Temporal Dislocation and Theoretical Reconstruction in the History of Science: A Unified Interpretation from Ion Channels to DNA Replication

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Abstract:

Many major breakthroughs in modern life sciences display a prominent feature of phenomenon observation preceding structural analysis in the historical timeline. To fill cognitive gaps, classical theoretical systems often rely on auxiliary hypotheses to maintain logical consistency, which inadvertently increases theoretical complexity and violates the principle of simplicity pursued by science. This paper systematically reviews the complete course from the cognition of neuron structure, the discovery of cellular bioelectric phenomena, and the proposal of the sodium-potassium pump hypothesis to the structural elucidation of ion channels and the DNA double helix, clearly identifying the inherent theoretical contradictions caused by the lag in observation timing. On this basis, returning to the fundamental laws of biophysics, this paper proposes the ion channel windmill model for explaining action potentials and the DNA tetramer whole-chain transmission model for interpreting genetic information transfer. The new model system abandons redundant hypotheses, features a more concise logical chain, and puts forward several key experimentally testable predictions, providing a more internally consistent unified theoretical framework for neuroscience and molecular biology.

Key words: temporal dislocation; logical reconstruction; ion channel; sodium-potassium pump; action potential; DNA replication; tetramer model; biophysics

1 Introduction

Human exploration of natural laws generally follows a progressive path from macroscopic phenomena to microscopic mechanisms, and from functional description

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to structural interpretation. However, in the eventful development history of neuroscience and molecular biology, restricted by technical means at specific historical stages, the discovery order of multiple fundamental mechanisms has been inverted from their proper positions in the logical causal chain, forming a unique phenomenon of temporal dislocation. This dislocation does not stem from researchers' negligence, but is an inevitable outcome of opportunistic breakthroughs in the free exploration of science. Many Nobel Prize-level discoveries also bear the phased characteristics of a "blind man feeling the elephant". This paper aims to analyze how such temporal dislocation has profoundly influenced the construction of classical theoretical systems, and attempts to reconstruct a simpler, self-consistent and verifiable theoretical framework based on more recent structural biology evidence and grounded in biophysical principles. The full text adheres to full respect for the historical contributions of scientific predecessors, and only examines the inherent logic of theoretical evolution from the perspective of objective limitations of the times and technical conditions.

2 Temporal Dislocation in Scientific Discoveries: Key Nodes and Historical Causes

2.1 Early Limitations in Neuron Structure Understanding

In 1906, Santiago Ramón y Cajal and Camillo Golgi shared the Nobel Prize in Physiology or Medicine for their outstanding contributions to the study of nervous system structure[1]. Nevertheless, limited by techniques such as Golgi staining that could only label approximately 1%–5% of neurons at that time, the debate between these two giants remained at the level of cellular architecture, failing to touch the physicochemical essence of nerve signal transmission—ion channels.

2.2 Preceding Electrophysiological Research and Lagging Channel Structure

Foundations of electrophysiology: Alan Hodgkin and Andrew Huxley launched experiments on the giant axon of squid in 1939 and published a series of papers in 1952, establishing the Hodgkin-Huxley (H-H) model named after them, which quantitatively describes the ionic mechanism of action potentials[2]. They jointly won the Nobel Prize in Physiology or Medicine with John Eccles in 1963.

Proposal of the sodium-potassium pump hypothesis: After the H-H model successfully described action potentials, explaining how the intracellular and extracellular sodium and potassium ion concentrations could recover after each potential occurrence became an unavoidable question. To this end, Danish scientist Jens Christian Skou discovered Na^+ /K^+ -ATPase through experiments in 1957 and formally proposed the "sodium-potassium pump" hypothesis as an active transport mechanism for ion concentration recovery[3]. He was awarded the Nobel Prize in Chemistry in 1997.

Late breakthrough in structural biology: It was not until 1998 that Roderick MacKinnon first resolved the atomic-resolution structure of potassium channels [4]; in the same year, Peter Agre discovered aquaporins. The two shared the Nobel Prize in Chemistry in 2003. Nearly half a century had passed since the elucidation of electrophysiological mechanisms when this key structure was resolved.

The discovery order of "electrophysiological phenomena–pump hypothesis–channel structure" is completely inverted from the logical order of "channel structure–electrophysiological mechanism". This forced early theorists to introduce new hypotheses (the sodium-potassium pump) to fill cognitive gaps when facing a "black box". This was a reasonable choice under historical constraints, but it also planted the seed of theoretical redundancy.

2.3 Similar Temporal Dislocation in DNA Research

In 1953, James Watson and Francis Crick proposed the DNA double helix model [5] and won the Nobel Prize in 1962. However, discussions on the possible higher-order structures of DNA (such as G-quadruplexes) and their potential intrinsic correlation with ion channel functions lagged far behind the establishment of the double helix model. This temporal gap led the traditional semi-conservative DNA replication model to rely on a complex set of enzyme systems (helicases, topoisomerases, various DNA polymerases, etc.) to overcome topological challenges in double-strand unwinding and replication, resulting in high theoretical complexity.

3 Inherent Contradictions of Traditional Theories: Examination of Biophysical Feasibility and Simplicity

3.1 Historical Value and Contemporary Limitations of the Sodium-Potassium Pump Hypothesis

Pioneering scholars including Skou keenly realized when constructing their theories that, according to the classical membrane ion theory and mathematical models at that time, the transmembrane ion flow triggered by a single action potential could not accurately restore the membrane potential to the resting state and support high-frequency continuous discharge only by diffusion equilibrium. Driven by the rigorous pursuit of theoretical logical consistency, they introduced the active transport mechanism of the "sodium-potassium pump" to bridge this logical gap. This measure was an insightful and responsible major theoretical contribution under the cognitive conditions of that era, and its historical value is beyond doubt.

However, from a biophysical perspective, the transmembrane ion flux involved in a single action potential accounts for only an extremely small proportion (on the order of one ten-millionth) of the total ions at the local cell membrane interface, belonging to a local and microcirculation. One can imagine a counterfactual historical scenario: if MacKinnon's resolution of the atomic structure of ion channels had preceded Hodgkin and Huxley's electrophysiological experiments and Skou's pump research, researchers would have first recognized a channel "machine" with exquisite conformational changes and ion selectivity. Starting from this cognitive point, it might have been unnecessary to introduce a global, energy-consuming active transport system to explain local potential reset, and the theoretical system might have been constructed in the direction of "local ion circulation" from the very beginning. This is not a criticism of predecessors' mistakes, but a clear revelation: temporal dislocation in scientific discoveries is an important reason why the "sodium-potassium pump" evolved from a necessary transitional hypothesis to a core link of classical theory.

3.2 Room for Simplification Optimization of the Traditional DNA Replication Model

The traditional semi-conservative DNA replication model has achieved great success, but its heavy reliance on the "unwinding–replication–rewinding" process coordinated by multiple enzymes leaves room for theoretical optimization and simplification from the perspective of biophysics in terms of energy efficiency and system robustness. This complexity is also related to the cognitive timing of "the double helix structure being preconceived, while more efficient physical pathways for its replication were not prioritized".

4 Theoretical Reconstruction: A Unified Framework Based on Biophysical Mechanisms

4.1 Ion Channel Windmill Model

This model argues that the generation, conduction of action potentials and the reset of resting potentials can be entirely driven by the conformational cycle ("windmill-like rotation") of voltage-gated ion channels themselves [6]. Triggered by changes in membrane potential, this cycle guides the selective and sequential transmembrane flow of sodium and potassium ions along the electrochemical gradient through conformational changes of channel proteins, forming local ion microcirculation. This process has extremely high energy efficiency, does not require the participation of global active transport by the sodium-potassium pump, and is highly compatible with the known atomic structure and gating dynamics of channel proteins.

4.2 DNA Tetramer Whole-Chain Transmission Model

This model proposes that DNA does not necessarily unwind into single-stranded templates during replication; instead, it can form a transient "tetramer bundle" composed of four strands as a transition state. Genetic information is transferred and copied in whole segments through the overall rotation and synergy of this four-stranded structure. This model can greatly reduce the demand for auxiliary factors such as helicases and topoisomerases, making the replication process more direct and efficient physically, in line with the basic principle of simplicity favored by living systems.

4.3 Unified Interpretation of Bioelectromagnetic Signals

The information transmission between neurons is essentially the propagation and coupling of bioelectromagnetic fields. The above ion channel model based on physical laws provides a more fundamental physical explanation for neural electrical activities, and is expected to unify cellular electrophysiology, neural network information coding and macroscopic electroencephalographic activities under a common bioelectromagnetic field framework.

4.4 Experimental Verification and Key Predictions of the New Model

4.4.1 Reinterpretation of Existing Unconventional Phenomena

(1) Membrane potential homeostasis and pump inhibition: Some experiments show that after the sodium-potassium pump is pharmacologically inhibited, the resting membrane potential of cells does not collapse immediately but can maintain relatively stable for a long time. This suggests the existence of a potential maintenance

mechanism independent of the active pump, consistent with the idea of local ion circulation in the "windmill model".

(2) Complex dynamics of DNA replication forks: Single-molecule techniques have observed behaviors such as pausing and backtracking of replication fork movement, which are difficult to be fully explained by traditional models. These behaviors may be related to the complex dynamic characteristics of inter-strand synergy and torque transmission in the "tetramer model".

4.4.2 Key Testable Predictions

(1) Predictions of the ion channel windmill model: Under alternating electromagnetic field stimulation of specific frequencies, the action potential threshold and conduction velocity of neurons will exhibit resonant non-monotonic changes; in a closed membrane system (e.g., liposomes embedded with channel proteins) with complete sodium-potassium pump inhibition, periodic membrane potential oscillations maintained purely by channel dynamics can still be observed.

(2) Predictions of the DNA tetramer model: Time-resolved cryo-electron microscopy is expected to directly capture the possible four-stranded bundle transition state structure during DNA replication; after partial knockdown of helicase activity in vivo via gene editing, if replication can still proceed with high efficiency by applying physical torque (e.g., magnetic tweezers), it will constitute strong support for the tetramer model.

4.4.3 Feasible Technical Paths for Verification

Electrophysiological verification can adopt techniques such as patch-clamp, fluorescent ion imaging and microfluidic chips; DNA replication mechanism verification can rely on cutting-edge technologies including time-resolved cryo-electron microscopy, single-molecule magnetic/optical tweezers, high-throughput sequencing and CRISPR-Cas9 gene editing to conduct empirical tests on the model from multiple perspectives.

5 Conclusion

Reviewing the century-long history of life sciences, the classical theoretical systems we are familiar with today are largely products of the phased development of observation technology, bearing a profound imprint of "discovery timing". Major scientific breakthroughs have never been predictable by human effort; chance and necessity in free exploration have jointly written the chapter of cognition, and also left "theoretical patches" composed of auxiliary hypotheses caused by "temporal dislocation".

Scientific exploration is like climbing a perilous peak, and every forerunner is a lighthouse illuminating the way behind. We deeply understand that today's thoughts all stand on the shoulders of predecessors. Pioneers such as Skou introduced the sodium-potassium pump in pursuit of logical consistency at the cognitive boundary of their time, which is the highest embodiment of scientists' rigorous and truth-seeking spirit. They were not unaware of the debatable points in their theories; on the contrary, it was precisely because they perceived the inconsistencies in the old framework that they made this transitional and connecting expedient arrangement. This effort to strive for theoretical completeness within historical limitations deserves our highest respect.

The discussion in this paper is by no means negation, but tribute and continuation. We attempt to reorganize the logical timing on the new basis provided by today's structural biology and biophysics, return to the physical essence behind life phenomena, so as to strip away historical redundancy and construct a more concise, self-consistent and empirically testable theoretical framework. This is not only the integration and sublimation of the great work of predecessors, but also expects to provide a possible path with distinctive characteristics and core competitiveness for China to seek original breakthroughs in the field of life science basic theory.

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