Bibliometric Characteristics of a "Paradigm Shift": the 2012 Nobel Prize in Medicine

Andreas Strotmann[1] and Dangzhi Zhao[2]

[1] *andreas.strotmann@gmail.com*
ScienceXplore, F.-G.-Keller-Str. 10, D-01814 Bad Schandau (Germany)

[2] *dzhao@ualberta.ca*
University of Alberta, 3-20 Rutherford South, Edmonton, Alberta (Canada)

Abstract
This research-in-progress paper reports bibliometric characteristics that illustrate and give credence to the claim of the Nobel Prize committee that its 2012 Nobel Prize in Physiology or Medicine was awarded for a "paradigm shift". An all-author co-citation analysis (ACA) of stem cells research 2004-2009 provides an interesting characterization of this paradigm shift, which was triggered by a mid-2006 publication by the younger of the two 2012 laureates. In particular, while ACAs of 2-year time slices for the period consistently indicate the presence of a single cohesive subfield in which the "paradigm shift" occurred, with some fluctuation in membership throughout the period, an ACA of the entire six year period shows instead a closely interlinked pair of subfields, which on closer inspection turn out to represent the pre- and post-paradigm shift states of the same subfield. This bibliometric characterization also correctly identifies the name of the researcher primarily responsible for the paradigm shift, namely, Shinya Yamanaka, as that of the dominant post-shift cited author in that subfield. The relative lack of dominant figures in the subfield in the pre-shift period also underlines the area's pre-paradigmatic state of multiple conflicting and relatively unsuccessful research directions attempting to address a fundamental crisis in that field at that point.

Conference Topics
Mapping and Visualization; Citation and Co-citation Analysis; Methods and Techniques

Introduction
The 2012 Nobel Prize in physiology or medicine was awarded to John B. Gurdon and Shinya Yamanaka for having triggered, the latter with a discovery first reported in his mid-2006 publication (Takahashi & Yamanaka, 2006), "a paradigm shift in our understanding of cellular differentiation" (Nobel.org, 2012).

In the present paper, we report bibliometric evidence and characteristics for this paradigm shift. Results from this study may contribute to research that combines relational and evaluative citation analysis methods to extend the research problems that are addressed by citation analysis.

Methodology
We examined the evolution of the stem cell research during 2004-2009 through an author co-citation analysis (ACA) of three 2-year time slices using the same dataset as in Zhao and Strotmann (2011), which reported results from a study of the full 6-year time period. We adapted methods from that study.

The data set was constructed by retrieving about 60,000 full PubMed records of stem cell research articles published during 2004-2009 with MeSH heading "stem cells", enriched by their cited references from Scopus records corresponding to these PubMed records (Strotmann & Zhao, 2009). Automatic author name disambiguation was performed on this dataset (Strotmann, Zhao, & Bubela, 2009).

For each of the three 2-year time slices, the 200 most highly cited authors were identified by fractional author citation counting, and their exclusive all-author co-citation counts were

calculated (Zhao & Strotmann, 2008). An exploratory factor analysis with oblique rotation was performed on each of these co-citation matrices (SPSS Direct OBLIMIN) with the number of factors to extract determined by Kaiser's rule of eigenvalue greater than one. Only factor loadings greater than 0.3 were retained in the factor analysis results in order to focus on the most important relationships.

The visualization used here is similar to that in Strotmann and Zhao (2012), improving on the one introduced in Zhao and Strotmann (2008). It visualizes directly the results of a factor analysis, with authors as square, and factors (research specialties) as circular nodes. An author node is colored according to the factor that it loads most highly on in the pattern matrix result of the factor analysis. Node sizes are proportional to citations received (author nodes) or to the sum of member author citations weighted by each author's loading (factor nodes). The visualization merges information on both the pattern and the structure matrix results of the obliquely rotated factor model, using the latter for automatic layouting (Kamada-Kawai algorithm in Pajek) and the former for gray-scale values of lines that link authors to the factors that they load on. Interpretation of the factor nodes (i.e., research specialties identified) proceeded exactly as in earlier papers, by manually examining highly co-cited papers of authors that load highly on a factor.

Results

Figures 1-3 show the intellectual structure of the stem cell research field for three consecutive 2-year periods.

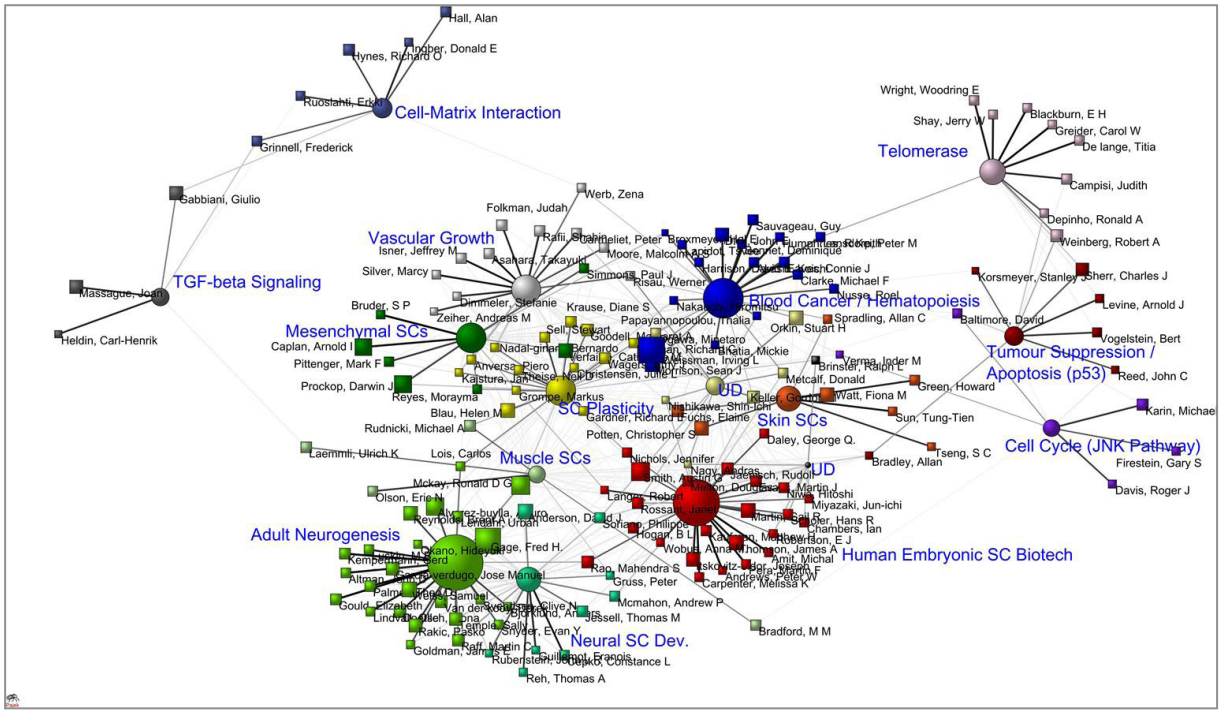

Figure 1. ACA of stem cell research 2004-05.

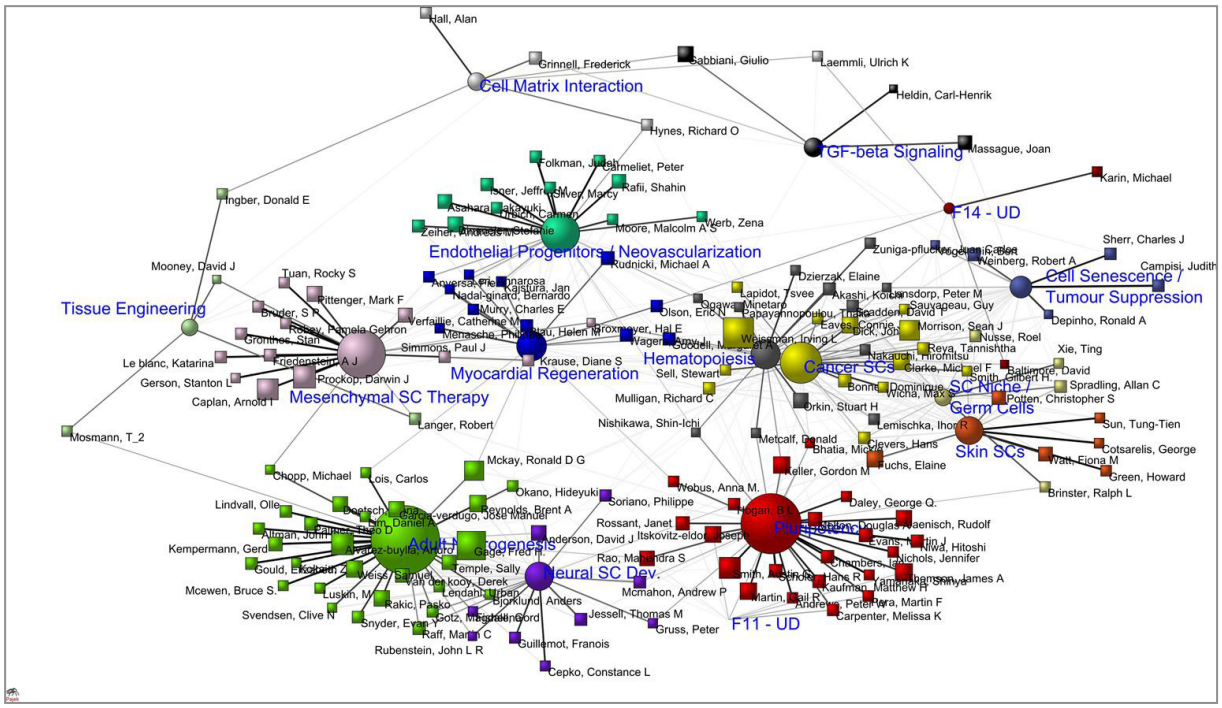

Figure 2. ACA of stem cell research 2006-2007.

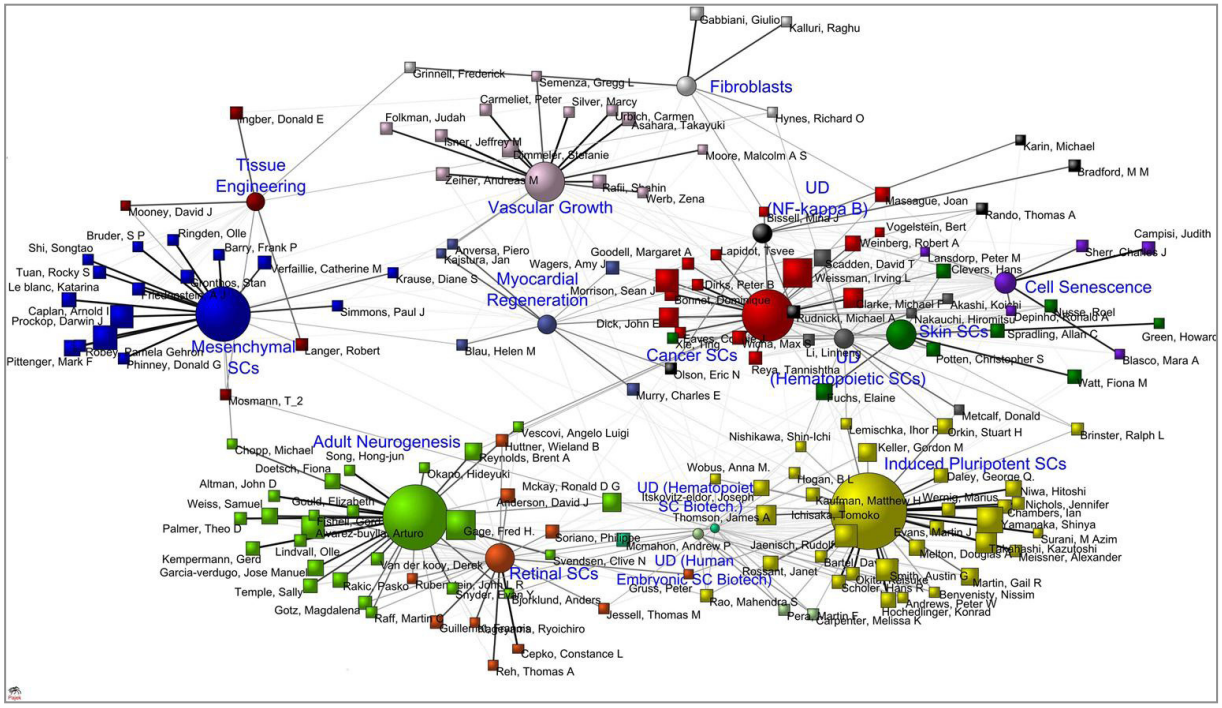

Figure 3. ACA of stem cell research 2008-2009.

While many interesting features of the international stem cell research field may be observed by examining these maps closely, we focus here on one particular major development in this field during the 2004-2009 time period as seen from changes over time. During the entire 2004-2009 time period, a subfield is shown prominently in the bottom right area of these maps as one of the two dominating specialties in stem cell research (the other being neural stem cells, bottom left). However, the entire focus appears to be shifting from (human) embryonic stem cell research in 2004-2005 (Fig. 1) through the study of pluripotency in

2006-2007 (Fig. 2) to the study of (human) induced pluripotent stem cells in 2008-2009 (Fig. 3). With this renewed focus on induced pluripotent stem cells, this subfield overtook the Neural stem cells specialty to become the most prominent specialty in the entire stem cell field in 2008-2009.

The transformation of this subfield is linked to the phenomenal rise of Shinya Yamanaka in these maps. Yamanaka was awarded the 2012 Nobel Prize in physiology or medicine for his discovery of induced pluripotent stem cells in mid-2006. He was not a highly influential researcher yet in 2004-05 as measured by citation impact (his name does not appear in Fig. 1); his name emerges in 2006-2007 (a small square in Fig. 2) and dominates this subfield by 2008-09 (the largest square in Fig. 3) with a citation impact reaching that of the two long-time most highly influential authors in the entire stem cell research field: Irving Weissman in the cancer stem cells specialty (red) and Fred Gage in the Neural stem cells area (green).

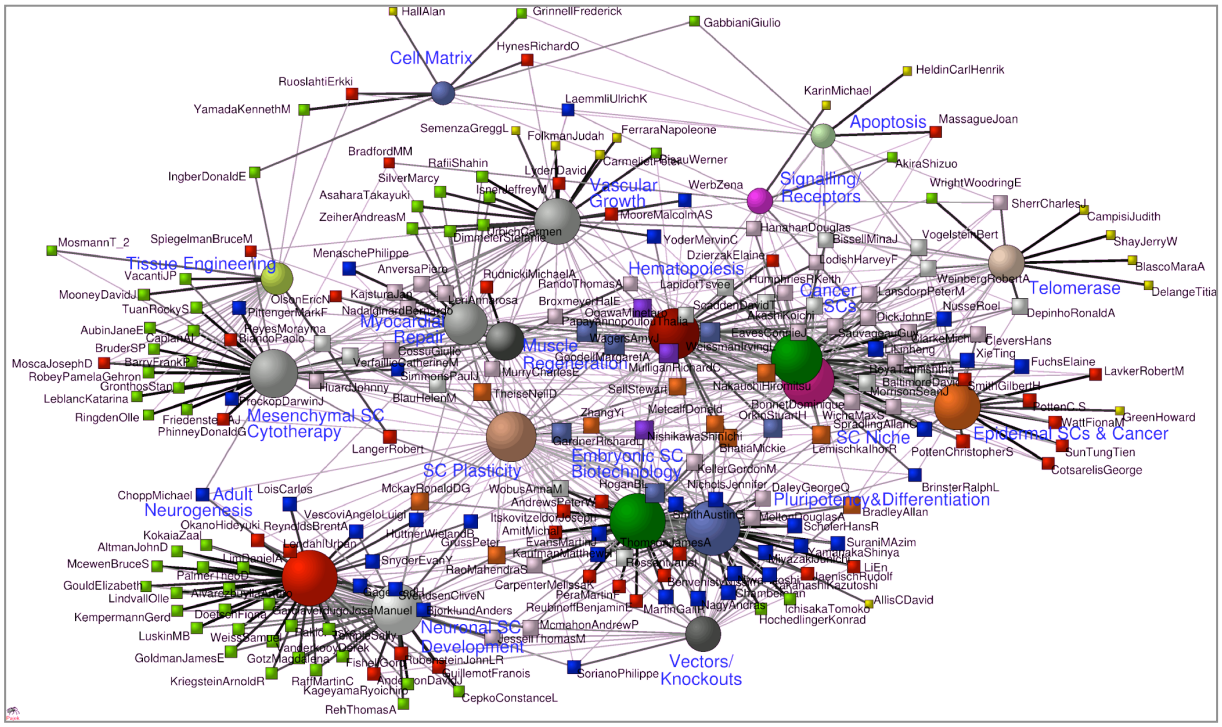

Figure 4. ACA of stem cell research 2004-2009.

By contrast, Figure 4, reproduced from (Zhao & Strotmann, 2011), which covered the entire 2004-2009 period in a single visualization, shows this subfield as consisting of two heavily interlinked research areas (bottom center), namely embryonic stem cell research (left, green) and (induced) pluripotent stem cell research (right, blue). This clarifies that what at first blush looks like it might have been a gradual change within this subfield when considering only Figures. 1-3 in fact constitutes a major in-place shift of research focus. Taken together with Figures 1-3, this confirms that the entire knowledge base for this subfield of stem cell research shifted from the former to the latter within just a couple of years of the publication of the key transformative paper – a true paradigm *shift* indeed. Most authors in this subfield co-loaded strongly on both these areas in the 6-year visualization, indicating a widespread realignment of researchers. A major paradigm shift becomes apparent.

Discussion

Kuhn's main criterion for a scientific revolution, or paradigm shift, is that something previously unthinkable becomes standard knowledge in a scientific field and a major crisis within the field is resolved as a result (Kuhn, 1970). In the case of stem cell research,

Yamanaka found that differentiated cells can be "reset" (induced) to undifferentiated (pluripotent) state, which essentially reverses the arrow of time in cell development biology, something previously unthinkable indeed.

It had been known in principle since Gurdon's 1960s paper (Yamanaka's co-laureate) that adult cells could be turned into even totipotent cells. For decades, stem cell research had been attempting to make this process feasible and controllable for therapeutic use, hoping someday to be able to regrow any type of damaged tissue (hence, the term regenerative medicine). The insurmountable research problem was a practical one: all methods for manipulating cells to this end produced stem cells that carried an unacceptably high risk of growing into malignant cancers rather than viable organs. Yamanaka's methods appear to have been the first (among uncountable failed attempts by others) to promise a fully viable resetting of cell development to the pluripotent or even totipotent state.

At the same time, Yamanaka's methods promised "safe", "natural", and abundant sources of pluripotent stem cells for research on early stages of cell development, which provided an immediate solution to a major social crisis that faced stem cell research in this subfield. This crisis came from the huge ethical and legal problems of obtaining and handling the embryonic stem cells that it required. By triggering a "natural" reset switch of much less problematic adult cells to the pluripotent state, as it were, the resulting stem cells not only side-stepped the ethically problematic use of embryos as a source, but did so without the kinds of major intervention such as genetic manipulation that had severely limited the usefulness of earlier versions of such cells for studying the "natural" biology of cell development.

As the Committee points out, Yamanaka's solution was also quite simple, so that human embryonic stem cell research was able to rapidly shift its entire focus to the study of induced pluripotent stem cells, in the remarkably short time of just a couple of years. Yamanaka's methods became standard knowledge very quickly – "textbooks were rewritten".

In the visualizations produced from an ACA of the type we performed here, this paradigm shift is characterized, somewhat paradoxically, by a stable visual appearance of the affected research subfield, accompanied by a shift in topic focus (factor labels). That a major topic shift took place can be confirmed through an analysis of a larger time slice spanning the triggering event, as we saw above. The initiator of the paradigm shift, Yamanaka, stands out as the author whose node shows explosive growth in citations received within the area as the shift occurs. The success of the paradigm shift is also seen from a rapid growth spurt of the shifting subfield relative to other subfields.

Interestingly, our visualization appears to also capture the "pre-paradigmatic" stage of this subfield, during which no single proposed solution managed to dominate the field (or subfield) that is undergoing a crisis (Kuhn, 1970). Unlike e.g. Gage in Neural stem cell biology or Weissman in bone marrow stem cell medicine research, whose citation impacts (indicated by relative node sizes) clearly dominated their respective subfields, no individual stood out in the embryonic stem cell research to that degree in Figure 1 (2004-2005). By 2008-2009, however, with the paradigm shift from embryonic to (induced) pluripotent stem cells as primary research tools completed, Yamanaka clearly plays that role in this area.

This ACA was actually performed, and Figures 1-4 were created, well before the 2012 Nobel Prize was announced (Strotmann & Zhao, 2011; Zhao & Strotmann, 2011). It appears that this paradigm shift could in principle have been identified and the 2012 Nobel Prize predicted through bibliometric studies of this kind (we did identify it as a "major development" of the field). Now that we have an idea what to look for, we could perhaps proactively look for patterns of this kind in bibliometric research in order to identify scientific breakthroughs and to make interesting predictions for major research awards. Research of this kind could enhance previous attempts to predict who among millions of scientists might qualify for the

honor of a Nobel Prize (Garfield & Malin, 1968) by combining relational and evaluative citation analysis methods to provide more convincing evidence.

Conclusions

This paper provides bibliometric evidence that the 2012 Nobel Prize in Physiology or Medicine was indeed awarded for a paradigm shift, through ACA of three consecutive 2-year time periods of stem cells research 2004-2009 compared to a single 6-year ACA for the same data. The success of this paradigm shift is seen on the ACA maps from the explosive growth in node size (citations received) of the researcher whose research initiated the shift, along with a complete shift of research focus in a subfield of stem cells research and a rapid growth spurt of this shifting subfield relative to other subfields. An ACA of the full period confirms that a major shift in the knowledge base of the subfield took place over this short time period; indeed, it shows signs of moving from a Kuhnian "pre-paradigmatic" to a "normal science" stage.

We hope that results from this study will contribute to research that combines relational and evaluative citation analysis methods to extend the research problems that are addressed by citation analysis.

Acknowledgments

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