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DYNAMICS OF DISSEMINATION IN THE CASE OF AFFINITY CHROMATOGRAPHY

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1. INTRODUCTION

Within the structure of developing scientific knowledge, techniques are the links between the various subject areas and this is clearly shown in the citation networks. Thus if we link subject areas (research specialties) through the co-citations[1]*, then we find that biochemistry and biomedicine form a macro-cluster, consisting of individual clusters formed by the 29 most cited methodological articles[2].

Of all the scientific disciplines biochemistry and molecular biology are the most method-oriented: they show a clear predominance of methodological papers amongst the most cited articles. According to our estimates, made on the basis of the most cited articles in biochemistry, biomedicine and psychology (as indicated in *Current Contents*[3]) 75% are intrinsically methodological and monopolize 85% of the citations (the total number of 156 articles examined offer 210,759 citations, while the methodological articles (118) have 178,488 citations, *i.e.* on the average 1512 per paper). In the field of biochemistry, one such methodological paper gives 1996 references, while a non-methodological one has 949. (In biochemistry the proportion of references to methodological articles within the "classics" reaches 92%[4].) Hence an understanding of the patterns involved in the creation and diffusion of new scientific methods in biochemistry and molecular biology is of great importance for the forecasting of developments and the planning of scientific policies.

Affinity chromatography represents an important methodological innovation in chemistry and biochemistry in the second half of the twentieth century. First

* The most commonly cited papers, when linked through co-citations in other publications, form consistent groups (clusters) of key works, representing the state-of-the-art of the corresponding subject area.

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developed at the end of the 1960s, it emerged on the "map" of biomedicine as a scientific speciality in its own right already in 1972. Its links with other areas of knowledge grew rapidly; in 1972 it was linked with the "immunology" cluster by 125 co-citations, in 1973 the linkage increased to 235 co-citations and a new link with the "cyclic AMP" cluster emerged with 192 citations[2].

There are a number of reasons why the history of the dissemination of affinity chromatography is of special interest for the study of science as a whole. First, as indicated above, the method has been used in many subject areas, it is part of the "methodological skeleton" of modern biochemistry and has quickly become an element of modern paradigm in this area. Secondly, affinity chromatography has a long prehistory —the scientific community had practically awaited the emergence of such a method— a fact that reduced to a minimum any delays in its dissemination, which might otherwise have occurred due to a non-awareness of its existence on the part of the research community. Thirdly, since the utilization of affinity chromatography does not involve the acquisition and mastering of sophisticated and expensive equipment, it represents a graphic example of "soft" technology. This eliminates yet another factor hampering the dissemination of this method. Apart from that, the method exhibits a specific and very interesting peculiarity due to the fact that it was arrived at almost simultaneously by two groups of workers, one in Sweden[5,6], the other in the U.S.A.[7], which makes it an ideal case for comparison of the dynamics of dissemination.

2. METHOD OF INVESTIGATION

The evidence which is found in the literature provides an objective insight into the way a given scientific method is utilized. Therefore, we adopted for our investigation the information approach, *i.e.* the study of the dynamics shown by references to publications of the inventors of affinity chromatography. The quantitative data characterizing the utilization of affinity chromatography from 1968 to 1979 were taken from the *Science Citation Index*[8]. We proceeded on the assumption that a worker using affinity chromatography would necessarily cite the authors of this method. This is especially true with new methods which have not yet become routine. The yearly number of citations was taken from the *Citation Index*, the patterns of co-authorship and titles of articles from the *Source Index*, and the countries in which the journals are published from the *Journal List*.

3. RESULTS AND DISCUSSION

In many studies on the dissemination of technological innovations, diffusion is described with the aid of a logistic curve, *i.e.* as a process which is accelerated in its initial stage[9]. Scientific methods such as affinity chromatography represent in their essence an integral technology of research (see ref. 10 for this concept). And indeed the number of citations of the first work on affinity chromatography[5] has grown exponentially (Fig. 1). This figure alone clearly demonstrates the speed with which affinity chromatography was introduced in the research laboratories.

However, a more comprehensive idea regarding the dynamics of its dissemination is provided by the extent to which all publications by P. Cuatrecasas, an

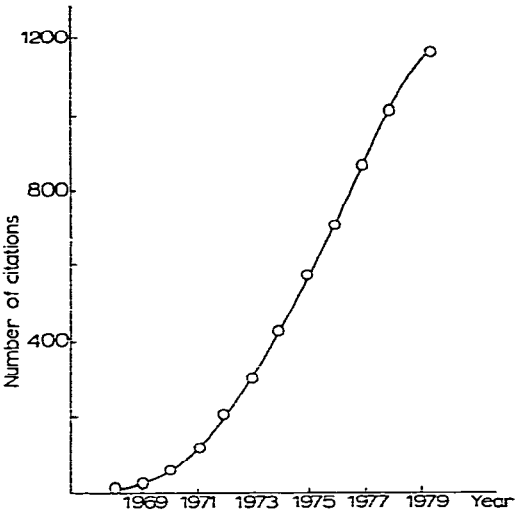

Fig. 1. Cumulative citation curve for Axén *et al.*'s paper[5].

author from the American group of inventors of the method, are cited. It is interesting to compare these dynamics with those of the dissemination of paper chromatography during its first years. Fig. 2 shows the rise in the total number of citations of the inventors' papers after the first publication on affinity chromatography (Curve 1) and the rise in the number of papers carrying references to paper chromatography (Curve 2).

Fig. 2 shows that, following the creation of paper chromatography in 1944, the method passed through a four-year induction period before its rapid dissemination began. Until 1947 the number of workers using this method remained almost constant. Conceptually and technologically affinity chromatography is far more intricate

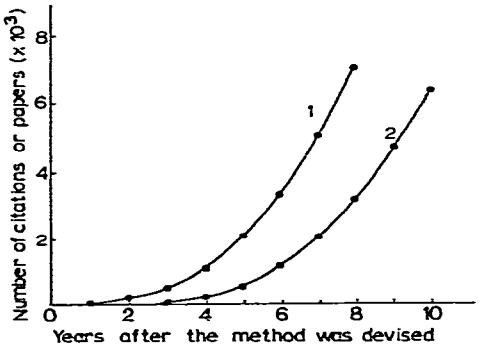

Fig. 2. Dynamics of dissemination of affinity chromatography (since 1968) and paper chromatography (since 1944). 1, Cumulative citation curve for Cuatrecasas *et al.*'s and Axén *et al.*'s papers. 2, Cumulative curve indicating the growth in the volume of publications on paper chromatography, as reflected in the bibliography in ref. 11.

than paper chromatography, but its dissemination was preceeded by a far shorter induction period. This goes to show that affinity chromatography was fully in accord with the methodological paradigm that had obtained in biochemistry by the 1960s whereas paper chromatography required a change in conceptual pattern for its mastery.

Innovators in the production field who have mastered an new technology earlier than others receive an additional remuneration. Transposing this to the scientific scene, if one takes the number of citations as a measure of professional remuneration in science, it may be expected that the faster the authors master a new method the more often they will be cited in the literature. To check this hypothesis, we selected at random 20 authors who cited ref. 7 in 1970 (group 1), and 20 authors who cited this work for the first time in 1974 (group 2). Table 1 indicates citation averages relating to the authors of both groups. As is evident from Table 1 "innovators" are cited considerably more often than those workers who mastered affinity chromatography only four years later. Of course, this correlation does not allow cause and effect to be identified, because productivity and innovation tend to complement each other. However, the fact that the correlation does exist at all is eloquent enough. One may also note that already a year after the publication of the papers in which affinity chromatography was utilized (1975) the citation frequency of the work of the second group of scientists increased considerably: from 16.4 to 23.1 citations per year.

TABLE 1

CITATION RATES OF PUBLICATIONS OF SCIENTISTS WHO BEGAN TO APPLY AFFINITY CHROMATOGRAPHY IN 1970 (GROUP 1) AND IN 1974 (GROUP 2)

Group	*Average number of citations per author per year*		
	1970–1974	*1975*	*1977*
Group 1	62.6	67.3	73.0
Group 2	16.4	23.1	35.0
Ratio of citation rates of group 1 to group 2*	3.8:1	2.9:1	2.1:1

* If, in an effort to reduce the influence of extreme values, we omit the values for the three most cited and the three least cited authors in each group, the following ratios are obtained: 6.1:1 (1970–1974), 2.8:1 (1975) and 2.2:1 (1977).

Technically the variants of affinity chromatography, as developed in the Swedish and the American laboratories, differed only insignificantly, in contrast to the dynamics of their dissemination, which differed sharply. Already in the first publications the differences in the citation pattern are clear (Fig. 3).

Whilst the annual number of citations of Axén *et al.*'s[5] paper increased until 1977, the number of citations of the paper of Cuatrecasas *et al.*[7] stabilized already by 1972. However, as was already pointed out above, it would be more rational to

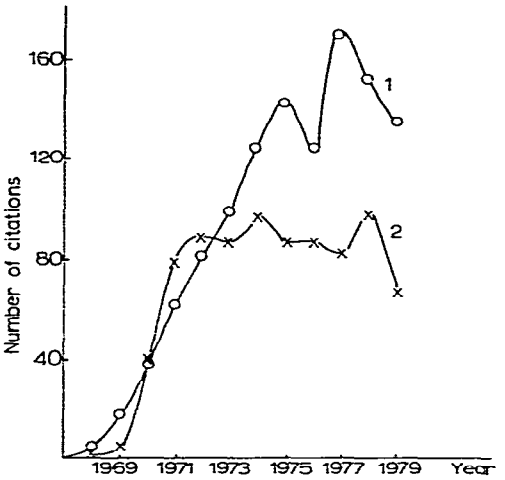

Fig. 3. Breakdown by years of citations of papers by Axén *et al.*[5] (curve 1), and Cuatrecasas *et al.*[7] (curve 2).

characterize the dissemination of both variants by the citation dynamics of all publications by Cuatrecasas, beginning in 1968, and by that of ref. 5. (For a more detailed validation of this approach see ref. 12.)

It is reasonable to assume that some references to the work of Cuatrecasas should be related to the results of his other research, rather than to affinity chromatography, but the error that this may cause is relatively small. A case in point is the fact that though the citation rate of Cuatrecasas' work published prior to 1968 is rather high (67 citations in 1970), it corresponds to the general laws of obsolescence, to which scientific information of "normal" values is subject (a two-fold reduction in the citation rate occurs every five years). No doubt, since 1968 Cuatrecasas published highly valuable results (due in no small measure to the utilisation of affinity chromatography, or methods allied to it; for example, the method involving the quantitative measuring of the coupling of insulin to its receptor on the surface of the cell[13]), but the mistake arising from the citation figures can surely be offset by the fact that we thus omit a large number of references to work on which his name was not the first on the list of authors*. However, a considerable number of those papers are devoted to applications of affinity chromatography.

Fig. 4 indicates the citation dynamics of the publications by Cuatrecasas and by the Swedish authors[5]. Towards the end of 1979, the number of citations of the American work reached 9000, while that of the Swedish work was only 1100**. How can this enormous difference in the dissemination of such similar variants of a method be accounted for? The difference is all the more surprising in view of the fact that the

* During the 1970–1974 period, Cuatrecasas published 96 articles, but in only 39 of them he was the first named on the list of authors.

** We leave out of account subsequent publications by the Swedish authors, because they, judging by their titles, apply to other topics (immobilized enzymes). However, even if they are taken into account, the parameters of curve 2 in Fig. 4 will not change substantially because Axén *et al.* were referred to 365 times up to and including 1976.

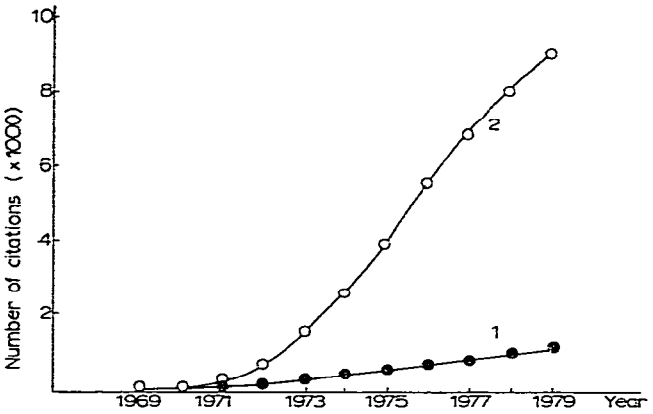

Fig. 4. Cumulative citation curves for papers by Axén *et al.*[5] (curve 1), and Cuatrecasas, published beginning from ref. 7 (curve 2).

article by the Swedish authors[5] appeared one year earlier in a widely read journal, and one of its authors was J. Porath, who had gained a world-wide reputation as the inventor of gel filtration.

The first reason for this lies in the fact that, despite the breadth of scientific contracts and the intensity of communications in modern science, geographical proximity to the place where a new method is developed, still tends to play a significant role.

Table 2 illustrates the citation dynamics of refs. 5 and 7, taken from journals published in various countries. It is evident that the American scientists tend to cite more often the American authors of affinity chromatography, while in the Scandinavian countries the Swedish authors are more often cited (7.7 times more). And furthermore the American "market" for the new research technique is substantially larger.

However, the main differences between the dissemination patterns of the two variants manifested themselves later. We believe that the reason for this lies in the

TABLE 2

BREAKDOWN OF REFERENCES TO THE FIRST PAPERS ON AFFINITY CHROMATOGRAPHY ACCORDING TO NATIONAL JOURNALS

Country of publication	*Total number of references for 1969–1974*	*Ratio of the number of references to ref. 5 to that of ref. 7*
U.S.A.	378	0.71
France	17	0.90
Great Britain	91	0.62
G.F.R.	25	1.27
Japan	25	1.50
Scandinavia	45	7.60
Others (taken together)	46	1.50
International journals	163	2.50

personal and active involvement of Cuatrecasas in the introduction of affinity chromatography for a wide range of problems, which cannot be said regarding the Swedish inventors of the method. Cuatrecasas personally helped a large number of workers in various areas of biochemistry and chemistry in overcoming the difficulties (mostly psychological) connected with the mastering of the new method, demonstrated its efficiency and created many "centers of proselytism", which played a large role in promoting a swifter adoption of the innovation. In fact, Cuatrecasas played the role of the innovation "champion" needed in a technology transfer. Indeed, that this function is indispensable has been confirmed in the course of numerous researches into the development of scientific and technological innovations. The difference of approach to the introduction of this method by the two groups of workers is seen already in the fact that the first main article by the Swedish inventors contains about 12.000 typographical symbols, while that of the Americans contains about 22.000.

The latter paper contains a detailed, step-by-step description of all the manipulations performed in applying affinity chromatography, which is of the utmost importance in overcoming the psychological barrier experienced by people mastering a new technology. A brief report has a much poorer didactic effect. However, what is most important, in our view, are the broad scientific contacts maintained by Cuatrecasas.

Evidence as to the breadth of such contacts can be found in the *Science Citation Index*. Fig. 5 shows a "map" of the contacts maintained by the authors of ref. 7. This shows not only the scientists who published certain papers in 1968 in co-authorship with Cuatrecasas, Anfinsen and Wilchek, but also some leading "co-authors of the co-authors".

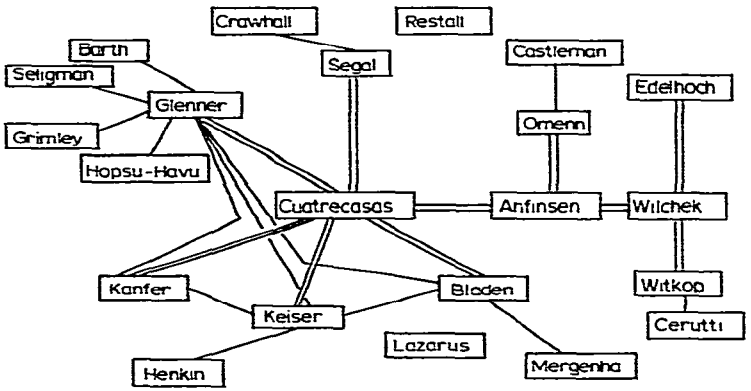

Fig. 5. Scientific contacts of the authors of ref. 7 in 1968. The double line is used to connect immediate co-authors and the single line the co-authors of Cuatrecasas', Anfinsen's and Wilchek's co-authors.

Indicating them on the "map", we proceeded from the assumption that a co-author of the co-author can be found in the group of scientific contacts of a given researcher because an informal contact can easily be established through a common acquaintance. It is evident from Fig. 5 that the group of Cuatrecasas' scientific contacts encompasses eminent scientists, working in many areas of research. This is confirmed by the data in Table 3, in which the lines of activity of these scientists and the number of articles published by them in 1968 are indicated.

TABLE 3

LINES OF ACTIVITY OF RESEARCHERS COMING WITHIN THE "FIELD" OF CUATRECASAS' SCIENTIFIC CONTACTS IN 1968

Name	*Number of papers published in 1968*	*Field of activity*
Glenner, G.	21	Histochemistry
Keiser, H. R.	6	Antibiotics
Bladen, H. A.	4	Bioorganic chemistry
Kanfer, J. N.	5	Lipids
Segal, S.	15	Active transport
Crawhall, J.	7	Medicine
Restall, C.	4	Anasthaesiology
Barth, W.	6	Connective tissues
Seligman, A.	16	Histochemistry
Grimley, P.	8	Cytology, virology
Hepsu-Haru, V.	10	Enzymology
Henkin, R.	9	Endocrinology
Lazarus, G.	6	Connective tissues
Mergenha, S.	12	Polysaccharides (endotoxins)
Castleman, B.	49	Medicine
Witkop, B.	27	Bioorganic chemistry
Cerutti, P.	6	Bioorganic chemistry
Edelhoch, H.	6	Bioorganic chemistry

It should be noted that the co-authorship "map" contains interesting evidence on the closeness of both variants of the affinity chromatography technique: Wilchek had as his co-author in 1968 an eminent specialist in bioorganic and fine organic chemistry, Witkop, who in 1966 and 1967 was a co-author of the Swedish research group.

The evidence characterizes Cuatrecasas as a scientist maintaining intense communications with a large number of research groups, which can, by itself, contribute to the dissemination of the method. In 1967 he published 13 articles as co-author of 15 other scientists. However, his activities after the year 1968 have assumed the character of a purpose-oriented co-operation with a large number of other scientists, largely for the popularization of affinity chromatography. Cuatrecasas published a large number of papers, while the list of his co-authors increases annually. Thus what we see here is a non-recurring co-operation rather than a broadening of constant contacts. Again, in the list of co-authors we see eminent scientists and heads of research groups.

Table 4 contains evidence as to the number of publications, the number of co-authors and the new co-authors of Cuatrecasas (those which first appeared in 1970 or later). It is noteworthy that, taken year by year, the number of "new co-authors" first showed a maximum and then started to decrease in recent years. This is easily explained; the method can now be considered to have been introduced into all of the main areas of its application: it has been given a large coverage in manuals and is included in the university curriculae. Thus there is no longer a need for the urgency with which the author introduced the technique previously.

TABLE 4

NUMBERS OF PUBLICATIONS BY CUATRECASAS AND HIS CO-AUTHORS AFTER AFFINITY CHROMATOGRAPHY WAS DEVISED

Year	*Number of publications*	*Number of co-authors*	*Number of new co-authors**
1970	10	12	4
1971	21	17	6
1972	15	13	8
1973	28	15	10
1974	22	21	9
1975	23	14	5
1976	16	16	3
Total (1970–76)	135	108	45

* "New" co-authors are those who, in the period from 1968 and until the specified year, did not have any joint publications with Cuatrecasas.

The activities of the Swedish authors have developed differently. Since 1967 their publication activity or their co-operation with other scientists have evinced no changes. During 1968–1976, Axén published 22 papers (many in co-authorship with Porath), while Porath published 50 articles (of which only 16 were devoted to affinity chromatography as such). And those 16 pursued the objective of arriving at a new technique whereby active molecules can be bonded to their matrices, rather than the extension of the technique to new areas of application. This may explain the continuous growth until recently of the number of citations of ref. 5 as this seems the only work that could be cited by scientists working with this variant.

The retrospective comparison of the diffusion dynamics of the two variants of affinity chromatography highlights the regularity of the process of introduction of a technological innovation.

The combination of the two key roles in the person of Cuatrecasas, as creator of the method and as its propagatori, has resulted in a synergic effect that accelerated the introduction of this important scientific technique.

4. SUMMARY

The *Science Citation Index* was used to study the dynamics of the dissemination of scientific knowledge, using the two main affinity chromatography procedures developed by Axén, Porath and Ernback and Cuatrecasas, Wilchek and Anfinsen. It is suggested that the higher rate of citation of the latter group may be due to a more intensive method of propagation.

REFERENCES

1 H. G. Small and B. C. Griffith, *Sci. Stud.*, 4 (1974) 17–40.
2 E. Garfield, *Citation Indexing —Its Theory and Application in Science, Technology and Humanities*, Wiley, New York, 1979, pp. 110–118.
3 E. Garfield, *Curr. Contents*, 9, No. 29 (1977) 5–12.

4 E. Garfield, *Curr. Contents*, 9, No. 25 (1977) 5–12.
5 R. Axén, J. Porath and S. Ernback, *Nature (London)*, 214 (1967) 1302.
6 J. Porath, R. Axén and S. Ernback, *Nature (London)*, 215 (1967) 1491.
7 P. Cuatrecasas, M. Wilchek and C. Anfinsen, *Proc. Nat. Acad. Sci. U.S.*, 61 (1968) 636.
8 E. Garfield, *Citation Indexing —Its Theory and Application in Science, Technology and Humanities*, Wiley, New York, 1979, pp. 18–36.
9 E. Mansfield, *Industrial Research and Technological Innovation*, Norton, New York, 1968.
10 S. G. Kara-Murza, *Vestn. Akad. Nauk SSSR*, No. 1 (1979) 44–52.
11 I. M. Hais and K. Macek, *Handbuch der Papierchromatographie*, Bd. II, Gustav Fischer, Jena, 1960.
12 S. G. Kara-Murza, *Nauchno-Tekh. Inf.*, No. 1 (1979) 7–12.
13 P. Cuatrecasas, *Proc. Nat. Acad. Sci. U.S.*, 68 (1971) 1264.