The prehistory of biology preprints: a forgotten experiment from the 1960s

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PeerJ Preprints | https://doi.org/10.7287/peerj.preprints.3174v1 | CC BY 4.0 Open Access | rec: 22 Aug 2017, publ: 22 Aug 2017

Abstract

In 1961, the NIH began to circulate biological preprints in a forgotten experiment called the Information Exchange Groups (IEGs). This system eventually attracted over 3600 participants and saw the production of over 2,500 different documents, but by 1967 it was effectively shut down by journal publishers' refusal to accept articles that had been circulated as preprints. This article charts the rise and fall of the IEGs and explores the parallels with the 1990s and the biomedical preprint movement of today.

Introduction

Since 1991, physicists and mathematicians have been using the arXiv preprint repository to circulate articles and ideas. Many biologists have looked on with envy, and wondered whether a similar approach could be used in the life sciences. After a number of failed attempts, including ClinMed Netprints (1999-2005) and Nature Precedings (2007-2012), in 2013 two major biology preprint servers were launched – Peer J Preprints and bioRxiv (Cold Spring Harbor Laboratory). Many journals are now happy to consider an article that has previously appeared on a preprint server, and key grant-awarding bodies on both sides of the Atlantic allow preprints to be cited in grant and fellowship applications.

This is widely seen as an example of biology finally catching up with physics [1, 2], but in fact the first large-scale adoption of biological preprints occurred 30 years before arXiv. From 1961-1967, the National Institutes of Health (NIH) in the USA pioneered a system known as the Information Exchange Groups (IEGs). IEGs were the model that the physicists used for their informal exchange of information in the late 1960s, which eventually led to the creation of arXiv. The IEGs, forgotten by all except a handful of historians of

documentation [3,4,5,6], have been the subject of only one investigation – published, appropriately enough, as an unrefereed report in 1971 [7]. The IEGs have not been systematically studied by science historians – for example, there is no record of the documents they produced. They eventually fell prey to a campaign by commercial publishers and learned societies, who perceived preprints to be a threat to their financial interests and to their self-proclaimed status as guardians of scientific integrity.

This article outlines the rise and fall of the IEGs and tells the cautionary tale of the ability of commercial scientific publishers and entrenched interests within the academic community to restrict the free sharing of knowledge.

Launching the IEGs

In 1961, Francis Crick received a letter from Errett C. Albritton, a 70-year old administrator at NIH (Fig 1 – for a photo of Albritton see http://hsrc.himmelfarb.gwu.edu/historical_photos/91/), inviting him to join an informal network for circulating preprints, called an Information Exchange Group (IEG) [8]. Crick gave Albritton the brush-off, saying he was 'strongly opposed' to the scheme [9], even though he had spent much of the previous six years circulating his own informal papers in such a network, called the RNA Tie Club [10]. 'There is far too much careless and rapid communication already in every area of this field of study,' Crick replied, 'The idea of increasing it even in this semi-public manner fills me with horror'. Albritton's response was good humoured [11] – Crick's hostility was not widely shared, and there were enough positive responses for the first IEG to be set up shortly afterwards.

The IEG concept had been dreamt up in January 1961 by Albritton, along with two biochemists – David Green of the University of Wisconsin-Madison and Philip Handler of Duke University [12]. Albritton later described the IEGs as an 'experiment' or a 'natural history study' that would enable researchers working

on a tightly focused research area to send 'any communication whatever' (preprint, comment, discussion...) to NIH, who would then physically reproduce the 'memo' and circulate it by the postal service to all members of the network, with all costs met by NIH. Although the initial proposal was focused on 'leading investigators' [13], IEG membership was soon broadened to anyone 'above the level of graduate student', although the IEG chair had the final say on who could join [14]. All memos were confidential and could not be referred to without permission, but could be taken as evidence of priority. This process was intended to increase informal communication between scientists, and to avoid the delays imposed by traditional publication methods. Albritton's conception of the IEG was summarized by a brief slogan that was included on the front cover of each memo: it was a 'continuing international congress by mail' [12].

At one level, there was nothing new about circulating unrefereed documents. Previous examples were linked to specific institutions, such as the MIT Research Laboratory in Electronics which began producing unrefereed technical reports in 1946 [5] or the preprints circulated by the Petroleum Chemistry Division of the American Chemical Society from 1921 [15]. Other sets of unrefereed documents were tightly focused on the needs of a particular research community, such as the *Drosophila Information Service* [16]. Albritton's NIH proposal was far more ambitious. It involved systematically circulating copies of all submitted preprints to subscribers, rather than issuing them on request from an institution [17]. The scale of this experiment was immense, given the technology of the time: by the end of 1965, 3,663 researchers, from 46 different countries, were involved and 2,561 different memos had been physically mailed out, involving millions of pages of paper [7].

The first IEG was focused on oxidative phosphorylation and terminal electron transport. It initially had only 32 members, but grew to 386 within four years [7]. The IEG chair, David Green, underlined the advantages of the system: 'The exchange makes it possible for all of its members to be fully informed in record time of all important developments in the field' [18]. Other advantages included

avoiding the danger of being ‘ambushed by some overzealous or overopinionated reviewer’, thereby providing ‘an outlet for anyone who feels choked by editorial intransigence’ [19]. Green insisted that despite the lack of review, the IEG memos did not consist of a ‘flood of rubbish’; indeed, it was possible that informal review via the IEG might lead to a reduction in the number of weaker articles submitted to journals.

In October 1963, Albritton began soliciting suggestions for more IEGs, and approached Sydney Brenner, Jacques Monod and many others [20]. Like Crick, Brenner gave a negative response: ‘the informal contacts that already exist facilitate enough exchange of information’, he wrote [21]. However, five new IEGs were soon created, covering Hemostasis (IEG2), Computer Simulation of Biological Systems (IEG3), Molecular Basis of Muscle Contraction (IEG4), Immunopathology (IEG5) and Interferon (IEG6). IEG7, focused on Nucleic Acids and the Genetic Code, was launched in early 1966 by Jim Watson and Marshall Nirenberg; over 1,100 scientists immediately signed up [7]. Crick’s hostility to the IEG project diminished, and by October 1965 he was proposing Brenner and others as members of the future IEG7, although he warned Albritton that having multiple copies of IEG documents ‘pouring into our laboratory is more than we can stomach’ [22]. Among the most significant memos submitted to IEG7 was Francis Crick’s ‘wobble hypothesis’ explanation of codon-anticodon binding [23,24].

Overall, about 80% of the IEG memos were articles. About 1/3 of these were circulated after acceptance by a journal but before publication, which in pre-electronic days could involve a delay of many monthss. The remaining 2/3 were submitted to the IEG before peer review, and would be what we would now classify as preprints. There were also technical notes and – occasionally – debates. Over one third of IEG members were from outside the USA (mainly from the UK, Japan and Australia), and over 90% of the memos were written in English [7]. David Green later claimed that the system enabled researchers

outside the USA, including some in Communist countries, to be as clued up about recent developments as their North American colleagues [25].

The publishers strike back

The 1960s marked a period of substantial growth in the scientific publishing industry, in particular through the activities of Pergamon Press, set up by the British businessman Robert Maxwell. The number of journal titles published by Pergamon rose from 40 in 1959 to 150 in 1965; some were created as money-spinners by Maxwell's company, others were learned society journals that Pergamon took over [26]. The financial model that now dominates scientific publishing, with large numbers of for-profit journals paid for by institutional library subscriptions, began at this moment [27].

At about the same time, there were repeated discussions in the scientific community about the slowness of publication and the need for more informal and automated methods of communication [28], including a CIBA Foundation conference on the topic [29]. The IEGs began to attract attention from outside the biomedical community: historians and librarians explored the consequences of the IEG for collaboration [15, 30] while an influential article in the *Bulletin of the Atomic Scientists* [31] argued that physics should use the IEGs as a model to resolve their communication problems. This eventually led to the idea of a Physics Information Exchange (PIE) modelled on the IEGs. In July 1966, in the pages of *Physics Today,* the theoretical physicist Michael Moravcsi proposed setting up PIE. There would be a crucial cost-cutting difference compared to the IEGs –a single copy of each preprint would be sent to participating libraries, rather than to each individual member [32, 33].

The growth of preprint circulation led some journal publishers – both commercial companies and learned societies – to feel threatened in terms of both their prestige in the scientific community and their finances. The counter-offensive

began in April 1966 at a meeting of the American Association of Immunologists (AAI). Since 1916 the AAI had published *The Journal of Immunology* and it clearly felt threatened by the creation of IEG5 (Immunopathology) [34], which had gained over 600 members and had produced over 300 memos in a little more than a year [7]. The AAI meeting accordingly adopted a resolution criticizing the IEGs, claiming that the circulation of IEG memos by NIH was an 'improper' activity for a government agency, while the fact that memos were in reality 'complete publications' meant that they posed 'a real danger' to immunological journals and might 'ultimately supersede them'. By a majority of 56:39, the AAI meeting voted that the publication of articles that had been previously circulated by IEG5 'should not be continued' [34].

The massive growth in IEG membership (Fig 2) and the looming possibility of PIE, coupled with the hostility of the AAI, prompted *Nature* to wade into the debate. It was not that journal's finest hour. In a series of articles and editorials in July and August 1966, including the unapproved reproduction of one of Albritton's documents [35], *Nature* attacked the growth of the IEGs and the PIE proposal in sometimes sarcastic terms [36,37]. *Nature's* first target was PIE – a proposal the journal considered to be 'so offensive' that it hoped it would be 'stillborn'. The opening of one editorial, particularly condescending and alarmist, revealed the concern of the commercial publishers: 'Next to downright villainy, misguided zeal is one of the most dangerous forces in society,' they wrote [36].

Next in *Nature's* sights were the IEGs, which a few weeks later were attacked by the journal as 'suspect' and a waste of money, and for being 'in the publication business' no matter what NIH might claim. The defects of preprints, thundered the journal, included 'inaccessibility, impermanence, illiteracy, uneven equality, and lack of considered judgment' [37]. The traditional journal system, it boasted, had by contrast 'encouraged thoroughness and measured judgment [and] discouraged triviality and repetitive work'.

This claim that journals act as guarantors of scientific quality was a key part of *Nature*'s criticism, as was the issue of priority. *Nature* was particularly irked by the fact that the IEG members agreed to treat the memos as priority-laden. As Albritton put it: 'a paper sent through the IEG is better protected than one published without prior circulation through the IEG' [12]. Inevitably, financial considerations were also to the fore. A fraction of the money lavished on circulating preprints, argued *Nature*, should be devoted to 'helping the journals become more efficient'. The for-profit journal was suggesting that NIH should keep out of 'the publication business' and instead use that money to help commercial journals. The editorial closed with the same tone it had used throughout its coverage: 'If the National Institutes of Health are as well-disposed towards the cause of effective publication as they seem to be, they could do a lot to help. The energy they choose to dissipate in Dr Allbritton's print shop will be a lot less valuable.' [37]

A similar tone was adopted by the editor of *Science*. Philip H. Abelson suggested the products of the IEGs could be seen as 'government-subsidised shoddy merchandise' and concluded that while the growth of the IEGs was born of understandable frustration with 'the inefficiency of many publications', it also revealed 'a desire on the part of some scientists to avoid a discipline essential to the integrity of science.' [38]

The fate of the IEGs was finally sealed not by the leading gatekeepers of scientific publishing, but by a group of specialist journal editors. In September 1966, editors of leading biochemical journals met in Vienna to discuss the widespread circulation of preprints by the IEGs. There were 13 journals represented at the meeting, including the *Journal of Chemical Biology* and the *Journal of Molecular Biology* [39]. Like the AAI, this group decided – mostly without consulting their societies or editorial boards [7] – that no article that had been circulated as an IEG memo would be accepted for publication. It is striking that these journals and those published by the AAI overlapped with the two IEG

areas that had the largest memberships: immunopathology and molecular biology, which together represented nearly 2,000 researchers.

This decision was soon leaked to *Nature* – an editorial crowed 'Preprints made outlaws' and praised the 'firm... lethal steps' the Vienna meeting of journal editors had taken against the IEG system [40]. The editorialist was right: no one would submit a preprint to an IEG under these conditions. Faced with the inevitable, the NIH caved in, and in November 1966 announced that the IEGs would be closed in the following March. Albritton accepted that the IEGs were not financially viable without external funding [9], and growth in the number of preprints meant the IEGs were stretching NIH's financial and physical resources. Each copy of a memo cost $0.10 – $0.50; by 1967, the IEGs were projected to cost NIH $400,000 per annum, or over $3m in today's values [7,41].

Meanwhile, the letters pages of *Science* [42] and *Nature* [43,44] began to bulge with positions for and against IEGs. In *Science* Philip Siekevitz, a cell biologist at Rockefeller University, claimed that the IEGs were 'a dangerous nuisance' while *Nature* pointed out in a note that it had received seven letters in support of the IEGs, and only one against, but complained that Theodore Spaet, the Chair of IEG2, had encouraged its members to write in.

After the IEGs had been killed off, *Nature* produced a slightly more considered editorial, entitled 'Secret colleges end' [45]. The journal recognized that there were problems of slowness and rigidity in the traditional journal format, but insisted that if successful, the IEGs 'would have been an offence against scholarship'. The *New England Journal of Medicine* followed suit, going so far as to praise the 'morally sensitive scientists' who had opposed the IEGs, before finishing on a contradictory note by calling for the IEG idea to be taken up again once the lessons had been learned [46]. The journal's real position on preprints was made clear two years later, when it stated it would not accept any articles that had been previously published, including by 'controlled-circulation journals' [47]. Strict application of this principle, known as the Ingelfinger Rule after the

journal's editor, later prevented the journal from publishing material that had appeared on any kind of website [48].

The PIE proposals met a similar fate. They were vigorously opposed by Simon Pasternack, the editor of *The Physical Review*, probably the most prestigious journal in physics, who described the project as 'a great disservice' [49]. Pasternack denied that PIE would be any quicker than traditional publication routes and predicted it would 'dilute orderly communication and add confusion'. Going into rhetorical overdrive, Pasternack claimed PIE threatened physics research communication with 'obscurity, incompleteness, polemics, inadequate references, discursiveness and irresponsibility'.

PIE was not stillborn as Pasternack and *Nature* wished, but it was instead launched for a trial year, with a much-reduced ambition. There was no central circulation of documents, not even to a single library per institution. Instead, PIE functioned primarily as an announcement service of new articles and discussion documents that was circulated to a mailing list; anyone interested had to request the document directly from the author.

After the IEGs

After minor pushback [50], and some policy discussion of the significance of the experiment [29], most of the IEGs immediately folded. Albritton had hoped that because many IEG members – and even some IEG Chairs – were also Editors or Associate Editors of journals (including the *Journal of Molecular Biology* and the *Journal of Biological Chemistry*), peaceful coexistence with traditional journals would be possible [12]. This turned out to be naive. The power of the Vienna editors' meeting and of the AAI, coupled with the hostility of *Science* and *Nature* and the financial strain on NIH, stopped the IEGs in their tracks. Only

IEG6 decided to keep going; the group continued to circulate material until at least the late 1970s as the Interferon Scientific Memorandum [51].

The perception of the IEGs by those who had been involved was overwhelmingly positive. Professor Michael Woodruff of the University of Edinburgh chided *Nature* for its 'timid' attitude, stating that he found his membership of IEG5 to be of 'enormous value' and that he was 'most delighted' with reading and writing memos [52]. Surveys of IEG members showed 94% of the respondents said reading a memo had positively influenced a research decision, while 68% considered that the memos had saved time and money [7]. However, in most cases the key memos were articles that eventually appeared in print; although the IEGs increased the rapidity and efficiency of communication, there was no evidence that it led to greater debate, one of the Albritton's key objectives.

Albritton's colleagues at NIH were unrepentant and continued to emphasize the value of preprints [17]. In an understandably embittered article reviewing the rise and fall of the IEGs, David Green, the chair of IEG1, described the 'strangulation' of what he considered to be 'one of the most revolutionary innovations in the history of science communication.' [25] After dismissing the three criticisms leveled at the IEGs by the Vienna meeting and by *Science* and *Nature* – duplication, copyright infringement and potential misunderstandings from lack of review – Green explained why the IEGs had really been killed off:

> "It is my opinion that the stated reasons are not the real reason. Rather, the stated reasons merely hide the fact that the editors were apprehensive that the status and prestige of the journals would be downgraded if another agency (IEG) were distributing to its members, from 6 months to a year earlier than the journals, the very papers which would eventually appear in the journals, though not necessarily in the same final form."

In *Nature's* final statement on the affair, in February 1967, an editorial suggested preprints should be renamed 'impersonal communication' or 'postal circular' and reiterated the 'offense' the IEGs had given to the established journals because of the claimed potential of duplicate publications. However, the editorialist was also keen to turn his article into an advert, reassuring his readers that the rapid circulation that was so attractive a feature of the IEGs would soon be found at *Nature*, which in a few months would 'be operating consistently with a time lag of a few weeks'. The aim was for *Nature* to 'beat the IEG at their own game' [53].

Debate about how to enable more rapid communication of scientific discoveries continued into the 1970s [54,55]. The solution was finally found in physics. In January 1969, following discussion of the brief experience of PIE and of the preprint services run by Lawrence Radiation Laboratory at Berkeley and the Stanford Linear Accelerator Center (SLAC), a similar service, Preprints in Particles and Fields, was run out of the SLAC Library, reaching around 1600 subscribers within a year [56]. Over the next two decades, rapid progress in information technology enabled the development of increasingly complex and cost-effective schemes for circulating information, culminating in the launch of arXiv by Paul Ginsparg in 1991. This server hosts submitted preprints that can be freely read by anyone with access to the Internet. Initially set up for high energy physics, it gradually extended into other fields and gained NSF funding in 1993 [2,3]. The concerns of the journal publishers and the learned societies were placated by the gradual introduction of the system and the evident fact that it did not damage journal prestige or finances [4].

Life science researchers, who had either forgotten the IEG affair or never know of it, could not help but notice the growth of arXiv. In May 1999, following a series of informal discussions by biomedical scientists, Harold Varmus, the head of NIH, proposed that an electronic repository of preprints should be created in the form of E-biomed, clearly modelled on arXiv [48,57]. Varmus opened a consultation on his proposal and received overwhelming support from

the individual scientists who responded to his call, but the journal publishers were deeply hostile.

An editorial in the *New England Journal of Medicine* warned of 'a potential threat to the evaluation and orderly dissemination of new clinical studies' – they were concerned that unrefereed and potentially incorrect clinical papers would gain the imprimatur of NIH's authority and could have significant negative consequences for patient health and well-being. But the journal also revealed that one of its major concerns was the 'probably disastrous effects' on the paid circulation of journals [58]. FASEB, a powerful umbrella group of learned societies, even threatened to use their lobbying power in Congress to affect the NIH budget should the E-biomed proposal go ahead [48].

Within four months the project was dead in the water. Varmus admitted defeat, and it would be another decade and a half before biologists, their funders and their editors accepted what had become commonplace in most parts of physics.

A third attempt in over 50 years to introduce preprints into biology occurred in 2013, with the launch of Peer J Preprints, biorXiv and others. This time around, there appears to have been a shift in opinion amongst funders and publishers of biomedical research – there has not been the kind of hostility that appeared in the 1960s and 1990s. This apparent change in attitude has yet to be systematically analysed. One explanation might be that it is linked to the widespread adoption of open access publishing and the free circulation of data and ideas – opposing preprints just looks churlish in the age of the Internet. Another is that despite immense changes in technology, the time from submission to the first journal to final publication often remains the same as in the 1960s – 12-18 months – and frustration with this situation is growing [59]. Or it may be that so many key decisions affecting the lives of scientists – recruitment, promotion and funding – are often reduced to the titles of the journals we publish in, rather than a direct estimation of the quality of the research we produce. In such a world, the journal will not go extinct – indeed,

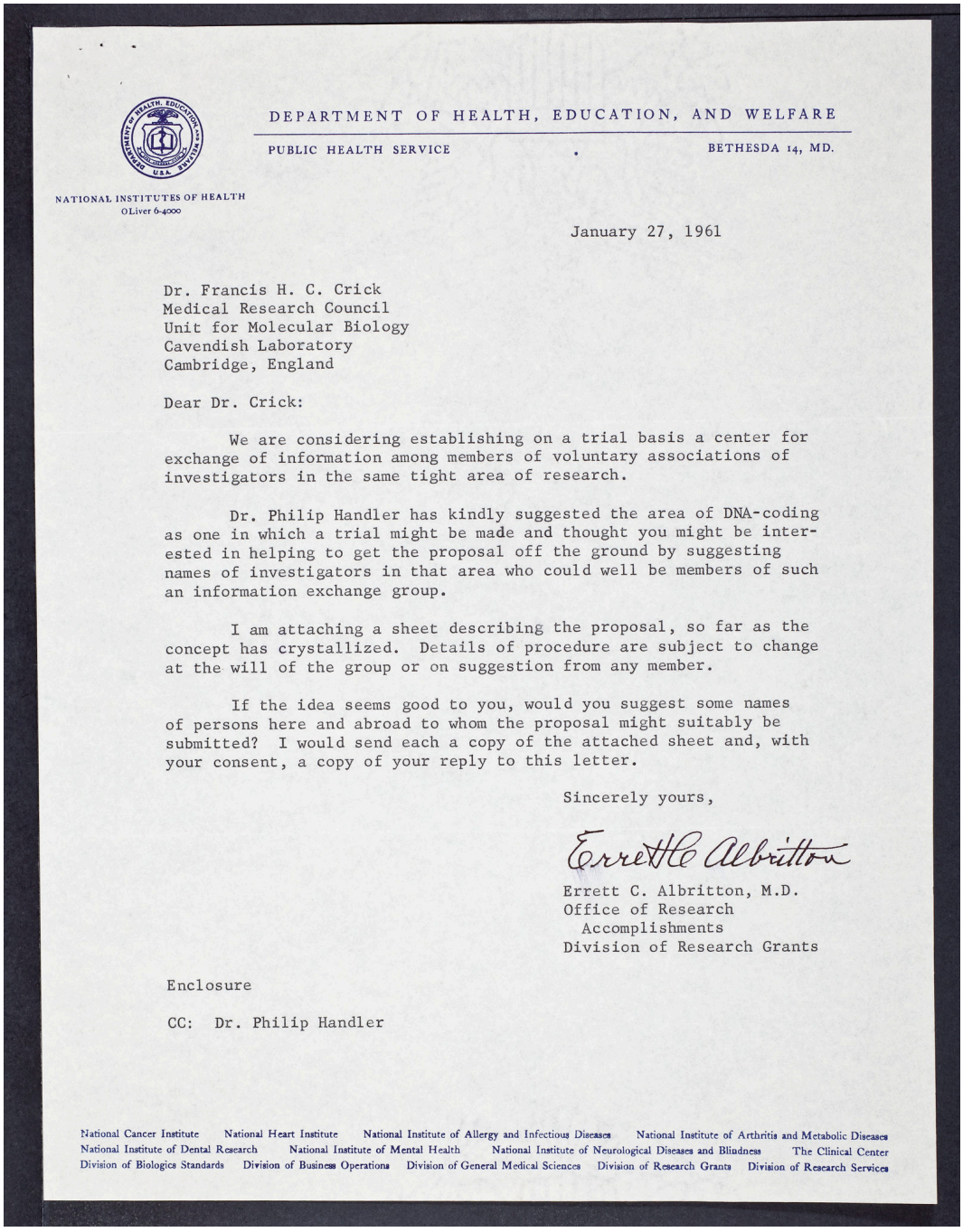
journals can make money by charging for open access, and can scout out promising papers on the preprint servers.

Whatever the case, on the third attempt, it appears that a culture of preprints has been established in the biosciences, but the fate of the IEGs should warn us of the power of commercial publishers and of vested academic interests to restrict the free circulation of knowledge.

The digital world we now live in is far beyond the dreams of Errett C. Albritton and his printed IEG memos, individually sent out in the mail to eager subscribers. But much of what we now value in the culture of the free circulation of knowledge and debate was envisioned by him over half a century ago. His name, and his ambitions, may have been forgotten, but his influence is all around us.

Acknowledgements: Stephen Curry and Leslie Vosshall are thanked for their comments and encouragement.

Funding disclosure: This article was supported by a Sydney Brenner Research Scholarship from Cold Spring Harbor Laboratory.



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
OLiver 6-4000

January 27, 1961

Dr. Francis H. C. Crick
Medical Research Council
Unit for Molecular Biology
Cavendish Laboratory
Cambridge, England

Dear Dr. Crick:

We are considering establishing on a trial basis a center for exchange of information among members of voluntary associations of investigators in the same tight area of research.

Dr. Philip Handler has kindly suggested the area of DNA-coding as one in which a trial might be made and thought you might be interested in helping to get the proposal off the ground by suggesting names of investigators in that area who could well be members of such an information exchange group.

I am attaching a sheet describing the proposal, so far as the concept has crystallized. Details of procedure are subject to change at the will of the group or on suggestion from any member.

If the idea seems good to you, would you suggest some names of persons here and abroad to whom the proposal might suitably be submitted? I would send each a copy of the attached sheet and, with your consent, a copy of your reply to this letter.

Sincerely yours,

Errett C. Albritton

Errett C. Albritton, M.D.
Office of Research
Accomplishments
Division of Research Grants

Enclosure

CC: Dr. Philip Handler

National Cancer Institute National Heart Institute National Institute of Allergy and Infectious Diseases National Institute of Arthritis and Metabolic Diseases
National Institute of Dental Research National Institute of Mental Health National Institute of Neurological Diseases and Blindness The Clinical Center
Division of Biologics Standards Division of Business Operations Division of General Medical Sciences Division of Research Grants Division of Research Services

Fig 1 – Letter from Albritton to Crick, January 1961 [8]. Credit: Cold Spring Harbor Laboratory Archive.

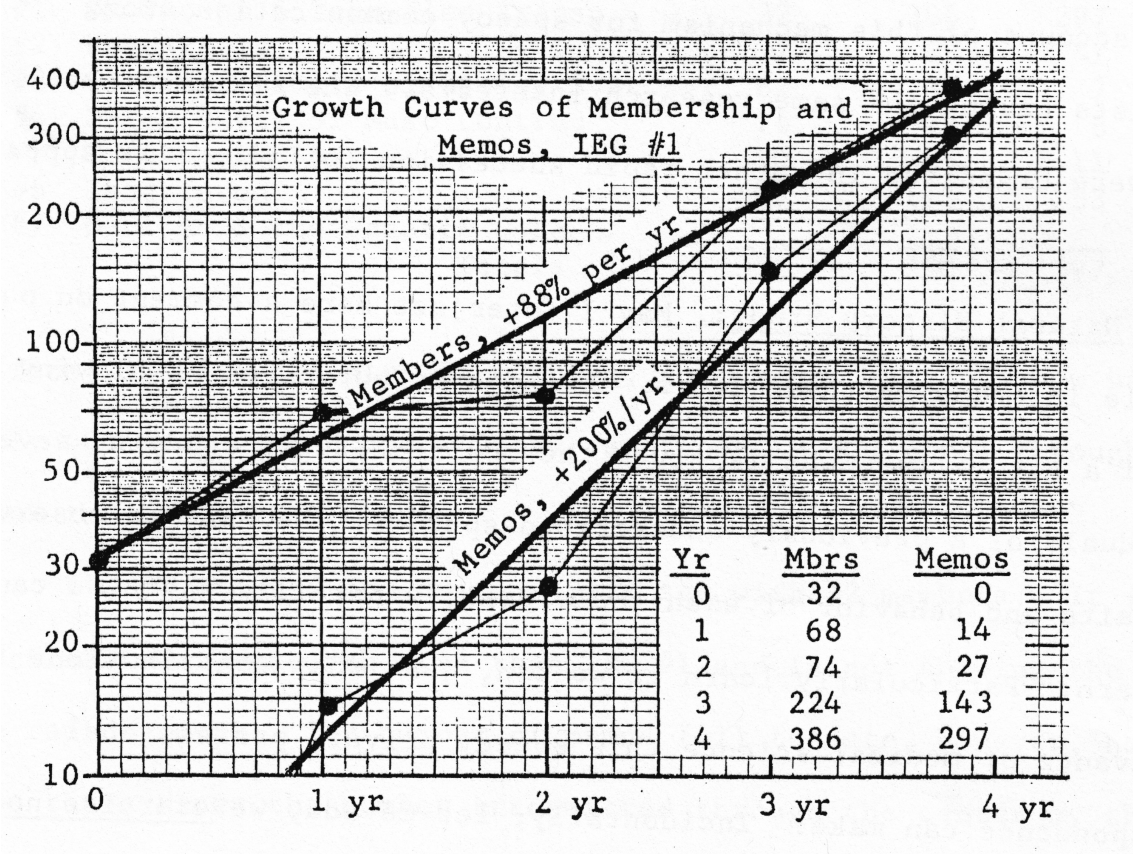


Fig 2 – Growth of IEG1 1961-1965, as reported by Albritton [12]. Credit: Cold Spring Harbor Laboratory Archive.

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