

Metabolic Structure and Regulation

A Neoclassical Approach

There is a renewed interest in the fundamentals of energy metabolism, yet most people base their understanding on the views of generalists expressed in elementary textbooks. New techniques that enable analysis of thousands of metabolites provide useful data, but do not themselves substitute for an understanding of the fundamentals of metabolism. While classical ideas of metabolism are also valuable, some earlier ideas have not withstood further investigation. This book presents a personal philosophy but rests on what is broadly accepted by metabolic biochemists over the past few decades.

Some principles developed in this book include:

Kinetics – The kinetics of isolated enzymes is placed in a metabolic context. For example, the K_m is a useful concept, but it can be misleading when considered as a means of interpreting enzyme inhibition, and it can be different yet in a pathway context.

The pathway view – This is a holistic perspective, in contrast to the reaction view, which is reductionist. For example, reaction cofactors such as NAD and ATP are connectors in the pathway view, but substrates or products in the reaction view.

Reversibility – Thermodynamics has been applied to metabolic pathways in earlier studies in ways that remain relevant today. This work rekindles the concept of near-equilibrium versus metabolically irreversible as separate classes of enzymes with distinct characteristics. A further type of reversibility emerges from the pathway view.

Signals and Pathway Flows – The richness of currently available information concerning signal molecules itself becomes a barrier to a broad understanding of function. This treatment considers just a few signal molecules: cyclic AMP, Ca^{2+} , AMP, and diacylglycerol, using balance and pathway considerations to place signalling in a metabolic context.



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