were encountered during the study of digestive processes. Selectivity of proteases was exploited, and they served as useful reagents to cleave and study protein structure. The field of molecular biology has benefited enormously from enzymatic tools to cut, ligate, and replicate information molecules like DNA and RNA. Metabolic and cellular regulation is unthinkable without involving enzymes and their response to various environmental cues. The complexity associated with life processes owes it largely to their catalytic versatility, exquisite specificity, and ability to be modulated.

Current advances in crystallography, electron microscopy, NMR, mass spectrometry, and genetic engineering have made it possible to view an enzyme closely while in action. Reverse genetics and genomics have made enzymology more powerful. Enzymology begins with a defined function and its purification; after which homing on to the corresponding gene has become very easy. Picomoles of pure enzyme protein are enough to determine its partial peptide sequence and obtain a fingerprint. From here it is a well-beaten track of gene identification, cloning, overexpression, and manipulation.

Enzymes are superbly crafted catalysts of nature, and they are at the heart of every biological understanding. Life has literally preserved its past as chemistry. The book of life is written in the language of carbon chemistry, and enzymes form a major bridge between chemistry and biology. Enzymology is the domain where chemistry significantly intersects biology and biology is at its quantitative best. From early history the evergreen tree of enzymology was nurtured by chemical and biological thought. We will take a look at this rich history in the next section.

Suggested Reading

Cleland WW (1979) Enzymology-dead? Trends Biochem Sci 4:47-48
Khosla C (2015) Quo vadis, enzymology? Nat Chem Biol 11:438–441
Kornberg A (1987) The two cultures: chemistry and biology. Biochemistry 26:6888–6891
Zalatan JG, Herschlag D (2009) The far reaches of enzymology. Nat Chem Biol 5:516–520