Investigating Development Trends of Science-Technology Linkages Through Patent Citation Analysis: A Case Study of HCV (Postprint)

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Abstract

[Objective/Significance] An analysis of the development trends in knowledge diffusion and cross-integration between scientific research achievements and patent technology innovation constitutes an important decision-making foundation for disciplinary domain planning, research and development investment, and the allocation of scientific and technological resources. The measurement indicators employed in existing studies have failed to comprehensively capture the characteristics and evolutionary patterns of science-technology linkage relationships. This paper proposes novel measurement indicators and methodologies for domain-specific science-technology linkage relationships, with a focused emphasis on evolutionary trend analysis. [Method/Process] Through systematic analysis and synthesis of existing measurement indicators, this study expands the conventional single-dimensional metrics of scientific linkage degree and/or linkage time lag into a hierarchical framework of measurement indicators encompassing three dimensions: closeness, timeliness, and diversity, thereby enabling a more comprehensive revelation and identification of the extent and characteristic patterns inherent to science-technology linkages. [Results/Conclusion] By applying the measurement indicators constructed in this study to the HCV research domain, we conducted empirical calculations and discussions that reveal the developmental trends of science-technology linkages in this field. The results demonstrate the advantages of the proposed indicators in terms of systematic measurement dimensions and underscore the reference value of their conclusions for patent technology research and development activities.

Exploring the Development Trends of Domain Science-Technology Linkage Based on Patent Citation Analysis: A Case Study of HCV

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Abstract

[**Purpose/Significance**] The analysis of knowledge diffusion and cross-integration development trends between scientific research outcomes and patented technological innovations serves as a crucial decision-making basis for disciplinary field layout, R&D investment, and scientific resource allocation. Existing measurement indicators fail to comprehensively reflect the characteristics and evolutionary patterns of science-technology relationships. This paper designs new indicators and proposes a method for measuring domain science-technology relationships that focuses on evolutionary trend analysis.

[**Method/Process**] By analyzing and summarizing existing measurement indicators, we expand the single metrics of science linkage degree and/or linkage time lag into hierarchical measurement indicators across three dimensions: compactness, timeliness, and diversity, thereby comprehensively revealing the degree and characteristic patterns of science-technology relationships.

[**Results/Conclusion**] Using the measurement indicators constructed in this paper, we calculated and discussed the HCV research field, revealing its science-technology linkage development trends and demonstrating the systematic advantages of the new indicators in measurement dimensions and the reference value of their conclusions for patent technology R&D activities.

1. Introduction

With the accelerating integration of science and technology, their relationship has transformed from mutual separation to interaction, integration, penetration, and mutual transformation. While science exerts multifaceted influences on technology, it is also influenced and constrained by technology. As early as the 1960s, Professor D.J. Price pointed out that science and technology possess unique knowledge accumulation structures, and under certain conditions, knowledge may flow from science to technology or vice versa. Subsequently, numerous scholars conducted more in-depth research and verification from different perspectives, employing methods such as surveys and bibliometrics to evaluate and analyze the “science-technology relationship” across various disciplines or countries.

Some studies examined collaborative R&D activities between public research institutions and enterprises or tracked talent mobility between scientific and technological sectors. Others borrowed approaches from statistics and econometrics. The majority of research, however, treats academic papers and patents as manifestations of scientific research outcomes and technological innovations respectively, using co-occurrence and citation analysis methods to mine relationships between papers and patents. On one hand, basic research serves as a prerequisite and catalyst for applied research, representing an important driver of technological innovation. On the other hand, the increasing phenomenon of patents directly citing scientific papers or monographs indicates increasingly close connections between science and technology, with knowledge flows becoming more direct and frequent. Therefore, analyzing the knowledge diffusion and cross-integration development trends between scientific research outcomes and patented technological innovations has become an important decision-making basis for disciplinary field layout, R&D investment, and scientific resource allocation.

However, within the mainstream method of patent-based citation analysis, existing indicators and their applications cannot yet reflect the characteristics and patterns of science-technology relationships in detail. Consequently, improvement efforts are needed, such as making subtle adjustments to existing indicators and designing new ones. While the relationship between patent inventions and basic innovations in biomedicine has been macroscopically demonstrated and analyzed, this study focuses on the HCV (Hepatitis C Virus) research field, employing new indicators and methods to analyze its science-technology linkage development trends over the past decade. This aims to provide references for research activities and scientific development planning management in this field, while offering insights for similar studies in other medical domains.

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2. Related Research Overview

Patent-based citation analysis examines the citation characteristics and patterns of non-patent references (NPRs) such as journal papers and conference proceedings in patents, quantitatively revealing the driving role of basic scientific research in technological innovation. F. Narin pioneered the use of patentometrics to measure the interaction between science and technology, with subsequent scholars further developing these methods. Although patents do not represent the entirety of technological innovation, they constitute its core content and foundation. Analyzing non-patent citations in patents can reflect the dependence of technological innovation on basic research or, conversely, the contribution of basic research to technological innovation. Meyer's research further demonstrated that patent citations to academic publications represent an important indicator for measuring science-technology interactions, with varying linkage strengths, interaction patterns, and knowledge transfer mechanisms across different fields necessitating different science and technology policies.

Compared to other science-technology linkage analysis methods, patent citation analysis has yielded more research outcomes. For instance, Meyer, Henderson, and Bacchiocchi examined science-technology linkages in nanotechnology, across the United States, and between European public research institutions and innovative enterprises respectively, using patent-to-paper citations as a “link” to explore correspondences in content, direction, structure, and level. Hiroyuki’s analysis of high-impact patents in Japan revealed that university basic research serves as the primary theoretical source for invention patents, while Lo’s analysis of non-patent literature citations in genetic engineering also demonstrated the important role of public institution basic research in technological development.

The Science Linkage (SL) indicator is commonly used internationally to examine relationships between national patent technology and basic science. For example, Japan’s Ministry of Education, Culture, Sports, Science and Technology’s *Annual Report on the Promotion of Science and Technology* compares and analyzes changes in this indicator across the US, UK, Germany, France, and Japan. Zhao Zhiyun et al. studied Chinese patents in biotechnology filed in the US, demonstrating growth in science linkage, citation sources by journal, author countries, and institution types. Pei Yunlong et al. used non-patent citation analysis and negative binomial regression models to quantitatively study the impact of nanoscience on nanotechnology. Wen Xiaofen conducted empirical research on the relationship between technological innovation and basic research across four fields: chemistry, medicine, computer & communications, and machinery. Zhang Lingling et al. selected patents in the man-made fiber technology field from USPTO, constructing a co-citation network of cited journals to identify important foundational disciplines influencing the technology and summarizing how basic disciplinary knowledge represented by journals affects technological innovation.

3. Measurement Indicators for Science-Technology Linkage

Current indicators for measuring science-technology relationships based on patent citations primarily include science linkage, linkage time lag, and statistical analysis of involved journals. This paper categorizes science-technology linkage measurement into three dimensions: compactness, timeliness, and diversity. Compactness quantitatively characterizes the overall degree of closeness and its changing trends between patent technology and corresponding basic research in a specific period. Timeliness reveals whether patent technology keeps pace with scientific research innovation processes and to what extent. Diversity measures the diversity of scientific knowledge sources referenced by patent technology. Based on this understanding, we construct the indicator system framework shown in .

3.1 Compactness: Science Linkage

The CHI research school defines science linkage as the average number of scientific literature citations (including academic papers and conference proceedings) in patents. For trend analysis requiring period-specific examination (e.g., annual), this paper modifies the science linkage formula as:

$$SL = \frac{\text{Number of non-patent references (NPR) cited by patents in a given period}}{\text{Number of patents (P) in that period}} \quad \text{(Formula 1)}$$

After obtaining SL values for multiple consecutive periods and plotting them on a curve, we can observe the evolving trend of linkage degree between technology (represented by patents) and science (represented by non-patent references). The trend may show increase, decrease, or fluctuation. Higher SL values indicate greater technology dependence on science or more scientific knowledge flowing into technology R&D and innovation. Some scholars suggest this indicator "examines the degree of association between technology and latest scientific development; a large number indicates that R&D activities and technological innovation keep pace with the latest scientific advances." This paper argues that this view is appropriate only when considering the time dimension. SL quantitatively characterizes the overall closeness between technology (in a given period) and corresponding basic research, reflecting technology's dependence on basic research or basic research's contribution to technology, while whether it keeps pace with the latest science should be evaluated through linkage time lag indicators.

3.2 Timeliness: Linkage Time Lag

Theoretically, science-technology linkage time lag comprises two aspects: the time required for scientific knowledge to flow from the "science community" to the "technology community" to generate new technological knowledge, and the time required for technological information to act on the "science community" to generate new scientific knowledge. Short time lag indicates fast interaction and high innovation activity, though this also relates to field-specific characteristics. Long time lag may reflect slower interaction but also demonstrates that older scientific or technological knowledge retains applicability and value over time, highlighting its precious worth.

This paper focuses on time lag in patent citations to scientific literature. The division of time periods is merely illustrative, designed to examine citation patterns of relatively recent publications and demonstrate the flexibility of this indicator for setting different intervals based on research needs. The formula for calculating the overall time lag for a specific patent set is:

$$LTD_{P_i} = \text{Patent year } P_i - \frac{\sum_{j=1}^{n} \text{Publication year of scientific literature } j}{n} \quad \text{(Formula 2)}$$

where n is the total number of scientific literature cited by patents in year P_i. This formula is designed for examining annual science-technology linkage time lag in a specific field. For a patent set not limited to one year, the patent year would need to be averaged or otherwise processed.

The formula for counting the number and proportion of cited scientific literature by time interval is:

$$V_i = \sum_{j=1}^{n} X_j \quad \text{where } X_j = 1 \text{ if } P_j \in TZ_i, \text{ otherwise } 0 \quad \text{(Formula 3)}$$

$$PRO_i = \frac{V_i}{\sum_{i=1}^{m} V_i} \quad \text{(Formula 4)}$$

where TZ_i is the i-th time interval, n is the total number of scientific literature across all intervals divided by publication year, and m is the number of intervals. The reference time interval definitions are shown in .

Table 2. Time Interval Definitions and Examples

Scientific Literature Publication Year	Example Year ($P_i = 2015$)
P_i (current year)	2015
$t_{1-2} : P_i - 1, P_i - 2$	2014, 2013
$t_{3-5} : P_i - 3, P_i - 4, P_i - 5$	2012, 2011, 2010
$t_{6-10} : P_i - 6$ to $P_i - 10$	2009-2005
$t_{11-20} : P_i - 11$ to $P_i - 20$	2004-1995
$t_{21-} : P_i - 21$ and earlier	1994 and earlier

Notably, existing studies use either patent priority application year or publication year. Considering that scientific literature has several months between submission and publication, and patents have delays between application and publication, using patent publication year may be more reasonable when scientific literature year uses publication year, as this places both innovation outcomes on the same standard.

After dividing reference years into intervals, comparing quantities or proportions across intervals reveals whether specific period's patent technology references newer or older scientific knowledge. For example, [Figure 1: see original paper] shows that t_{1-2} interval has the most scientific literature, followed by t_{3-5}. This timeliness characteristic relates to technology's inherent nature. Across a technology's lifecycle, different stages may show different timeliness features in referenced scientific knowledge, requiring case-specific analysis.

3.3 Diversity: Source Journals and Disciplines

Typically, journal papers constitute the vast majority of scientific literature referenced in patents, with books and reports being relatively rare. Since existing databases provide more detailed and standardized information for journal literature with mature classification systems, using only journal papers for measuring diversity does not affect conclusions (books and reports are negligible). Therefore, this paper defines Journal Diversity (JD) based on journal categories of cited scientific literature:

$$JD = \frac{\text{Number of journals cited by patents in a period}}{\text{Number of patents (P)}} \quad \text{(Formula 5)}$$

In Web of Science (WoS) and similar databases, journal papers are assigned to one or more disciplinary categories, with many journals belonging to the same discipline. Therefore, we can consider a higher level based on disciplinary categories (e.g., SCI subject categories) to measure diversity:

$$SD = \frac{\text{Number of disciplinary categories cited by patents in a period}}{\text{Number of patents (P)}} \quad \text{(Formula 6)}$$

In both formulas, λ serves as a constant to adjust the value range of JD and SD for subsequent analysis. Notably, the denominator uses the total number of patents in a period, not just those with NPRs, to maintain the same baseline as classic science linkage and serve as a complementary indicator. This approach examines linkage from the overall technology field perspective, whereas using only patents with NPRs would be a narrower, linkage-object-focused perspective.

With the same or similar number of patents, more journal or disciplinary categories yield higher JD and SD values, indicating broader scientific knowledge sources for patent R&D. Like linkage time lag, source journal and discipline analysis can examine overall categories and proportions.

Counting journals or disciplines reveals those with larger proportions, which can be considered core scientific foundations for the technology field. These provide references for R&D personnel in subsequent innovation processes for locating, absorbing, and utilizing scientific knowledge. JD helps identify core journals and emerging journals closely related to patent R&D, while SD helps identify core and interdisciplinary fields. TOP journals or categories can be identified from complete datasets or examined across periods to detect changes or patterns.

4. Analysis of Science-Technology Linkage Development Trends in the HCV Field

4.1 Data Sources

Hepatitis C, caused by Hepatitis C Virus (HCV) infection, is primarily transmitted through blood transfusion, needle sharing, and drug use. According to WHO statistics, the global HCV infection rate is approximately 3%, with an estimated 180 million people infected and about 35,000 new cases annually. HCV infection causes chronic inflammatory necrosis and liver fibrosis, with some patients developing cirrhosis or hepatocellular carcinoma (HCC). HCV-related mortality is projected to continue increasing over the next 20 years, posing serious social and public health challenges. Investigation shows that HCV patents cite numerous scientific papers, and WoS data indicates high and sustained research activity in this field in recent years. Therefore, this study selected this field for science-technology linkage trend analysis to provide references for its innovative development.

Patent data were collected from the Derwent Innovations Index (DII) using the search strategy TS=(hepatitis C OR HCV OR BCV) for 2008-2017, yielding 6,662 patents. Among these, 3,767 patents referenced scientific papers or books, with 30,854 cited scientific literature records. Non-patent citation data were obtained from Lens on July 20, 2018. Due to missing and erroneous information in the downloaded data, self-programmed scripts were used to supplement and clean the data, followed by manual verification.

4.2 Analysis Results

4.2.1 Linkage Compactness Using Formula (1), we calculated annual science linkage for HCV patents published from 2008-2017 and compared them with annual patent counts and patents with NPRs, as shown in [Figure 2: see original paper].

Figure 2. Trends in Patent Counts and Science Linkage

The results show that patent counts over the past decade exhibit a relatively flat wave trend, remaining above 600 except in 2015. The number of patents referencing scientific literature increased before 2013 but gradually decreased thereafter. Correspondingly, science linkage increased from 2008, peaked in 2011, then decreased annually with only a slight rebound in 2016. Overall, the compactness between HCV patent technology and scientific literature has shifted from increasing to decreasing.

In 2011, 651 patents were published, with 467 referencing 6,648 scientific papers/books (average 14 per patent). This year had the most references of both scientific literature and patent literature types, indicating particularly active knowledge absorption activities by inventors. Notably, although science linkage was relatively low in 2016 and 2017, scientific literature citations in these years exceeded patent citations by at least 25%, suggesting inventors increasingly draw inspiration from scientific knowledge, with potential for future science linkage growth.

4.2.2 Linkage Timeliness First, we calculated overall linkage time lag (LTD) for each annual patent subset using Formula (2), with results shown in .

Table 3. Annual Linkage Time Lag and Scientific Literature Publication Year Characteristics

From the time lag values, HCV science-technology linkage time lag showed a 平缓增长 trend from 2008-2017. The average publication year of cited literature was 1999 for 2016 patents, with other years within 5 years, indicating relative stability. The median publication year was 2001 in early years and mostly 2004 in later years (2007 for 2017). The earliest publication year shifted from around 1900 in early years to after 1920 in later years (1954 for 2017). The linkage span exceeded 100 years in early years but gradually shortened to 63 years in 2017, meaning 2017 patents cited literature published from 1954-2017.

These changes show that older scientific knowledge is gradually replaced by newer knowledge in supporting technology R&D, with earlier knowledge being replaced faster. However, the slower change in average and median publication years compared to patent knowledge updates reflects the sustained value of basic research knowledge.

Second, we calculated the distribution of cited literature by time period using Formulas (3) and (4), with proportions shown in [Figure 3: see original paper].

Figure 3. Proportion of Scientific Literature by Publication Year Interval

Overall, except for 2016, over 50% of citations in each year referenced literature published within the previous 0-10 years, and over 80% referenced literature within 20 years, indicating significant influence and value of recent literature. The proportion of literature published over 20 years ago gradually increased, approaching 20% from 2012 and exceeding 25% in 2016. Literature from the 1980s-1990s has more citations and longer-lasting influence than earlier works.

Specifically, citations to current-year literature (t_0) are minimal, visible only for 2008 (below 0.7% otherwise). Citations to literature from the previous 2 years remain stable around 10% (except 2008, 2009, and 2016). Citations to literature from years 3-5 exceeded 20% in 2008-2010 and 2013 but were 15-18% in other years. Literature from years 6-10 accounted for 19.8-25%, with minimal variation across years.

Dividing t_{11-20} into t_{11-15} and t_{16-20} shows the first five-year period's proportion fluctuated, while the latter five-year period showed inverse fluctuations. The t_{11-15} literature remains a key citation source, but the t_{16-20} proportion increased noticeably from 2014, indicating the growing importance of these years' literature for current patent R&D.

Combining t_{1-2} and t_{3-5} into 5-year periods shows literature published within the previous 5 years consistently represents the largest proportion (maximum near 40%, minimum about 24%), followed by years 6-10 (1-14 percentage points lower). The gap narrowed in recent years (2013-2017), with differences of only 3-6 percentage points, indicating increasingly similar reference value between these periods.

4.2.3 Linkage Diversity After reviewing, verifying, and cleaning the journal and disciplinary category information of annually cited scientific literature, we calculated Journal Diversity (JD) and Subject Diversity (SD) using Formulas (5) and (6), comparing them with annual patent counts in [Figure 4: see original paper].

Figure 4. Trends in Journal Diversity and Subject Diversity

Subject Diversity (SD) shows a relatively flat trend around 0.2, much smoother than patent count changes, indicating relatively stable foundational science quantities supporting this field's invention patents. Four of ten years exceed 0.2, peaking at 0.24 in 2016 and bottoming at 0.17 in 2008. Journal Diversity (JD) fluctuates more widely (0.67-1.46), with higher values in 2010-2013 and 2016 due to inventors referencing more scientific literature (average >10 NPRs per patent) and more journals (843, 952, 936, 825, and 761 types respectively). Since each journal focuses on relatively specific topics, more journal types indicate broader thematic attention and reference, suggesting higher technical complexity or innovation degree in those years' patents.

Table 4. Distribution Characteristics of TOP10 Journals by Year

The 20 journals include both comprehensive and specialized titles, demonstrating rich knowledge sources. The top two journals each exceeded 1,000 total citations (over 100 annually), constituting heavyweight reference journals. Journals ranked 3-9 each exceeded 300 citations. Most cited journals appear only once or twice annually, making those in Table 4 important sources.

Specifically, six journals (Table 4, ranks 1-6) consistently ranked in the top ten, particularly *Proceedings of the National Academy of Sciences of the United States of America* and *Journal of Virology*, which ranked first or second with significantly more citations than subsequent journals. *Nature* and *Science* citations highlight inventors' attention to high-quality papers and advanced research levels. *Journal of Medicinal Chemistry*, *Hepatology*, and *Nucleic Acids Research* form a second tier, appearing in 9, 7, and 6 years respectively.

Table 5. Distribution Characteristics of TOP10 Subject Categories by Year

The 16 subject categories show diversity from cell biology, molecular biology, and genetics to virology, immunology, and pharmacology, including the multidisciplinary category. This indicates patent inventors address HCV-related problems using interdisciplinary knowledge. Molecular Biology and Biochemistry each exceeded 4,000 citations (over 400 annually). Categories ranked 3-10 each exceeded 1,000 citations, representing important knowledge sources. Some categories outside TOP10 had similar citation frequencies to those within, such as Microbiology in 2010 (294 citations) and Genetics (288 citations).

Seven categories consistently ranked in the top ten annually: Molecular Biology, Biochemistry, Immunology, General Medicine, Cell Biology, Molecular Medicine, and Virology. Multidisciplinary studies narrowly missed the top ten in 2017. Pharmacology and Drug Discovery appeared in many years, while Infectious Diseases and Microbiology were prominent before 2011, and Cancer Research, Immunology & Allergy, and Oncology have emerged since, reflecting shifting research foci toward HCV-related cancers and immunological disorders.

4.3 Multi-Indicator Qualitative Analysis

The three-dimensional indicators measure different aspects of science-technology relationships, representing a refinement of the analysis. While quantitative integration may be inappropriate due to different attributes, qualitative synthesis of the three dimensions' conclusions is feasible. For the HCV field, the past decade shows: knowledge flow from papers to patents shifted from increasingly dense to relatively loose; knowledge transfer speed gradually slowed, though older scientific knowledge retains strong theoretical value; referenced journal types followed a similar divergent-to-convergent trend, while referenced disciplines remained relatively stable, reflecting field stability. Overall, patent R&D's dependence on basic research has decreased somewhat, particularly for recent scientific knowledge, though the magnitude is modest.

This paper refines existing metrics like science linkage and time lag with more objective descriptions and trend analysis orientation, implementing a three-dimensional, multi-layered approach (demonstrating five indicators: SL, overall time lag, segmented time lag, journal linkage, and discipline linkage) to explore knowledge interaction characteristics during domain development. This provides references for inventors selecting scientific knowledge sources and for research managers planning R&D investments. The new indicators, though relatively simple, reveal useful patterns, such as which years' scientific knowledge receives more attention from inventors and which serves as important R&D support. The Lens website facilitates patent-scientific literature analysis but requires time-consuming data verification and cleaning.

While demonstrated in the HCV field, the indicator design has no field-specific limitations and should apply to other disciplines. Future work will expand empirical fields and use technology themes as analysis units to compare differences across themes and disciplines. Additionally, patent-to-paper citation analysis (e.g., technology linkage) represents another important approach for measuring science-technology relationships, and combining both directions may offer meaningful insights.

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