Temporal Analysis of Frontier Evolution in Biological Sciences Research (Postprint)

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Abstract

Identifying and monitoring the evolution and migration of scientific research frontiers facilitates understanding the patterns of knowledge flow in scientific and technological fields, tracing the development trajectories of these fields, and provides reference and guidance for effectively selecting and tracking key research areas. Based on the 2013-2016 "Research Frontiers" reports, and taking the field of bioscience as an example, this study interprets and analyzes the temporal evolution and development trends of 40 hot research frontiers in this field, determines the evolutionary types of research frontiers, and reveals the patterns and characteristics of their evolution. This method can be used to capture the dynamic evolution of frontier fields and to identify the developmental timeline and evolutionary lineage of research frontiers.

Full Text

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Analysis on Time Sequence Evolution of Biological Science Research Fronts

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Abstract

Identifying and monitoring the evolution and migration of scientific research fronts is crucial for understanding knowledge flow patterns in science and technology fields, tracing their developmental trajectories, and providing references for effectively selecting and tracking key research areas. Based on the 2013-2016 *Research Fronts* reports and taking the field of biological science as an example, this study analyzes the temporal evolution and development trends of 40 hotspot research fronts in this domain, identifies the evolution types of these fronts, and reveals their evolutionary patterns and characteristics. This methodology can be applied to capture dynamic evolutions in frontier fields and identify the developmental timelines and evolutionary contexts of research fronts.

Keywords biological science, research fronts, time sequence, evolution
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Introduction

With the acceleration of technological evolution and interdisciplinary integration, scientific research landscapes are continuously extending and transforming in numerous directions. The constant renewal and transformation of research fronts drive disciplinary development, indicate the evolution of scientific fields and the direction of technological innovation, and reflect changes in scientists' focus and research priorities across different periods. For administrators in research universities, government agencies, and corporate R&D departments, identifying and monitoring the evolution and migration of scientific research fronts is essential for grasping knowledge flow patterns in science and technology fields, tracing developmental trajectories, and is also crucial for science and technology management agencies to identify development priorities and formulate science and technology policies.

The identification and detection of research fronts has become a hot topic in informatics research in recent years. Numerous scholars have conducted extensive studies on its concepts and identification methods, yielding many achievements. However, there is currently no unified definition of research fronts, which can be summarized into three main perspectives: (1) defining a set of highly cited documents as the scientific front, as proposed by D. D. Price and H. Small; (2) defining a set of citing documents as the scientific front, as suggested by S. Morris; and (3) defining emerging or hotspot topics as the scientific front, represented by Chen Chaomei [1]. The above definitions of research fronts are almost all tailored to suit the proposed identification methods, yet these definitions invariably revolve around several key characteristics: advancement, timeliness, and concentration [2]. Research on detection and identification primarily employs bibliometric methods such as co-citation [3], bibliographic coupling [4], direct citation [5], co-word analysis [6], and composite approaches using multiple methods [7], identifying or assessing research fronts through specific indicators. Studies on research front evolution are typically conducted in conjunction with identification method research. Small [8] demonstrated in collagen research how and when rapid changes in research focus occur. Morris et al. [9] employed an innovative timeline method to analyze and visualize the structure and temporal evolution of research fronts. Hou Jianhua et al. [10] analyzed the evolutionary context of nanotechnology research based on key node literature. However, among existing research outcomes, retrospective studies of known key research areas are more common, while studies that excavate and select potential "frontier fields" are relatively rare, and research that systematically organizes and analyzes the developmental context and evolution of research fronts at different stages of research fields is also scarce.

1 Development of the *Research Fronts* Report

1.1 Data Sources

The Essential Science Indicators (ESI) database, launched by the Institute for Scientific Information (ISI) in 2001, has become one of the most widely used tools worldwide for evaluating the international academic level and influence of universities, academic institutions, and countries/regions. ESI Research Fronts is a component of the ESI database, identifying research fronts in various disciplines through co-citation analysis and clustering analysis based on highly cited papers from the past five years. In 2013, Thomson Reuters released the *2013 Research Fronts: 100 Research Fronts in Natural and Social Sciences* report based on these clusters, identifying 100 important research fronts across multiple scientific fields [12]. In 2014, the "Joint Research Center for Emerging Technology Futures Analysis," established by Thomson Reuters and the National Science Library of the Chinese Academy of Sciences, released the *2014 Research Fronts* report, selecting the top 100 hotspot research fronts and 44 emerging fronts for 2014 [13]. The *2015 Research Fronts* report was subsequently launched in 2015. Based on 10,839 research fronts in the ESI database, it selected the top 100 hotspot fronts and 49 emerging fronts across 10 major disciplinary fields [14], attracting widespread global attention. In 2016, the Institute of Strategic Intelligence of the Chinese Academy of Sciences' Institutes of Science and Development continued to release the *2016 Research Fronts* report. Based on 12,188 research fronts in the ESI database from Clarivate Analytics (formerly the Intellectual Property and Science division of Thomson Reuters), it selected the top 100 hotspot fronts and 80 emerging fronts across 10 major disciplinary fields in natural and social sciences for 2016 [15].

1.2 Selection of Research Fronts

By tracking the world' s most important scientific research and academic papers, and analyzing citation patterns and clusters—particularly the frequent co-citation of clustered highly cited papers—research fronts can be identified. When the co-citation of a cluster of highly cited papers reaches a certain level of activity and coherence, a research front is formed, and this cluster of highly cited papers constitutes the "core papers" of that research front. Taking the *2016 Research Fronts* report as an example, the 12,188 research fronts from 21 disciplinary fields in the ESI database were first aggregated into 10 highly consolidated major disciplinary fields. Then, for each major field, the core papers of research fronts were ranked by total citation count, extracting the top 10% most citation-influential papers as research fronts. Based on this data, the fronts were re-ranked according to the average publication year of core papers to identify the "youngest" research fronts. Through these two steps, 10 hotspot fronts were selected from each major disciplinary field, totaling 100 hotspot fronts.

The ten major disciplinary fields in the *2016 Research Fronts* report are: Agriculture, Plant and Animal Sciences; Ecology and Environmental Sciences; Earth Sciences; Clinical Medicine; Biological Sciences; Chemistry and Materials Science; Physics; Astronomy and Astrophysics; Mathematics, Computer Science and Engineering; and Economics, Psychology and Other Social Sciences. The analysis of research fronts provides a unique perspective for revealing the context of scientific research. The data from these research fronts continuously document the emergence, convergence, and development (or decline and dissipation) of dispersed research fields, as well as their differentiation and self-organization into newer research activity nodes. As one of the ten major disciplinary fields mentioned above, biological science has published 10 hotspot fronts and varying numbers of emerging fronts annually since 2013. This paper uses 40 hotspot fronts (Table 1) and their core paper content as the basis to systematically organize the evolutionary pathways of research fronts in biological science, identify the evolution types of research fronts, and reveal their evolutionary patterns and characteristics.

2 Time Sequence Evolution of Biological Science Research Fronts

Among the 40 research fronts in biological science (Table 1), studies related to medicine and human health constitute a substantial proportion, followed by technological method breakthroughs and basic theoretical research. Below, combined with the spatiotemporal context of research fronts and based on research content, we categorize them into five major directions: HIV and immune system, neurodegenerative diseases, epidemiology, technology application and updates, and drug testing and mechanism research, to further demonstrate and explain the rationality of front evolution.

2.1 HIV and Immune System Domain

HIV/AIDS has spread widely worldwide, posing a serious threat to human health and social development. Research related to HIV and the immune system has consistently attracted scientists' attention. In the 2013 research fronts, researchers identified the mechanism by which the cytokine SAMHD1 protein inhibits HIV infection in myeloid cells, expanding understanding of how the immune systems of AIDS patients combat HIV and how HIV evades immune responses, laying a foundation for subsequent research. Subsequently, structural biology research achievements on important adaptors and sensor proteins in innate immune signaling pathways (2014) and analysis of the immune regulatory functions of innate lymphoid cells (2015) deepened understanding of autoimmune diseases and immunodeficiency disorders, enabling new strategies for vaccine development. In 2016, "Broadly Neutralizing Antibodies and HIV Vaccine Design" became a hotspot front, with recent articles reporting continuous major breakthroughs in HIV vaccine development, bringing new hope for conquering AIDS [16] (Table 2).

2.2 Neurodegenerative Diseases Domain

The research fronts in this domain primarily focus on neurodegenerative diseases such as Alzheimer’ s disease, frontotemporal dementia, and amyotrophic lateral sclerosis. The association analysis of pathogenic genes for these conditions has once again become a hotspot front (Table 3). Neurodegenerative diseases represent a class of conditions characterized by the loss of neuronal cells in the brain and spinal cord. With population aging intensifying, the prevalence of neurodegenerative diseases is rising steadily, and scientists have been continuously searching for pathogenic mechanisms and therapeutic approaches. Abnormal deposition of -amyloid protein in the brain is a primary cause of neuronal degeneration and death around senile plaques in Alzheimer’ s disease patients; however, targeting tau protein pathological processes shows greater therapeutic benefit for improving clinical symptoms than targeting -amyloid. Research on tau protein pathogenic mechanisms provides new ideas and clues for developing novel therapies or drugs for neurodegenerative diseases. The first human vaccine, ADAMANT, designed to modify tau protein to cure Alzheimer’ s disease, has successfully entered Phase II clinical trials [17].

In 2012, researchers identified the association between the C9orf72 gene and both amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Subsequent research has focused on explaining the pathological molecular mechanisms by which C9orf72 hexanucleotide repeat expansions cause these two diseases, and this research has been selected as a hotspot front for three consecutive years since 2014. Additionally, the 2016 research fronts also revealed that PINK1 protein, closely associated with Parkinson’s disease, helps cells eliminate dysfunctional mitochondria, uncovering new drug development targets for neurodegenerative diseases and holding significant importance for drug development targeting the mitophagy pathway (Table 3).

2.3 Epidemiology Domain

Epidemiology has developed through humanity’ s continuous struggle against severe diseases that threaten human health. In recent years, frequent contact between humans and various animal species in densely populated markets, along with human encroachment on natural animal habitats, has facilitated the emergence of new viruses. Emerging and re-emerging infectious diseases such as SARS coronavirus, Middle East Respiratory Syndrome coronavirus (MERS-CoV), avian influenza, and Zika virus pose threats to global public health. MERS-CoV is a newly emerged human coronavirus capable of causing severe respiratory infections, following in the footsteps of SARS coronavirus. Researchers have conducted extensive studies on MERS-CoV pathogenic mechanisms, and it was selected as a hotspot front for two consecutive years in 2015 and 2016. The discovery of functional receptors for MERS-CoV provides an important foundation for tracing the origins and cross-species evolution of novel human coronaviruses, as well as for research on viral transmission and epidemiological characteristics. Subsequently, scientists conducted in-depth studies on the mechanisms by which MERS-CoV recognizes these receptor molecules. The aforementioned research points to new directions for a deeper understanding of MERS-CoV pathogenic mechanisms. Avian influenza viruses, particularly highly pathogenic avian influenza, pose significant threats to animal and human health through outbreaks in the Asia-Pacific region. H7N9 avian influenza, as a novel type of avian flu, was discovered in 2013 and was selected as an emerging front in 2014. Subsequently, researchers conducted extensive studies on the origin, transmission routes, and biological characteristics of the H7N9 avian influenza virus, and its transmission and pathogenic mechanisms became a hotspot research front in 2015. In 2016, related research was selected as hotspot fronts in both biological science and clinical medicine fields (Table 4).

2.4 Technology Application and Updates

In recent years, gene editing technologies represented by ZFN, TALEN, and CRISPR-Cas have been widely applied in various aspects of life sciences and medicine. TALEN technology, officially invented in 2010, became a hotspot front in 2014. CRISPR-Cas technology, as the latest emerging genome editing tool, provides a novel platform for constructing more efficient site-specific gene modification technologies and has been successfully applied in functional studies of various animals and plants. The CRISPR-Cas system first appeared as an emerging front in 2014; subsequently, it became a hotspot front in 2015, while studies on its molecular mechanisms and applications in human cells were selected as emerging fronts. In 2016, it was once again selected as an emerging front, demonstrating its broad application prospects (Table 5).

Additionally, DNA methylation is one of the important mechanisms in eukaryotic epigenetics, playing crucial roles in maintaining normal cellular functions, genetic imprinting, and human tumorigenesis. The 2014 research fronts primarily explored and investigated genome-wide association study (GWAS) methods from the perspective of genetic statistics, while addressing issues such as "missing heritability" that emerged during GWAS analysis. The genome-wide association approach has first received significant attention and application in human medical research, enabling breakthrough progress in studies of many important complex diseases and becoming a key method in human genomics research.

3 Characteristics of Biological Science Research Front Evolution

From the aforementioned evolutionary pathways of biological science research fronts, it is evident that the distribution of research fronts in biological science is relatively concentrated, with more than half of the hotspot fronts closely related to human health. Their rapid research progress highlights the research focus and hotspots in biological science.

(1) Gradual-type fronts dominate the field in terms of quantity, demonstrating the long-term stability of scientific development. Research on

pathogenic mechanisms and drug action mechanisms of major diseases that continuously threaten human health (such as neurodegenerative diseases, HIV/AIDS, and cancer) has consistently received attention, accounting for 21 hotspot fronts. Over the past decade, with the rapid development of multidisciplinary research methods in molecular biology, neurobiology, and other fields, numerous new discoveries have been made regarding the pathological mechanisms of these major diseases. This research content primarily includes pathogenic mechanisms and clinical studies of the aforementioned diseases, extending to theoretical research on the roles of neural and immune systems in health maintenance and disease development, with an evident gradual evolutionary pathway. Additionally, the evolution of drug action mechanisms, such as melatonin —from its discovery in plants to studies of its biological functions, and then to research on its health benefits for humans—also demonstrates a clear pattern of deepening and progression.

(2) The number of emergent-type fronts is rising rapidly, demonstrating the phased and leapfrog nature of scientific development. Emergent research fronts typically signal major discoveries or breakthrough achievements in a research field, or are influenced by external sudden events (such as infectious diseases, terrorist attacks, environmental pollution, or new drugs), accounting for 10 hotspot fronts. The developmental direction of specific emergent fronts requires case-by-case analysis. For instance, research on the detection and hazards of new designer drugs will gradually transform into a declining-type front as detection technologies mature and relevant laws and regulations are perfected. The MERS-CoV and avian influenza research fronts have gradually evolved into gradual-type fronts, with their evolutionary pathways indicating that human society' s response cycle to new viruses—from discovery to analysis to public health response—is shortening. The application and breakthrough of technological methods are important drivers of disciplinary development and key factors in the emergence of emergent-type fronts. Meanwhile, the iterative updates of gene editing technologies and application research on genome-wide association methods exhibit significant gradual characteristics.

(3) Transient-type research fronts also exist in the analysis process. Examples include "Molecular Mechanisms of Rapid Antidepressant Effects of Ketamine," "Tracing and Imaging Neuronal Activity in Vivo Using Fluorescent Indicators," and "Application of Femtosecond X-ray Lasers in Nanocrystal Structure Determination of Biological Macromolecules." The specific formation mechanisms of these fronts may require further in-depth analysis, also providing new opportunities for improving research front identification methods.

4 Conclusion

The evolution of research fronts presents a metabolic process of disciplinary topics, reflecting the development trends and future directions of disciplines, which constitutes important content for studying disciplinary development patterns. To analyze the temporal evolution patterns and characteristics of research fronts, this paper takes the hotspot fronts in biological science from the 2013–2016 *Research Fronts* reports as examples, analyzes and evaluates their research content, and identifies the discipline-specific evolutionary patterns and development characteristics of research fronts in this field. This provides some reference for effectively selecting and tracking key research areas, particularly the dynamic evolution of frontier fields, and for identifying the developmental timelines and evolutionary contexts of research fronts. This study only analyzes the temporal evolution of the top 10 hotspot fronts selected annually in the biological science discipline, making it difficult to cover all research fronts across the entire discipline in scope. However, this method can partially reveal the development trends and characteristics of important research fronts in biological science. Subsequent research should build upon this foundation by integrating multi-source data, improving the identification methodology system with expert knowledge, focusing on the evolution directions and trends of emerging fronts, and enhancing the effectiveness of research front evolution judgment and prediction.

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Note: Figure translations are in progress. See original paper for figures.