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Indicators for the dynamics of research organizations: a biomedical case study

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Abstract This paper reports results on a bibliometric case study of the long-term development of research organizations, using an internationally leading biomedical institute as example. Using scientometric concepts, small group theory, organizational ecology, and process-based organizational theory, we developed a life cycle based theoretical model for analyzing long-term development of research groups and institutes. Three bibliometric indicators are proposed for growth, activity profile stability, and focus. With these, the research dynamics of the case institute are described. First, overall output growth matches developments internationally in developmental biology and stem cell research, and, in line with this, journal article output increasingly dominates the institute's activity profile. Second, superposed on the overall growth curve, a stepwise development is observed, consisting of long phases of growth and stabilisation. These steps reflect local conditions and events. Historical sources from the Institutes' archive and interviews with the current staff of the institute suggest that the pattern of life cycles reflects a strong influence of pioneering individuals. But once settled, pioneering directors who remain in function for many years delay adaptation of the institutes' mission to field developments. Furthermore, national science policies on PhD training, and on priority areas have influenced the life cycles, as did merging with other institutes. As in a social science case, also in this case study stabilized local conditions lead to adaptation to research field dynamics in a delayed fashion. In the present case stable output periods lasted at most 15 years, when local impulses led to new growth of research output and thus prevented onset of a lifecycle decline. The continued growth in the larger field both promoted and legitimized these local impulses.

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Introduction

We explore the dynamics of research organizations in an historical approach, based on an analysis of the long-term output. Through this, we identify the various domains of activity, and try to explain the development from the perspective of process-based organization theory. Our hypothesis is that research groups and institutes optimize and stabilize activities in order to realize its mission. This leads to a typical 'life-cycle', which can be disturbed by changes in the environment. We introduce life cycle indicators to analyze positioning and dynamics of research organizations.

Earlier, we used the approach to analyze a small institute within the social sciences (Braam and Van den Besselaar 2010). Are our life cycle indicators also useful in large research institutes, in other domains, and for long-term historical periods? To test this, we apply our life cycle model on an institute active in a very dynamic research area in the life sciences: stem cell research.[1] After testing the usefulness of the model, we discuss the practical implications.

Theoretical framework

Using process-based theorizing in organization studies, we analyze research groups[2] as units of change that follow a particular sequence of events, steered by an internal mechanism, in conjunction with external events and conditions (Scott Poole et al. 2000, pp. 36–37). Following this theoretical framework, one may describe research groups as follows. The internal mechanism that drives the activities of a research group is its mission: the shared (implicit or explicit) ambitions of the group members to realize specific results outside the group. Depending on its mission, a group will strategically position itself in a number of domains of activity, which can be summarized in an activity profile (Larédo and Mustar 2000). Therefore we expect that each group will optimize its 'primary activities' that directly contribute to its mission, and undertake 'secondary' activities to gain resources necessary for its survival. The latter contribute indirectly to the mission. Optimization of activities leads to (logistic) growth of output in primary domains up to a ceiling level that is given by the amount of available group resources (De Solla Price 1963). Within each domain of activity, the group has to be accepted (by its intended audience) as a legitimate player. Furthermore, it has to compete with other groups that produce the same or similar types of products for the same audiences. The success of a group in a specific domain of activity depends on the level of acceptance and specialization ('grade of membership') of the group as a producer of products in each domain (Hannan et al. 2007). Characteristics of the domains of activity influence the activities undertaken by a research groups, e.g. the dominant search processes in the scientific field the group is active in (Bonaccorsi 2008). The historical development of research groups can then be explained

[1] Hubrecht Institute for Developmental Biology and Stem Cell Research, Utrecht, The Netherlands.

[2] We use the concept of 'group' here interchangeable with 'laboratory', and 'institute'.

by a combination of internal and external processes and disturbing events/processes within the group (internal condition change) or in its domains of activity (external environmental change).

What can we predict about the development of groups? From *scientometrics* (De Solla Price 1963), we take the notion that growth of activities in science develops according to an S-curve: the growth pace first accelerates but then slows down by a ceiling of resources. We hypothesize that the growth of activities at the research group level will follow a similar pattern. From *organizational ecology*, we take the notion that a research organization must find a viable profile in its environment in order to survive (Hannan et al. 2007). We hypothesize, that if conditions are stable, a successful process of searching such a profile leads over time to a *stabilized set of activities* within specific domains[3] directed at specific target groups. If stabilization takes place, we will find that activity profiles do not change anymore from year to year. Similarity increases, probably in the form of an S-curve as well. In case environmental conditions change, research organizations may react in various ways to find a new balance (Sanz-Menendez and Cruz-Castro 2003). Finally, from *scientometrics* and *organizational ecology*, we take the notion that groups have to focus their activities to some extent. This is because their capacity is limited (Larédo and Mustar 2000), but also as legitimacy for the audiences in the selected domains increases by the level of specialization (Hannan et al. 2007). We hypothesize that the focus increases, and that the percentage of output for newly targeted (segments of) audiences gradually decreases over time to a low and stable level for each type of output. The more specialized the group is, the lower it will be.

Concepts from *process-based organization* theory help to model the development of research groups. Four types of 'change motors' influence processes of organizational development (Poole et al. 2000; Poole and Hollingshead 2005): (1) A *teleological motor*: processes driven by goal orientation, e.g., by the mission of a group, resulting in a recurrent discontinuous sequence of goal setting, implementation, and adaptation; (2) a *life cycle motor*: processes of unfolding stages of a prefigured program, e.g., ageing, resulting in a linear and irreversible sequence of development stages; (3) an *evolutionary motor*: processes of variation, selection and retention, e.g., competition, resulting in a recurrent sequence of variation, selection, and retention events; and (4) a *dialectical motor*: processes of conflict resolution, e.g., from reorganization, resulting in recurrent, discontinuous sequence of confrontation and conflict, and synthesis.

Distinguishing between primary forces that work from within groups, and other forces that work external to a group, results in various models of change (Arrow et al. 2005, pp. 324–330): The *robust equilibrium model* emphasizes internal evolutionary change in the early phase of self-organization of groups establishing a stable state, after which change requires external intervention. The *punctuated equilibrium model* focuses on the response of groups to periodic change in external circumstances resulting in stable periods punctuated by change. The *adaptive response model* focuses on (external) environmental opportunities for groups, the mix and change of which leads to idiosyncratic paths of development of groups thriving to reach their goals (teleological motor). *Sequential stage models* identify a series of stages a group goes through as part of its natural unfolding life cycle, from an endogenous process, i.e.: originating in the group. Dialectical processes within groups may lead to cyclic changes shorter than their lifetime.

[3] A domain is a relatively secluded social context wherein a research group performs activities. Larédo and Mustar (2000) distinguish five such domains: the scientific arena; the education system; the economic system; government; public media.

Based on the above notions, we hypothesize a basic life cycle model of development for research groups under stable conditions. Groups then go through three stages. In the first stage, the group formulates and/or internalizes its mission, and finds a strategic pattern of activities in domains that are suitable for realizing its mission. If a group succeeds in this, it will reach the next phase of robust equilibrium, and will remain functioning in a stable way until its mission is fulfilled and/or its members retire while key-members are not (adequately) replaced—thus reaching the third phase: (relative) decline. In the (second) stable phase, change only comes if forced upon the group from outside. This might lead to conflicts within or around a group, resulting, for instance, in change of the groups' mission or strategy, or in its organizational embedding. Further, in each domain of activity a group competes with other groups for scarce resources. Changes within domains may require a response of a group, e.g., more specialization. Changes in one domain may influence activities in other domains: if resources become scarcer in one domain, a group may have to intensify or diversify activities. All such changes will result in 'deviations' from the 'standard' life cycle. We use three output indicators to empirically describe the history of research groups:

(1) Growth of activities. The first indicator we use, the aggregated number of publications, is used to analyze the growth of activities, in all types and all domains of activity. It reflects to what extent the output of a group changes over time.
(2) Stability of the activity profile. The second indicator we use, activity profile stability, is meant to assess the stability of the activity profile over time: it reflects to what extent a research group produces a similar mix of output over the years.[4]
(3) Focus of activities. The third indicator, the percentage of output in a domain to new target groups, is meant to assess the focus of activities. It reflects to what extent a group is serving from year to year the same audience(s) within it activity domains.

Above we argued that each of the indicators[5] develops towards a stable high level (indicator 1 and 2) or stable low level (indicator 3). These patterns model the 'life cycle' of any research group (Fig. 1).

Under stable conditions, one expects (i) that the groups' output level will grow to a maximum level; (ii) the activity profile will stabilize after an initial period of searching the right output categories and target groups; and (iii) after initial fluctuations due to search processes, the level of focus will stabilize at a level that depends on the groups specialization. Patterns found in the indicators may help to determine the groups' life cycle phase.

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[4] $$\mathrm{Sim}\ (\mathrm{APyr}_t,\ \mathrm{APyr}_{t-1}) = \frac{\sum_{i=1}^{n} \left(\mathrm{Ai}_{\mathrm{yrt}}\right) * \left(\mathrm{Ai}_{\mathrm{yrt}-1}\right)}{\sqrt{\sum_{i=1}^{n} \left(\mathrm{Ai}_{\mathrm{yrt}}\right)^2} * \sqrt{\sum_{i=1}^{n} \left(\mathrm{Ai}_{\mathrm{yrt}-1}\right)^2}} = (0,1)$$

where APyr_t is the Activity Profile: items on activities of category i to n, in year t;
$\mathrm{Ai}_{\mathrm{yrt}}$ is the output items in Activity category i (e.g. journal publication) in Year t.
This 'Cosine' formula: Salton and McGill (1983), and Jones and Furnas (1987); the approach is similar to one earlier introduced to compare term profiles of document clusters (Braam, 1991).

[5] We use integer counts of items per year as for all output categories. At the item level, differences may exist in time and efforts to produce them, both between and within categories, but data to correct for this are lacking. In our analysis of long term patterns in output production this is not a large problem: each output category can be followed, and local fluctuations, due to the production of 'rare' items consuming much time and effort, are captured if other output decreases as a result. For performance comparison, it can be more sensitive (Moed 2005).

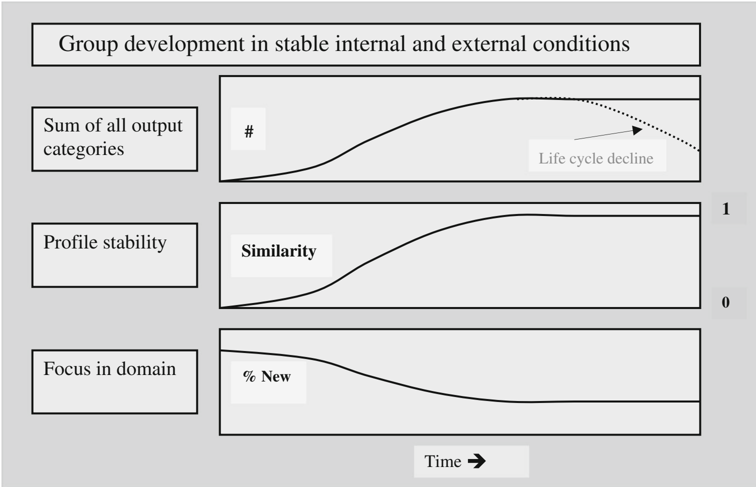


Fig. 1 Life cycle patterns of the indicators

Data and methods

Data on the output of a group or institute can be used to calculate the values of the three indicators over time. Comparing the actual patterns with the hypothesized life cycle, helps to interpret the trajectory of the group. This comparison is based on visual inspection and statistical (time series) analysis. In this way, transitions between life cycle phases, and gradual and sudden deviations from the 'normal' pattern are identified.

Change-Point Analysis (Taylor 2008) is deployed to locate significant changes in the time series. It identifies significant changes of the mean-levels in the time series of indicator values, given the expected life cycle patterns one would expect at least one level change for each indicator: the first and second indicator upwards, the third downwards. Of course, visual inspection of the curves is needed to secure interpretation.

Qualitative data on the history of the group help to identify critical events and processes that explain the observed dynamics. We use annual reports and other archived material of the Institute, as well as scholarly studies about the Hubrecht Institutes' history.

The case

The Hubrecht Institute[6] conducts fundamental research in the field of developmental biology and stem cells, and currently has a staff of somewhat over 150 FTE, organized in 17 units, each with a research leader. The Hubrecht Institute is part of the Royal Netherlands Academy of Arts and Sciences (KNAW), an umbrella organization with six research institutes in the life sciences, and eleven institutes in the social sciences and humanities.[7]

[6] *Sources*: www.hubrecht.eu/information/history.html; www.developmental-biology.org/about/about.html, Gerhart (1997).

[7] The KNAW has as its other main tasks science policy advice, promoting scientific cooperation, and quality assessment. In this latter task, the KNAW closely cooperates with the research council (NWO) and the association of Netherlands universities (VSNU).

The Hubrecht Institute started as Hubrecht Laboratory in 1916, when it was established as an Embryology Laboratory in the former residence of Ambrosius Hubrecht (1853–1915), professor of zoology in the medical faculty of Utrecht University. The laboratory was to contain the vast scientific collection of mammalian embryos of species from Europe and the East Indies, collected by professor Hubrecht. Based on a private fund, the laboratory maintained this collection to serve scientists in relation to the International Institute of Embryology, under the directorship of professor De Lange. In 1967, an additional collection of similar size was donated to the laboratory. In 2004 both collections were transferred to the Museum für Naturkunde in Berlin. Activities in experimental embryological research started with the pioneering work of Pieter Nieuwkoop, a student at Utrecht University zoology department who graduated in developmental biology in 1946, supervised by professor of zoology C. Raven, who also succeeded De Lange as director of the Laboratory in 1947. By 1953 Pieter Nieuwkoop had succeeded professor Raven as director of the laboratory. The Laboratory moved in 1964 from its original location in Utrecht to a new modern building at the university campus arising outside the Utrecht city area. After his retirement in 1980 professor Nieuwkoop in his turn was succeeded by professor De Laat as director. In 2000 the Laboratory moved to its present larger building, and was renamed Hubrecht Institute in 2007. Recently, the Institute affiliated with the University Medical Center Utrecht, intensifying the connections with Utrecht University. Funding comes from the KNAW, the Ministry of Science, from project grants, and recently from the Utrecht University Medical Center. The Institute obtained excellent scores by an international peer committee.

Data

Bibliographic data on the Hubrecht Institute's output for the period 1943–2008 come from publication lists on its website,[8] and data for the earlier years can be found in other documents of the institute. Data indicating the growth of the research field the institute is in, were obtained from the Web of Science.

In the period 1943–2009 the Hubrecht Institute produced a total amount of 1895 publications. Bibliographic data were organized in a database, that was used to categorize the items into seven categories: (1) articles in scientific journals: to international scientific environment; (2) conference papers: scientific environment; (3) book chapters/editorships: international scientific environment; (4) PhD theses: local university environment/educational setting; (5) lectures/teaching books: educational setting; (6) local language articles: to local/national scientific and public/lay audiences; (7) reports: to local organization/third parties, i.e. not-peers. These categories we then used in our analysis.

In the KNAW Yearbook 1942 we found an additional list of publications for the period 1917–1942. Director professor De Lange listed these publications at the occasion of the laboratory's 25th anniversary. The list contains 35 headings with 38 items (1.5 items a year, on average). The distribution over the mentioned categories and the development over time of Hubrecht Institute's output for the period 1916–2009 are represented in Fig. 2a, b.

From the archives of the Hubrecht Institute we were able to inspect Year Books, Annual Reports and Progress Reports, for the period 1937–2007. We also use a historical study about the Royal Academy's Life Sciences Institutes by Faasse (1999), and documents

[8] http://www.hubrecht.eu/information/publications.html.

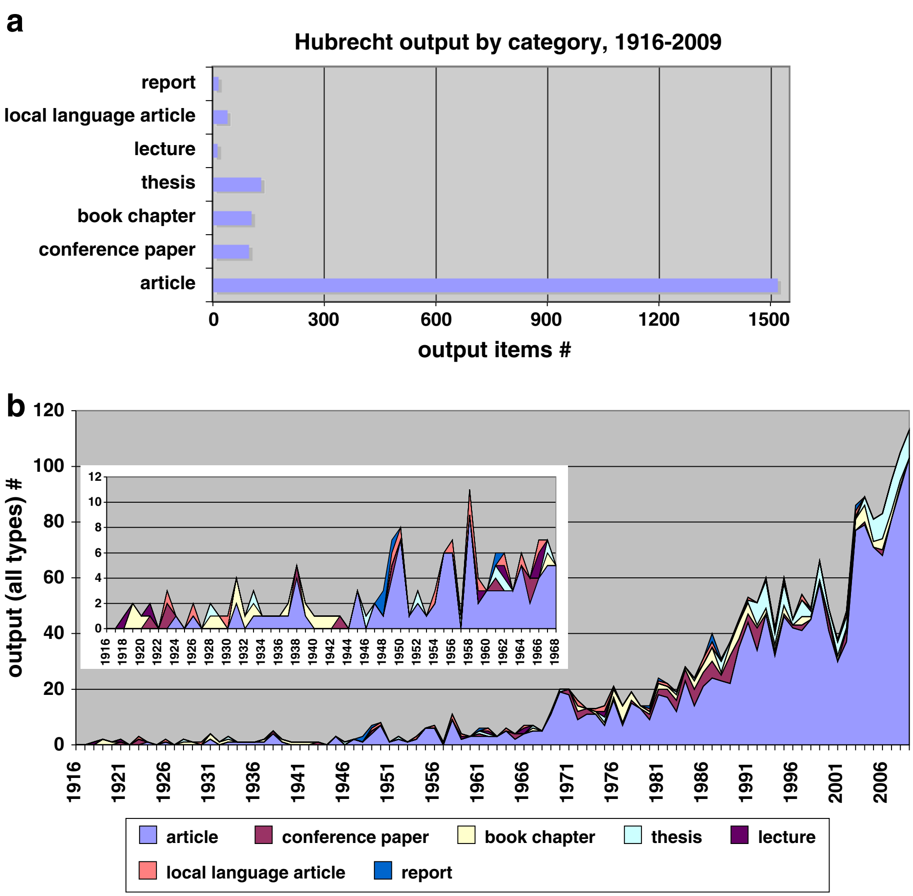


Fig. 2 **a** Hubrecht Institute publications, by category, 1916–2009. **b** Hubrecht Institute publications (*stapled graph*)

written on the occasion of specific events (Piekaar 1964; De Laat 1986, 1996; Clevers 2008). These sources are used to identify the main events in the history of the institute. The main events will be related to the output patterns.

As frame of reference for assessing the output development of the institute, we estimated the growth of the institutes' research field, by conducting a search in the Web of Science for the two main research topics of the institute: developmental biology and stem cell research.[9]

[9] Web of Science, 16 September 2009; Topic = (development * biology); Timespan = All Years. Databases = SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH. 28,218 records. The documents are classified in subject areas as biochemistry & molecular biology (3.192), cell biology (2.406), oncology (1.681), biotechnology and applied microbiology (1.397), genetics & heredity (1.386), plant sciences (1.383), biology (1.215), entomology (1.184), developmental biology (1174), and others. Of the 28.218 found documents, 15.177 were articles; 7.590 reviews and 3.909 proceedings papers. Of the found documents, 26.970 were in the English language. Most were from the USA (12.594), whereas the Netherlands came 11th with 646 records counted.

Web of Science, 16 September 2009; TI = (stem AND cell*); Timespan = All Years. DATABASES = SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH. 67.043 records. Note: As Topic search was larger than

Analysis

Comparison of the output growth of the Hubrecht Institute with Web of science data on its two main subjects, shows that the Institute follows the international growth path (Fig. 3). The continuous growth of Hubrecht institutes' output both contributes to an exponential growth of the field worldwide, and is dependent on the abundance of resources that enabled that growth.

Change point analysis of Hubrecht Institute output data 1916–2009

In order to identify significant changes in the level of output of the institute, we applied change-point analysis (CPA), developed by Taylor (2008), on the time series of summed raw scores over all output categories of the Hubrecht Institute over the period 1916–2009. This analysis identifies five change points where the time series shows a break (Table 1).

We plotted the average levels of the CPA-analysis in the graph with the total annual output (Fig. 4). Visual inspection of the graph and CPA-level line reveals that the change point of 1984, marks the start of continuous growth until 1991, followed by a stable output until 2003, rather then two periods with distinct output levels. Something similar holds for the most recent episode were output grows between 2003 and 2009—stabilization is not yet visible. The periods without changes lasted at most 15 years after the first growth phase around 1949.

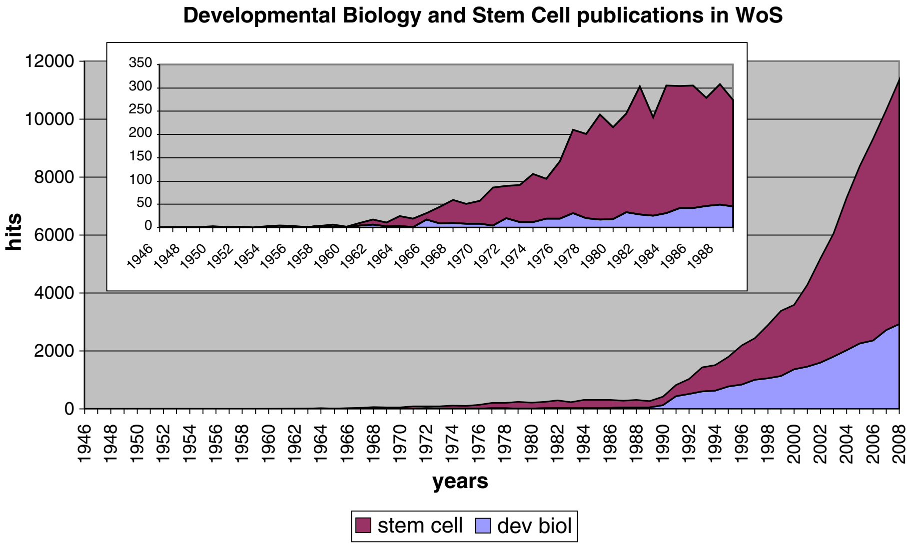
Given the CPA-analysis and visual inspection, we conclude to four periods of stable output each followed by a growth phase. After the first and second stable period, the growth takes place in a few years and the level change is small, whereas later on the growth is stronger, and the part of the phase in which we see growth is longer, with 2008 still growing (Table 2).

With respect to the first indicator (output growth), we have a mixed picture. The output of Hubrecht Institute follows the international trend, as well in terms of type of output (articles), as in terms of growth rate. However, looking more in detail, a pattern of escalating stages can be discerned, with periods of stability followed by short or longer periods of fast growth. This more detailed pattern may well point to changes in local conditions reflecting punctuated adaptation to international field dynamics: catching up with continuous exponential growth. Below we will discuss these local conditions in more detail.

Activity profile stability

If we look at our second indicator, the stability of the activity profile over the years, the increasing focus on international journal articles (=on the peer audience) is reflected in an increase of the profile stability, close to 1.0: profiles of subsequent years are similar

Footnote 9 continued
100.000, we used a TI search, so we underestimate the number of papers here. The documents were classified in many different subject areas, most in haematology (29.187), then in oncology (13.499), immunology (11.286), transplantation (10.495), cell biology (8.408), biophysics (7.912) medicine (6.168), biochemistry & molecular biology (4.167), and in biotechnology & applied microbiology (3.991), all others subject areas were below 5.000 documents for this search. Most records were from USA (24.674), the Netherlands was at 9th place with 2.052 records counted. Document types were: meeting abstracts (28.509), articles (25.875), reviews (3.645) and proceedings papers (3.103). The specific terms used in the search may underestimate activities worldwide, and for stem cell research even more (see above). Still, the general pattern is quite clear: a continuous growth of output in these particular research areas.



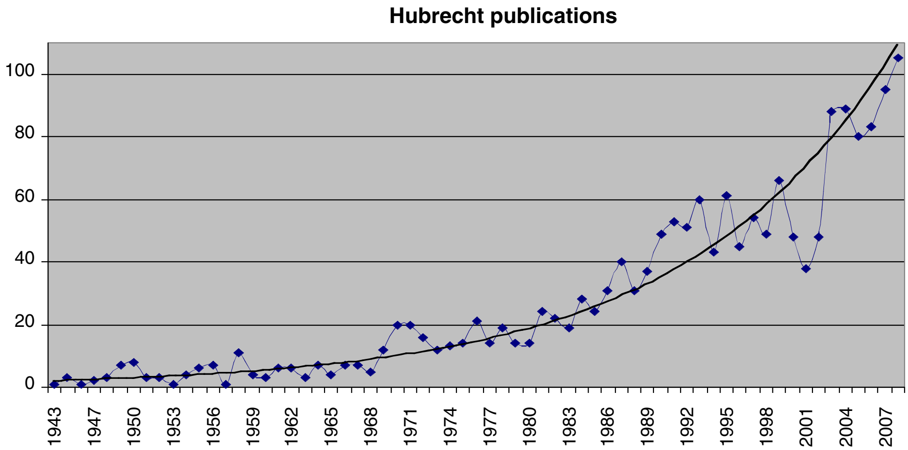


Fig. 3 Records in developmental biology and stem cell research, in WoS, 16-09-2009

(Fig. 5). In the early period from 1916 to about 1943, the value raised to about 0.8, indicating a stabilizing pattern of activities. This was interrupted by the Second World War when output diminished. The activity profile similarity then rises again after 1947, reflecting the continued increase of scientific article output. The outliers in 1957–1958 and 1965–1967 are due to incidental lower production (a single thesis in 1957) and differences in non-articles (book, thesis versus lectures, local language article).

In the long run, we observe an increased orientation to the international science audiences, as reflected in the growing share of articles, from 43 % in the early period (1916–1949), towards some 75 % in the middle periods, and 86 % in the most recent period (2003–2009). So, we find a doubling of the article share, leading to an activity profile dominated by the peer audience.

Table 1 Significant changes[a] in Hubrecht Institute output level[b]

Year	Level change documents/year	Confidence interval	Confidence level (%)	Years in between level changes
1949	From 1.4 to 4.9	(1948, 1955)	100	–
1969	From 4.9 to 16.8	(1968, 1969)	100	13
1984	From 16.8 to 31.2	(1984, 1985)	100	15
1990	From 31.2 to 50.7	(1990, 1992)	100	5
2003	From 50.7 to 92.9	(2003, 2003)	100	11

[a] Change-point analysis (Taylor 2008) (bootstraps = 1,000 without replacement, MSE estimates, >95 % conf.)

[b] Raw scores: all types of output

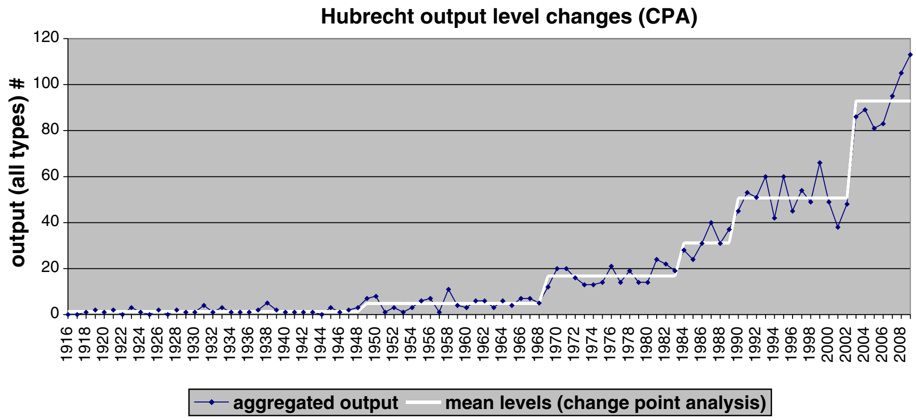


Fig. 4 Hubrecht Institute publications, all output categories, mean levels (CPA)

Table 2 Output change and level periods of the Hubrecht Institute (1916–2008)

Period		Growth type	Annual average
I	1916–1949	Stable output level	1.4
II	1949–1969	Initial increase then stable output level	4.9
III	1969–1984	Initial increase then stable output level	16.8
IV	1984–2003	Long growth period to a new stable output level	50.7
VI	2003–2008	Onset of new growth	92.9

If we leave out the articles, we get a more detailed picture of the other output categories (Fig. 6). We compare the periods discerned by the CPA-analysis, and calculated the number of output in each category for these periods. We left the first period out, because of the low numbers. Within the non-article output categories, one observes clearly a decline over time of the local language publications and lectures, and an initial increase but then again a decline of conference papers and books/book-chapters. Form 1986 onwards, the non-article output consists mainly of PhD theses.

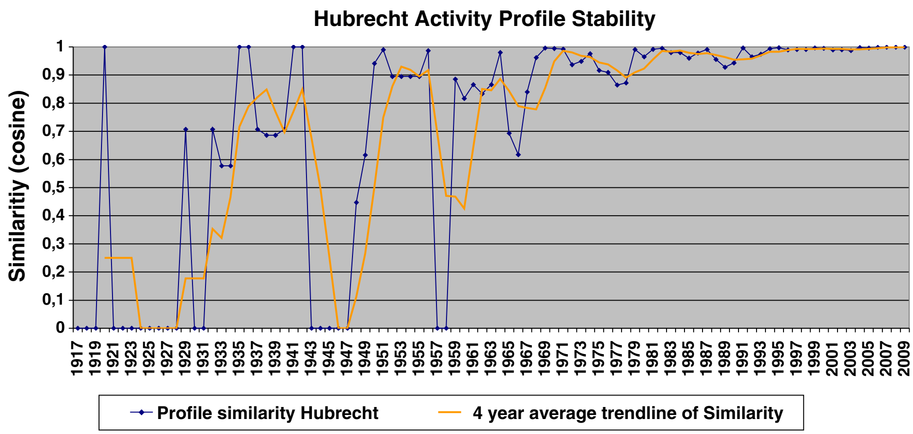


Fig. 5 Hubrecht Institute 'Activity profile similarity'

The increased role of peers as the intended audience of the Hubrecht Institute is also reflected in the language of its publications. Whereas in the early period contributions in the Dutch, French and German language do occur rather frequently, in later years almost everything is published in English.

Focus of activities

The third indicator relates to the changes in research topics of the institute. We extracted the title words from all publications, and identified for all title words the first year of appearance. We then inspected when new (crucial) keywords occur for the first time in the titles of the publications of the institute. First time use of these terms indicates changes in the research program. Several studies about the history of the institute (De Laat 1996; Faasse 1999) suggest that it has been following international research trends: from comparative to experimental to genetics and functional genomics.[10] This is indeed reflected in the selection of title words in Table 3. Interestingly, these new concepts start to appear in the Hubrecht publications around the transitions between the periods. In the fourth period (1984–2002) the new words are introduced during the longer output growth phase between 1984 and 1994.

This results in our third indicator. Figure 7a shows the annual percentage of new title words. The percentage of new title words of course shows a downward trend, as the number of 'old' title words becomes quickly larger over time. In the early period, the number of papers remains small, making the large fluctuations easy to occur. Figure 7b is the same figure, but now split over two y-axes, showing the fluctuations around downward trend more clearly. Around 1943, 1953, 1965, 1987, 2000 and 2003, we observe the share of new title words slightly increasing. This roughly corresponds to the changes in output level. More precisely, director changes co-occur with changing trends in new title words, suggesting change in scientific focus. The only moment where this is not the case is around 1960 when change in focus happens without a change of directorship. But there, the

[10] And of course contributed to these trends. Several directors were internationally leading pioneers in the field, and e.g., Nieuwkoop founded the International Society of Developmental Biologists.

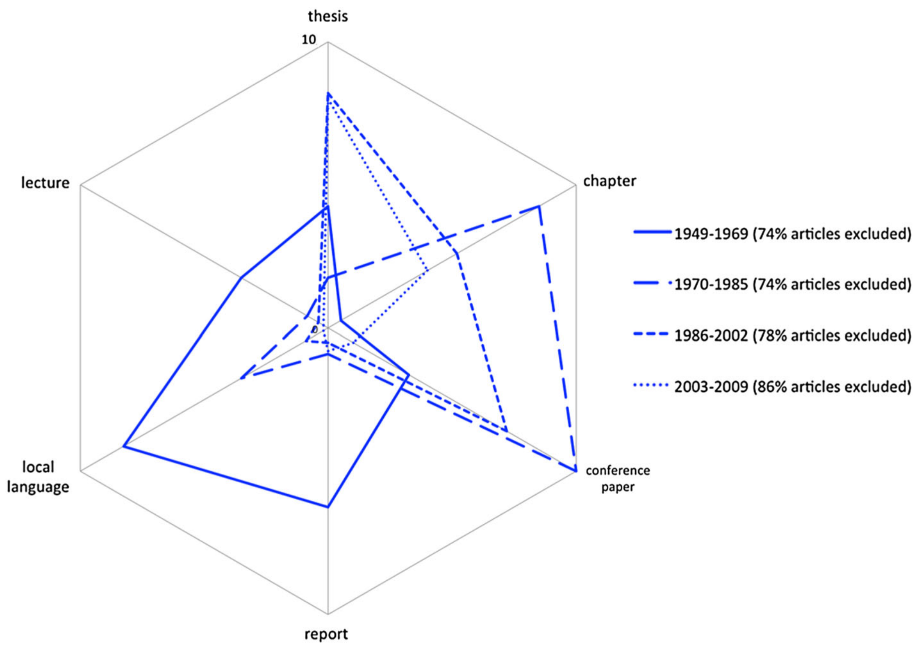


Fig. 6 Activity profiles, 5 periods

Institute moves to the Utrecht University campus, and shows a large increase of own research. Overall, Fig. 7 suggests that the changes in output levels go parallel with the exploration by the Hubrecht Institute of new developments within the field.

Summarizing, the development of the Hubrecht Institute shows the following characteristics, in terms of the three indictors introduced here. Firstly, a continuous growth of activities can be observed, leading to a stepwise growth of output. This growth has the form of a sequence of life cycles of varied duration. Secondly, The Hubrecht Institute's research profile shows an increasing emphasis on scholarly articles (for peers) and PhD theses (new graduates). Thirdly, the research focus of the institute increases in every growth phase and then slightly decreases when a new phase starts—followed again by gradually increase.

Explanation of found patterns

Above we first inspected the growth of output of the Hubrecht Institute over its entire life history, and compared this to the growth of international literature in its two core areas: Developmental Biology and Stem Cell Research. We did this by inspecting the Web of Science using keywords that indicate the international dynamics of *developmental biology* and *stem cell research*. Quantitatively the Institute appears in line with trend in these areas, but does so in a stepwise fashion. In order to link the patterns with the history of the institute, we inspected a number of historic sources to track events around the found change points. In that way we can find out whether events and/or processes can be identified explaining the periods of growth and stability that we discerned above. In Table 4 we

Table 3 Introduction of new title-words in Hubrecht Institute publications—examples

Keywords in title (>10 times used 1918–2008)	First usage
Development	1918
Ontogenesis	1919
Developmental *stages*	1921
Placenta(tion)	1919
Urodeles	1943
Germ cells	1945
Experimental	1946
Egg	1953
Influence	1953
Cellular	1965
Cell	1968
Genetic	1970
Cancer	1982
Stem cell	1987
Gene	1987
Genomic	1992
Heart	1995
Caenorhabditis	2000
Elegans	2000
Cardiomyopathie	2003
Intestinal	2003
MicroRNA (-producing enzyme)	2004
(Neuro) Progenitor (compartment)	2006
Mismatch (repair deficiency in germ line)	2008

list 'noteworthy events' and processes we took from the available sources mentioned in the data section.

1917–1943: collection as service to international science in comparative embryology

This period starts with a private fund and the establishment of an Institute for Embryology by members of the Royal Academy of Sciences in 1916, after the death of Prof. A.A.W. Hubrecht in 1915. The embryonic collection was to be maintained by a director, D. De Lange, who was appointed in 1917, to serve international scientists interested to perform research in comparative embryology at the laboratory. After retirement of Prof. De Lange in 1947, who had done sparse research himself, novel experimental research was introduced by the young and enthusiastic zoology student and PhD candidate from Utrecht University, P.D. Nieuwkoop. The start of experimental work at the laboratory was a delayed one, compared to the field of developmental biology internationally (Faasse 1999).

1949–1969: serving international science in experimental embryology

The post-war period is marked by activities of P.D. Nieuwkoop and Prof. Raven—the new director, and professor of zoology at Utrecht University—to make the Hubrecht Laboratory a 'truly international center for embryological science' providing working places and

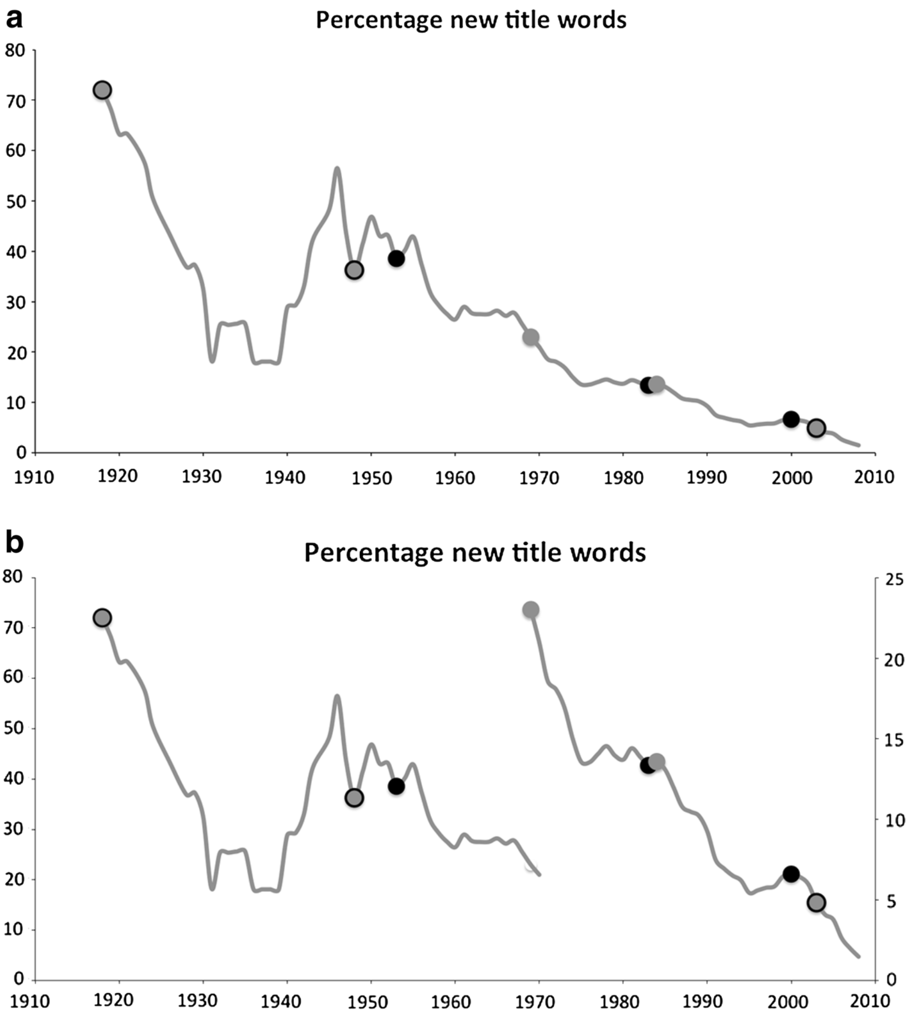


Fig. 7 **a** and **b**. New title words: periods of increasing focus and of focal change. % new word-stems, frequency >5 per year, 5 years moving average; *grey dot*: start new phase; *black dot*: new director; *grey dot with black border*: both

facilities for experimental research by visiting scientists.[11] Nieuwkoop and Raven increased the services to science in relation to the International Institute for Embryology (IEE).

- Maintain the Central Embryological Library and Collection;
- General Embryological Information Service (GEIS), a yearly publication (1949–1980);
- International Research Teams (IRT's) providing opportunity to groups of young students from all around the world to visit the laboratory for half a year of thematic work (1954–1968).

[11] KNAW Yearbook 1948, pp. 92–96; 1949, pp. 115–116; 1950, pp. 209–210.

Table 4 Noteworthy events in the history of the Hubrecht Institute

Year	Noteworthy events
–1915	Professor AAW Hubrecht, professor of zoology at Utrecht University, collects embryonic material from various species, for comparative studies
1910	Prof Hubrecht permitted to devote to study the embryological collection
1911	Institute International d'Embryologie IEE, founded by prof Hubrecht
1915	Death of prof Hubrecht (1853–1915)
1916	Foundation of Hubrecht Fund to the establishment of a laboratory for embryological research in the residence of the late prof Hubrecht
1916–1947	First director, appointed by KNAW, Prof. D De Lange (1878–1948†)
1941	25 years Hubrecht Laboratory; De Lange lists publications for 1917–1941
1943	First research publication by PD Nieuwkoop (1917–1996†)
1944	Prof. Raven, acting director, replacing De Lange because of illness
1946	PhD-thesis, Nieuwkoop (supervisor: prof. Raven UU)
1947	From June: Nieuwkoop acting director (replacing De Lange, who retired)
	Reorganization of the laboratory: more working tables for visiting scientists and facilities (aquarium unit) for experimental studies on living animals
1948–1953	Second director: Raven; Nieuwkoop to function as deputy director
	Several national and international subsidies for collection and library function
1950	Nieuwkoop full time at Hubrecht (before halftime at zoological lab. UU)
1951	Nieuwkoop to USA for a scholarly-visit of a year
1953–1980	Third director: Prof. Nieuwkoop, Prof. Raven member of steering committee
1964	Move to building at the university campus; research staff funding increased
1966	Hubrecht Laboratory 50th anniversary;
	Embryological collection of Professor Hill donated to Hubrecht Laboratory
1968	IEE reorganized as International Society of Developmental Biologists, ISDB, initiated from the Hubrecht Laboratory by Nieuwkoop
1970	J Faber deputy director of Hubrecht Laboratory
1974	Retirement Raven from University Utrecht, as professor of zoology
1978	Retirement of Nieuwkoop announced (formal retirement 1979)
1982–1983	Scientific Reorganization Committee (Faber secretary and acting director): renewed scientific program: 'Regulation of early embryo development'
1983–2000	Fourth director: De Laat (retires early because of illness, in 2000)
1985	Formation of Netherlands Centre for Developmental Biology NIOB, with UU New formation plan, including NIOB activities, accepted by the Ministry
1986	70th anniversary Hubrecht Laboratory. Internal reconstruction of building and expansion of laboratory research potential realized to carry out research plan
1987	First Hubrecht PhD-student thesis defended at University of Utrecht
1988	PhD graduate courses given at NIOB
1990	Developmental Biology appointed as focal theme at Utrecht University
1992	PhD Research School for Developmental Biology established at NIOB
	ESF fellowship program approved, with secretariat at NIOB, for 5 years
1993	Reorganization research program 1994–1998, approved by the KNAW board
	ISDB-Prize for Nieuwkoop for achievements in development biology
	Director De Laat absent for a year, recovering from a serious car accident
1996	Death of Nieuwkoop (1917–1996); 80th Anniversary of Hubecht Lab.
	Decision to make building of a new larger laboratory possible, planned: 1999

Table 4 continued

Year	Noteworthy events
1998	De Laat to retire ultimately 2000 (because of illness), search for new director
2000–2007	Fifth director: Prof. R Plasterk (until 2007, when he was appointed as minister)
	New larger building opened in 2000; addition of four new research groups
2001	Collaboration with Interuniversity Cardiology Institute ICIN, KNAW-funded
2002–present	Sixth director: Prof. H Clevers (from 2002 to 2007 co-director with Plasterk)
	Addition of new groups, based on funds from third parties (external funding)
	Restructuring of building to accommodate new additional research groups
2004	Collection to the Museum für Naturkunde, Humboldt University, Berlin
2007	Hubrecht Laboratory renamed as Hubrecht Institute
	Plasterk leaves to become minister of Education, Culture and Science
2008	Evaluation assessment, with committee site visit, results in excellent scores
	Growth by affiliation with Utrecht University Medical Center (adds 4 m€/yr)
	New building facilities started to facilitate new growth of staff

Sources Hubrecht Institute website, Progress Reports, documents; KNAW annual reports, yearbooks

To realize all this, several subsidies were acquired successfully. By 1950 the staff had grown to 10 people, and the building provided 20 workplaces for international visiting scientist.

1969–1984: increased research activities in a new modern building

By the midst of the sixties, the laboratory moved to a modern building on the new Utrecht University campus, providing more space and modern facilities to work with. In the period 1965–1970, after the removal, staff numbers vastly increased, mounting up to 57 staff members by the end of 1970: 3 management, 10 scientific and 44 support staff.[12] The collection of prepared embryos was enlarged by the addition of the collection from the late Prof. Hill. The Laboratory was developing as an 'international center for embryology' directed at fulfilling the goals of the International Institute for Embryology (IIE), that was reorganized in 1968 as the International Society for Developmental Biologists (ISDB), a section of the International Union of Biological Scientists (IUBS), with its administrative seat at the Hubrecht Laboratory. The 1971 Yearbook states: "The Laboratory is in a phase of stability. The Maximum number of eight research units is reached." Governmental subsidy had risen to €700.000 by then. The Laboratory was equipped for experimental work by its own staff as well as by visiting scientist, and still provided information services to international scientists in the field. At the end of the seventies, Nieuwkoop stepped back as director, after retirement, staying at the laboratory as a researcher until his death in 1996.

1984–2003: molecular genetics studies on multiple model animals

In 1982 an external scientific committee was installed by the Royal Academy (KNAW) to renew the research program. Main issues were the establishment of a new research unit on gene-regulation and discontinuation of the international service functions that the

[12] KNAW Yearbook 1971, p. 157.

Laboratory fulfilled. In 1983 the scientific committee proposed the new research program for the Hubrecht Laboratory (1983–1988), specifying needed resources and a new directorship. After acceptance of the program by the staff, De Laat was appointed as new director. In addition, the Ministry initiated a National Centre for Developmental Biology/Embryology (NIOB) at Utrecht, wherein the Hubrecht Laboratory would collaborate with Utrecht University.[13] By 1985 the new plans were formally accepted, the research staff had doubled since 1983, and the formal establishment of the Netherlands Centre for Developmental Biology (NIOB) took place, including collaboration with Utrecht University. After the reconstruction of the building and renewal of the institute, and with additional research capacity, 'conditions are now fulfilled to carry out the planned research program in the coming years'.[14]

In 1990, Developmental Biology was appointed as a focal theme, which intensified collaboration between the Hubrecht Laboratory and Utrecht University. The NIOB was appointed by the Ministry to organize a graduate school for developmental biology. By 1990, some 40 PhD students attended the school, 30 of which preparing a PhD thesis at the NIOB. Two years later the school acquired the status of National Graduate School for Developmental Biology, approved by the Royal Academy of Science.[15] In the same period, the Hubrecht Institute took the initiative to establish a European Science Foundation Network on developmental biology, with administrative seat at NIOB. An ESF-fellowship program in Developmental Biology followed in 1992, stimulating exchange of researchers. The growth of activities was largely realized by externally funded projects, and it lead to a pressing shortage of working space in the building. Governmental block funding did not follow the strong growth, and new reorganization seemed inevitable.[16] The process was delayed by the absence of the director for a year (because of a car accident). On return, he wrote: "The—drastic—reorganization has provided ample opportunities for a further strengthening of the research program of the Institute, and, most importantly, we may now look forward to the realization of a new, larger, laboratory building in 1998."[17]

2003–2009: further increase of activities and collaborations

After early retirement of De Laat, a new boost of activities started with the successive appointment of two new directors, both bringing in their own and other new groups to the Hubrecht Institute. The shifting focus from collection and service to research is now finalized with the shipping in 2004 of the collection to the Museum für Naturkunde of the Von Humboldt Museum at Berlin. Besides bringing in new groups, the new directors acquired additional resources, from collaboration within the Interuniversity Cardiology Institute of the Netherlands (ICIN) in developmental research of the heart, from participation in novel (competitive) national research programs, and from affiliation with the Utrecht Medical Centre. Output again grows to an even higher level, and continuous enlargement of building and research facilities is needed to accommodate new starting groups and research activities.[18]

[13] KNAW Yearbook 1983, 1984.

[14] KNAW Yearbook 1985, 1986.

[15] KNAW Yearbook 1989, 1990, 1991; Annual Report KNAW 1992.

[16] Hubrecht Laboratory, Progress Report 1993.

[17] Hubrecht Laboratory, Progress Report 1994.

[18] Hubrecht Institute/Laboratory Progress Report 2007, 2006, 2005, 2004.

Discussion

The analysis of the various phases reveals the role of a few factors that are summarized in the above Table 5. These factors are (i) the development of the research field; (ii) the institutional and organizational environment—especially the relations with the Utrecht University and with the Royal Academy of Science, and (iii) the role of individuals, especially the various directors of the institute.

The Hubrecht Institute and the field of developmental biology

The development of the Hubrecht Institute mirrors the development of the changes in developmental biology over a century (1916–2009). This is illustrated by accounts of the history of the Institute: "The Hubrecht Laboratory developed from a small collection maintaining institute, with a few staff members, to a multidisciplinary research institute with fifty FTE research staff in the 80s." (Faasse 1999). As the institute's director stated in 2003: "The Hubrecht Laboratory, established at the beginning of the twentieth century, has evolved through subsequent phases of the field of developmental biology: from comparative embryology (Hubrecht), to experimental manipulation of embryonic development (Nieuwkoop), to molecular studies of signal transduction, to genomics and functional genomics."[19] Besides the shift in content, the institute changed from a service center for international developmental biology research(ers), to an 'international center in this field of research' [developmental biology], attracting the best researchers from within the country as well as from abroad.[20] Where in the early period, under De Lange, Nieuwkoop and Raven, this regarded visiting scientists from other countries; research is now done by members of the institute staff itself, with a focus on young researchers. Other changes to be mentioned are the shift from maintaining a collection of gathered embryonic material to experimental work on living animals, which also had to be taken cared of, and the development of information technology and bibliographic databases that made the international library service obsolete.

The major changes in the scientific development of the institute, in sum, are thus threefold:

(1) A shift from serving international science/visiting scholars to research output by own staff.
(2) A shift from collection of prepared embryonic material for comparative studies to experimental research on—a growing number of—living model animals
(3) A shift from visual inspection and cell-related research to molecular analysis techniques.

These qualitative changes are reflected in the changes in output. Here we find an increase reflecting the (exponential) growth of the developmental biology field. The institute follows this growth in a stepwise delayed[21] fashion, as internal conditions had to be adapted to the external changes in the field, as discussed in the next sections.

[19] Hubrecht Laboratory Progress Report 2003.

[20] Hubrecht Laboratory Progress Report 2005, 2006.

[21] Stepwise, as we observe periods without output growth of the HI, whereas global output steadily increases.

Table 5 Development phases of the Hubrecht Laboratory/Institute

Phase	Time period	Local characteristics (leading people and events)
I	1916–1949 Collection comparative embryology serving guests	Establishment of Hubrecht laboratory with its collection, housed in Utrecht Director: Prof. D De Lange (until 1947; delayed retirement) Focus on collection of embryonic material as service material, and on contact with international scholars in comparative embryology. Some 38 publications by the director and a few others from the Lab
II	1949–1969 Empirical studies on living animals service to international scholars	Prof. C Raven, supervisor of P Nieuwkoop, director from 1947 Nieuwkoop, director from 1953 to 1980, Raven in steering com Enlargement of facilities for empirical studies by visiting scholars GEIS international oriented information service (until 1980) International Research Teams (1954, '56, '58, '60, '65, '68) Move to building at University campus + extra research staff (1964)
III	1969–1984 Intensification of activities	Nieuwkoop director until 1980 (retirement) Added collection prof. Hill (1967) + foundation of ISDB (1968) Move to new larger modern building at University Campus Hubrecht Institutes' staff's own research output to higher level
IV	1984–2003 Long growth period leading to higher stable level of output	Prof. De Laat, director (1980–2000), until retirement New program with gene regulation and multiple model animals Focus on multidisciplinary studies, new animal models, and novel molecular genetics techniques Growth period due to PhD Graduate School, ESF fellowship Program, and UU focal theme Developmental Biology Stabilization of output level: illness of director; lack of workspaces
V	2003–2009 Renewed output growth	Prof. R Plasterk (2000–2007) and prof H. Clevers (2002–present), directors Vast increase in the number of groups, affiliation with UMC To larger building (2000), for growing number of research groups Collection transferred to the Museum für Naturkunde, Berlin (2004) Affiliation with UMC, including additional budget (2008)

Organizational and institutional environment: Utrecht University and the Royal Academy

The Hubrecht Institute always had strong relations with Utrecht University, through personal affiliations, through collaboration, and through shared facilities. First of all, most of the core people were or became professor at Utrecht University (Hubrecht, Raven, Nieuwkoop, de Laat, Plasterk, Clevers). The PhD courses and later the graduate school were organized in collaboration with Utrecht University, as was the Netherlands Institute for Developmental Biology (NIOB). Furthermore, changes in mission, object, and method of study implied changes in need for lab space and for research facilities. Especially the size of the housing of the institute regularly formed a serious constraint. Large housing was realized at several occasions at the campus of Utrecht University. These relationships certainly facilitated growth of Hubrecht Laboratory.

More recently, the Hubrecht Institute has strongly integrated with the Utrecht University Hospital, while remaining an institute of the Royal Academy of Science. The development of the Hubrecht Laboratory is also closely connected to the Royal Academy, which at crucial moments repositioned the institute towards fundamental research (Faasse 1999), and stimulated multidisciplinary research themes in national collaborative settings—in line with national science policies.

The role of individuals

The subsequent directors played a crucial role in the development of the institute. It started with the assembling of a vast collection of embryonic material from mammalian species by Hubrecht. The pioneering research on germ cells by Nieuwkoop started experimental work at the Hubrecht Laboratory, while the initiatives of Raven and Nieuwkoop intensified the international service function of the institute. In fact, the stepwise growth of the research output coincides neatly with changes in leadership in the institute. This suggests that every new director was able to give the institute a new impulse, resulting a higher level of activities and output than before. However, this strong role of individuals also brings a risk. Most of the directors stayed very long in service, which may hinder the institute to keep up with new international developments. The skills and interests of the consecutive directors may get less central as the field develops. In the long run, this may have had a conservative effect and may have hindered sustained growth—as the sometimes rather long phases of stability suggest.

Preventing life cycle decline

We found long periods of stable output up to 15 years, which due to local impulses were followed by new periods of growth. So, absolute life cycle decline has not been observed, but in a continuously fast growing research field, long periods of non-growing output of the institute can be considered stagnation. As new growth phases correlate with changes in the institute's leadership, one may conclude that changes of leadership could have been implemented earlier.

Conclusions

In this paper we applied a theory based life cycle model with indicators on the long-term history of a leading research institute. The indicators suggested that the institute developed over five life cycles, in which the audiences, activities and focus changed. The indicators show that the increase of the institute's output follows the international growth within the relevant fields. The indicators also show an increased focus on the international peers, and a decline of service activities and local audiences. Finally, the indicators capture major and smaller shifts in the research focus, related to the international development of the field, to pioneering individuals, and to local science policy circumstances.

When comparing the bibliometrically identified life cycles with historical information about the field of developmental biology and about local changes and conditions, the relevance of the indicators could be validated. The stepwise growth path resembles a pattern of escalation of logistic growth (De Solla Price 1963). It can be interpreted as a sequence of life cycles, new ones starting at the ending of the former. In terms of organizational development models, we see a 'sequential stage' development with periodic adaptation to (increased) environmental opportunities, thus: 'punctuated adaptation'. Interestingly, the life cycles are related to local conditions and events, in particular the succession of directorships following each other after retirement.

In an earlier study, we focused on social science institutes (Braam and Van den Besselaar 2010). There we found a similar stepwise development was observed, and also there the long growth and stabilization phases (first stages of the life cycle) coincided with enduring directorship. Escalation (De Solla Price 1963) may result from attempts to avoid reaching a ceiling of growth, e.g. by searching extra resources. In that study, we found a strong growing market for applied research, leading to a boost of activities but here for societal and policy audiences. Overall this suggests that the indicators are useful for analyzing the developments of research institutes of different nature.

Further work

Moed (2000) found development phases in output of research groups of a biotechnology and molecular biology department in Flanders. In particular, he suggested that emerging groups (in the first phase of a life cycle) aim at quantity of publications, whereas more established groups aim more at quality of publications, e.g. by focusing on high impact journals. This should be visible by increase of high impact journals in a groups' research profile (Van Raan 2000), as indeed was found for the Hubrecht case (Van Leeuwen, personal communication). This observation suggests a fourth life cycle indicator.

How can we explain that the lifecycles of institutes coincide with the life cycle of the directors? First part of the explanation could be the following. When hiring a new director, one would expect the selection of an excellent and high reputation scholar who is in the center of the relevant research front(s). If that is the case, the new director will be able to successfully attract large research grants, organize other resources and facilities, and attract talented young researchers. This will lead to strong growth of output and to focusing of the research. However, if a director is long in office, the field may move on, and the directors' interests, skills and resulting research agenda may become less connected to the international developments of the field. This will result in stagnation of the further development of the institute and a stable situation (or decline) may be the result. This could be studied empirically by mapping the topical structure of an institutes' output over time, and comparing this with the topical structure of the field as a whole. This may also lead to a refinement of the third indicator (research focus), which is still rather rude. A second part of the explanation may refer to local conditions. Local organizational, institutional and financial factors may lead to reorientations of institutes, which may lead to a new life cycle. As these local dynamics often lead to changes in leadership, the two factors (leadership; local factors) may correlate strongly. The comparison of local and field dynamics may further better insights in this.

Implications

The results of our cases suggest that development phases of groups and institutes should be taken into account in science policy and research management and evaluation (see also Nederhof 1985; Moed 2000; Larédo and Mustar 2000). Furthermore, our analysis points to the conditions and events that influence the development of groups. The influence of individual initiatives, ageing and succession of directorships, seem to be superposed on the overall influence of the dynamics of the international field wherein groups are active. The case study results, so far, show that the combination of the *life cycle model* with the use of time series analysis of bibliometric output indicators is helpful to understand the development of research groups and institutes. In particular, the model and time series analysis helps to locate points and periods in time to look for crucial events and conditions. The developmental patterns and the crucial events help understanding the position(ing) of groups. Further case studies are needed to gain better insight in the implications of life cycles for research evaluation. If systematic relations can be found between research field dynamics, output growth and leadership changes, the proposed life cycle model can be used as a diagnostic tool for determining the appropriate moment for crucial changes in research institutes.

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