

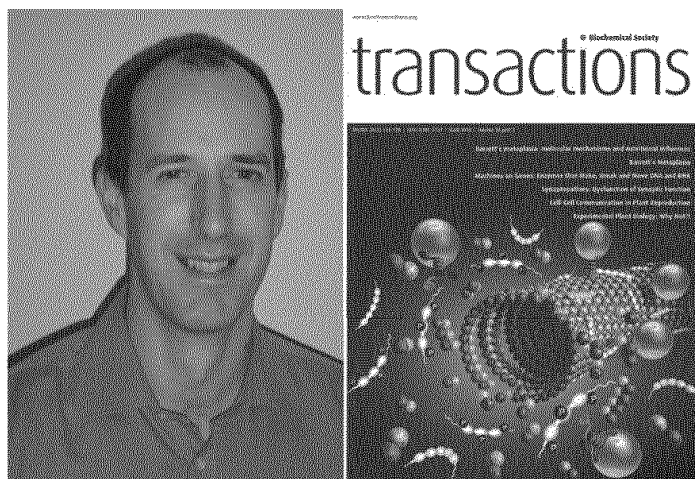
Biochemical Society Transactions

Over the past 25 years *Biochemical Society Transactions* has been transformed. It started the period as the means by which the Society recorded the communications at its scientific meetings. This led to a degree of unpredictability in the size and therefore cost of issues as they were dependent on the number of speakers and posters at meetings. In addition, as the papers were not peer-reviewed, there was a real and perceived lack of quality. The first turning point came in 1988 when the Publications Committee set up a working party to look at how *Transactions* could be improved. The working party consisted of Chris Pogson as Chair, Glyn Jones, and Alan Malcolm (the Society's Chairman). The Editor of *Transactions*, Dr David Watts, and Alan Beedle (the Editorial Manager), aided them. The working party distributed 1000 copies of a questionnaire to members (360 replies were received). In general, authors were content but recommended that systems of refereeing should be investigated. This would cause problems, as refereeing short communications would be very difficult given the timescales involved. The minutes of the Executive Committee meeting when the working party's proposals were reported show that there was some disagreement about how to proceed. After a vote it was decided that only one of the working party's recommendations – the immediate appointment of a Managing Editor – would be adopted and that the changes proposed by the other recommendations would be deferred until the Managing Editor was in place. However, it was agreed that Free Communications would no longer be published in the journal. Dr Catherine Rice-Evans took up the post of Managing Editor of *Transactions* on 1 January 1989, and in March 1991 the first issue of *Transactions* appeared in its new format.

The next round of major changes for *Transactions* came at the start of the new millennium. In 2000, the journal became fully online. Problems were soon to arise however and John Wrigglesworth who took over the editorship in 2002 from Keith Snell (Editor since 1993) was faced with the effects that the Society's planned changes to its meetings programme would have for *Transactions*. In 2001, it was announced that there would be a new structure to Society meetings. While 2003 would be a transitional year, in 2004, the pattern of meetings would consist of one main meeting, with stand-alone Focused Meetings dispersed throughout the year. This would obviously have implications for the frequency and quantity of papers for *Transactions*. The journal was marketed to subscribers on the basis of six issues annually and it was essential that sufficient copy would continue to be supplied so that this could be fulfilled.

Initially there was optimism about the new arrangements. Focused Meetings had proved to be very successful and it was hoped these would provide enough science content to fill the issues in the future. However, by 2003, Rhonda Oliver was reporting to the Portland Press Board on the failure of the new meetings structure to provide adequate copy for *Transactions* in 2004. To overcome the problem, it was proposed that the papers from the BioScience2004 meeting should be split between two hard-copy issues. To prevent the loss of credibility with speakers that would occur if publication of their manuscripts was artificially delayed, these issues would be published online simultaneously. But to avoid claims from institutional subscribers there would have to be a slight delay between the manufacture and despatch of these print issues. As well as the pressure that these arrangements would put on the editorial and production staff, the Board's unanimous opinion was that this sort of *ad hoc* action to protect *Transactions* was in danger of damaging the professional reputation of Portland Press. It was agreed, that if this situation could not be resolved, the Board would recommend that publication of *Transactions* should cease.

Another option to cover the predicted shortfall in papers was the possibility of combining *Transactions* and the *Biochemical Society Symposia* series. There were positive aspects to this solution: all the science from the meetings programme would be published in one place, rather than spread over two separate publications. *Symposia* authors would still get a dedicated publication, albeit in a different format, and it was also likely that this would have a positive effect on the Impact Factor for *Transactions*. However, there would be logistical problems in that the Annual Symposium would have to be held at the beginning of the year to



David Richardson, Honorary Editor of *Biochemical Society Transactions* in 2011.

enable papers from it to be fitted into a publishing schedule that had to cope with a large summer meeting. It was also noted that 85% of subscriptions to *Transactions* were combined subscriptions with the *Biochemical Journal*. This would need to be stressed to the Society's Executive Committee when discussing any move to discontinue publication of *Transactions*. The journal brought in a substantial amount in copyright sales and single-issue sales were also very popular. Eventually, in 2008, *Biochemical Society Symposia* was incorporated into *Transactions*, but with the online *Symposia* series available via subscription if required. The *Symposia* volumes continue to be made available as hardback books.

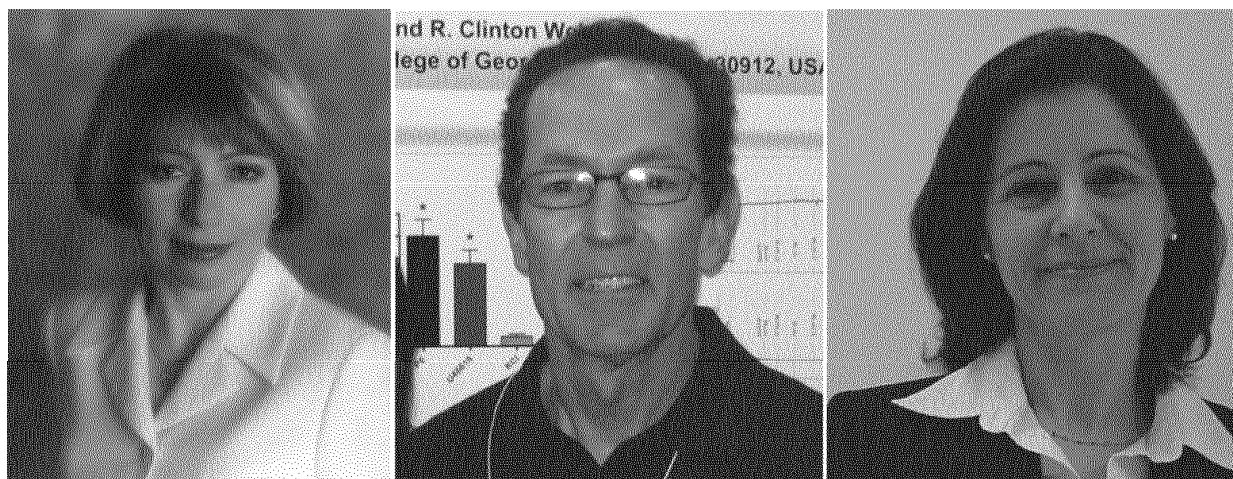
David Richardson from the University of East Anglia who was appointed Honorary Editor in 2005 has done much to improve the quality of *Transactions*, appointing an Advisory Panel and turning the journal into a respected educational resource. Its Impact Factor reflects this, increasing from 2.579 in 2004 to 3.989 in 2011, which is high for a journal of this type.

Manuscripts are written as mini-reviews, so that speakers are not precluded from publishing their primary data elsewhere. All the science in *Transactions* is meetings-led; it is the Society's Meetings Board that selects the topics for meetings from proposals from its Theme Panels. The production of a manuscript is a pre-condition of being awarded a Society Award (see also Chapter 3). Currently around 79% of speakers contribute manuscripts. *Transactions* is seen as a membership benefit for the Society and publication in *Transactions* contributes to the charitable objective for the Society to disseminate the science of biochemistry.

Clinical Science

The Biochemical Society and the Medical Research Society (MRS) had owned *Clinical Science* jointly since 1960. It was governed by a Committee of Management whose Chair alternated between the MRS and the Society. As decisions had to be taken jointly, its development was hampered; the MRS gave copies to their members as a membership benefit and had no real interest in developing the journal. By 2001, the Board of Portland Press had realized that *Clinical Science* could be a growth area and set in train negotiations that were to result in a Portland Press buy-out of the title from the MRS in 2002 for the very reasonable sum of £20,000. In practice, the cost to the Society and Portland Press was negligible as the fee Portland Press had received for the publication of the proceedings of the 'Endothelin-7' conference as a special supplement had almost covered the cost of buying the journal.

By July 1998, the journal was fully online and in 2004 the US Editorial Office at the Burnham Institute was extended to include *Clinical Science*. On taking over the journal, Portland Press proceeded to market it successfully and has tripled its turnover and increased its Impact Factor to 4.613 by 2011. These achievements



Key figures in the development of *Clinical Science*: (left to right): Anna Dominiczak, (Editor-in-Chief, 2004–2007), Clinton Webb (Editor-in-Chief, 2008–2011) and Rhian Touyz (Reviews Editor, 2005–2011).

are due in large part to the efforts of Anna Dominiczak (University of Glasgow; Editor-in-Chief 2004–2007), R. Clinton Webb (Georgia Health Sciences University; Editor-in-Chief 2008–2011) and Rhian Touyz (University of Glasgow; Reviews Editor 2005–2011), as well as the hard work by Portland Press staff.

Biotechnology and Applied Biochemistry

The Biochemical Society took over the publication of *Biotechnology and Applied Biochemistry* (BAB) on behalf of the IUBMB from February 1993. The journal had never been particularly successful and Portland Press debated as to whether its publication made commercial sense. It was agreed that, while it might not be profitable, its contribution to overheads was such that its continuation was worthwhile.

BAB was re-launched in 2003 with a new Editor-in-Chief, Parviz Shamlou (University College, London). Significant promotional activities were undertaken and the publication frequency increased resulting in an 88% increase in submissions to the journal in 2003 (230 papers compared with 122 in 2002). This increase was in no small part due to Parviz Shamlou's efforts in encouraging his colleagues and contacts at conferences to submit papers. BAB returned a small operating surplus in 2004.

However, in 2010, the IUBMB put the journal out to tender and Portland Press decided not to bid to renew the contract. The journal has now moved to Wiley-Blackwell who took over its publication from January 2011.

Biology of the Cell

In 2004 Portland Press won the contract to publish *Biology of the Cell* on behalf of the Société Française des Microscopies and the Société de Biologie Cellulaire de France. At the time that Portland Press began publishing *Biology of the Cell*, the journal had an Impact Factor of 2.23; this had increased to 4.898 by June 2011. During its time within the Portland Press portfolio the journal was rebranded and developed, increasing its international recognition. In 2011, the owners took the journal out to tender and from January 2012 the publisher will be Wiley-Blackwell.

Essays in Biochemistry

Essays in Biochemistry had started in 1965 under the editorial guidance of Peter Campbell who continued as Editor until 1985 when Keith Tipton of Trinity College Dublin took over. Academic Press had published *Essays* on behalf of the Society until 1991 when its publication was taken in-house by Portland Press. The following succeeded Keith Tipton from 1995 onwards: David Apps, Steve Higgins, Tom Cotter and since 2005, Melanie Welham.

Essays provides undergraduates and first-year postgraduates with a single source of information on the latest research in rapidly moving areas of biochemistry and molecular biology. Each chapter is written by an expert on the area of research and is a self-contained summary of the state-of-the-art of that topic. To date, 51 volumes of *Essays* have been produced and the series continues to sell well.

Other titles

Throughout its existence, Portland Press has sought new publishing ventures, either by starting new publications or seeking to publish existing journals on behalf of other organizations. Notable successes have included acquisition of the *Practical Methods in Electron Microscopy* series from Elsevier in 1994 and the launch in 2006 of an online reference work for students and researchers, *Cell Signalling Biology* written by Sir Michael Berridge. In 2010, *Cell Signalling Biology* was made freely available with sponsorship by the *Biochemical Journal*.

Bioscience Reports a journal owned by the Biochemical Society but published by Springer, was brought back in-house from January 2009. The current Editor-in-Chief is Wanjin Hong (A*STAR, Singapore).

In 2010 Portland Press took over the publication of *Cell Biology International* and launched *Cell Biology International Reports* on behalf of the International Federation for Cell Biology.

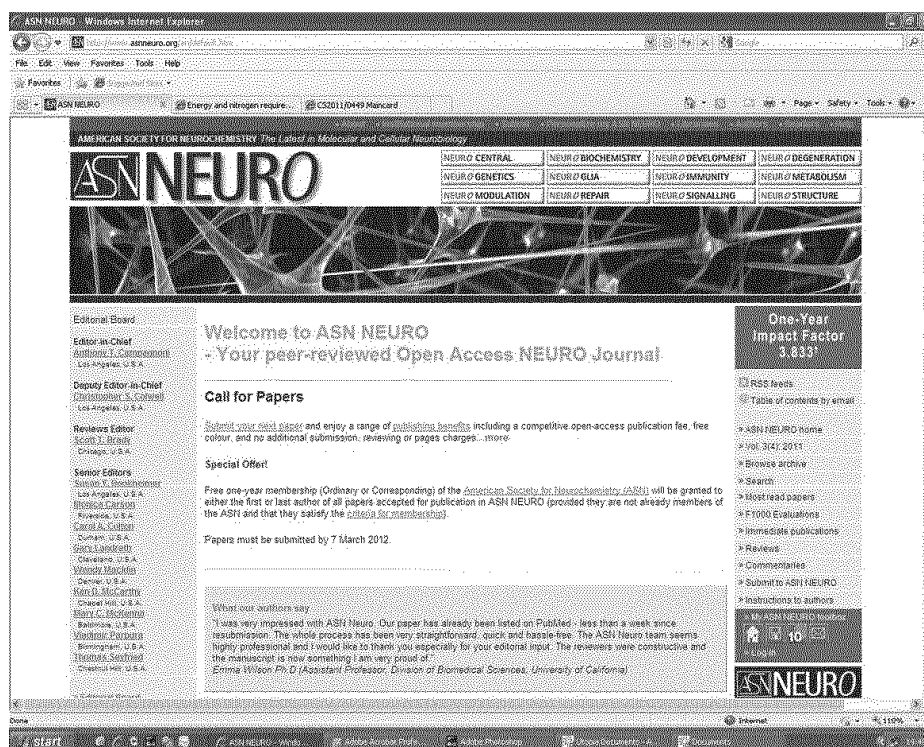
ASN NEURO was launched in March 2009 as a Gold Open Access online-only journal. Portland Press had been successful in its bid to publish this new journal on behalf of the American Society for Neurochemistry after a tender process in March 2008. In November 2010 *ASN NEURO* was accepted for indexing in MEDLINE®, and in June 2011 received a one-year Impact Factor of 3.833.

Some ventures have not been so successful; in 1997 a new journal, *Genes and Function*, was published by Portland Press and Blackwell Science Publishers as a co-operative venture between the Society, the Genetical Society and the Physiological Society. The journal had problems from the start as Blackwells simultaneously started a similar journal with the Genetics Society of Japan. The Editorial Board of the journal seemed reluctant to publish in it, further weakening its standing. Eventually it was decided to abandon the venture with a possible relaunch in 1999, but this did not happen.

The Biochemist

In 1985, the predecessor of *The Biochemist* was the *Biochemical Society Bulletin* (a publication that had metamorphosed from the old *Agenda Papers*) and as both names suggest, the *Bulletin* had been very much a vehicle for informing members about forthcoming meetings – and that was about it. It came out four times a year, to coincide with Society main meetings, and it is fair to say that its design values were not the highest. There was no thought given to securing any advertising revenue.

Robert Dale had joined the Society in 1985 as Assistant Meetings Officer to the redoubtable Doris Herriott. One of his responsibilities was to take over editing the *Bulletin*. Soon after this transfer of responsibilities, Glyn Jones, the Executive Secretary, set up a staff working party consisting of Robert, Dianne Stilwell, then Research and Information Officer, and Alan Beedle, the Editorial Manager, to look at ways in which the publication could be improved. Their recommendations (a new title, colour printing,



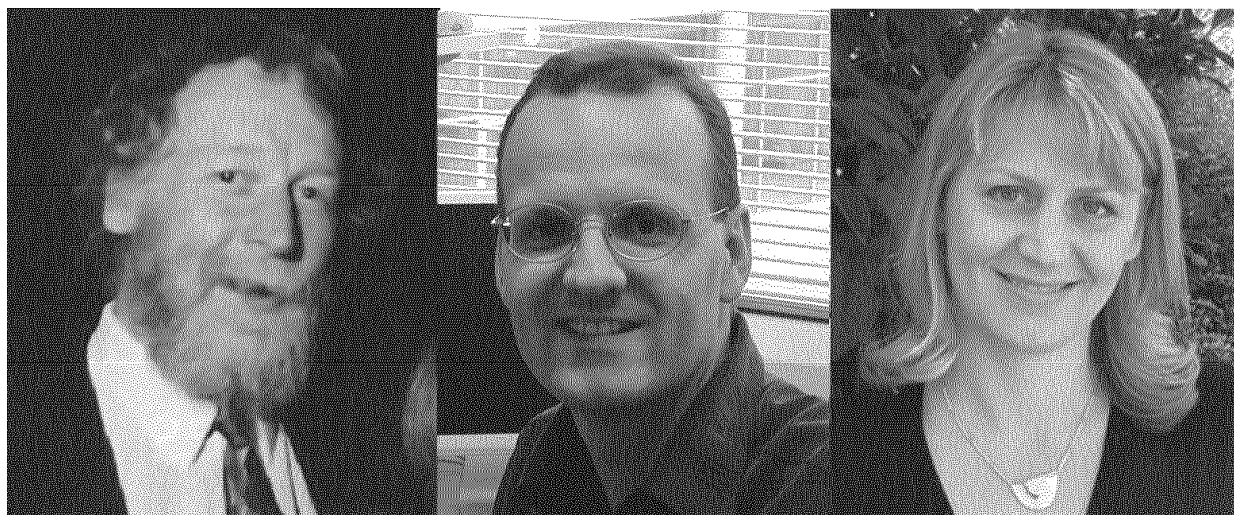
ASN NEURO became the first Gold Open Access online-only journal to be published by Portland Press when it was launched in March 2009.

a redesign and far more feature articles) were not at first approved by the Society's Executive Committee, who felt that the *Bulletin* did its job and they were reluctant to authorize the additional spending needed for the overhaul. Undeterred, the staff, especially Robert, proceeded to solicit advertisers, and, by 1987 the *Bulletin* was replaced with *The Biochemist*, a magazine with a colour cover. The changes were paid for by advertizing revenue and there was no additional cost to the Society. The members liked the transformation and the Executive Committee gave it its blessing. Publication moved to the current six issues per year.

Editorial responsibility for *The Biochemist* was split between the Society Honorary Secretary, then Roy Burdon, and the Meetings Secretary, Alan Malcolm. By 1989, Harry Bradford from Imperial College London (also the Society Archivist) had become Features Editor and in 1992 John Lagnado became Book Reviews Editor. As the magazine moved away from its origins as a meetings-focused publication, it was realized that to keep the content fresh and interesting, a dedicated Advisory Board was needed. Harry became General Editor of *The Biochemist* and chaired the Advisory Board meetings; he held this position until 1994 when Frank Burnet (University of the West of England) succeeded him.

One of the features of Frank's editorship was the Christmas-themed issues. Following the December 1991 issue where Dianne Stilwell had co-ordinated a series of articles relating to the biochemistry of Christmas, in which Richard Bruckdorfer provided his memorable piece on the biochemical secrets of the Christmas pudding, including the hitherto unknown organelle the 'pudosome', other Christmas issues dealt with the biochemistry of the seven deadly sins (1995), the biochemistry of fairy stories (1996), and the biochemistry of a Victorian Christmas (1998).

Christmas was not the only time the magazine took a more light-hearted approach to its subjects. A series of 'acrimonious debates' between Frank Burnet and David Weitzmann on 'course accreditation' held by the Society's Education Group and Professional and Education Committee at the December meeting in 1991 was heralded by a featured 'dialogue' in *The Biochemist*, illustrated with cartoons of the



Three of the General Editors of *The Biochemist*: (left to right) Frank Burnet, Richard Reece and Freddie Theodoulou.

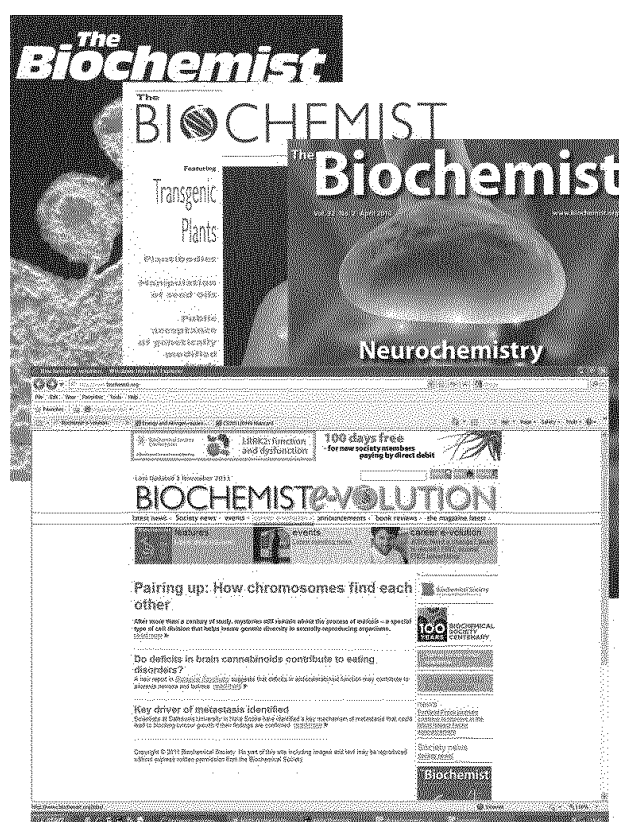
two protagonists. Other issues contained features discussing aspects of other topics close to biochemists' hearts – 'chocolate', 'cheese' and 'the movies' were three such issues.

As well as features, *The Biochemist* retained its primary role of informing the membership about Society activities. There had always been a letters page, but the information flow became a little less one-way when, in 1995, the Meetings Office (which still retained responsibility for production) started to accept email correspondence. By 2000, production and editorial responsibilities had passed to Portland Press.

The Biochemist got its first full-time editor in 2000 when Gary Burd became Executive Editor. Richard Reece (University of Manchester) took over as General Editor from the first issue in 2002 and continued until the last issue of 2009.

The year 2002 also saw the launch of the magazine's online counterpart, *Biochemist e-volution* (www.biochemist.org). As well as the content of the magazine, the site carries a daily news story and announcements of jobs, events and more. The idea was to allow greater interaction with members and the promotion of 'hot' *Biochemical Journal* papers and other Society initiatives. *E-volution* was 'highly commended' in the publishing innovation category of the ALPSP/Charlesworth Awards in 2003.

Until this time, advertizing revenue had seen a steady increase. However, from around 2002 revenue started to fall off. Different advertizing agencies were tried but nothing seemed to bring a revival. The overall economic



Since its launch, *The Biochemist* magazine has undergone several redesigns. Its online counterpart *Biochemist e-volution* was launched in 2002.

conditions no doubt played a part, but the changing profile of the Society's membership, with greater emphasis on students and young members (who do not control purchasing budgets) may also have been a contributing factor.

In 2003, Gary Burd was succeeded as Executive Editor by Mark Burgess. Mark oversaw the first redesign of the magazine for nearly a decade in 2007; this was largely the work of Peter Jones, who was Manager of Portland Press' design Studio at the time. After Richard Reece's term of office ended in 2009, Freddie Theodoulou of Rothamsted Experimental Station took up the reins as General Editor at the start of 2010.

The future

The year 2010 saw significant re-organization at Portland Press. John Coggins replaced John Clark as Chair of the Portland Press Board, and Sue Thorn and John Cox (both of whom have a lifetime's experience in scientific publishing) were appointed Non-Executive Directors. Rhonda Oliver left the company to take up a position as Managing Director of the RCN Publishing Company, and the post of Group Head of Publishing for the Biochemical Society and Managing Director of Portland Press was filled by Caroline Black in September 2011.

One of the highlights of 2011 was the opening in May of an Editorial Office for the *Biochemical Journal* at the prestigious Institute for Biophysics at the Chinese Academy of Sciences, in Beijing. China is seen as a burgeoning market and it was felt that an Editorial Office under the auspices of Tao Xu, the Journal's Vice-Chair, Asia-Pacific, would provide a real presence for the Journal which would help attract high-quality Chinese papers. The office was launched with a mini-symposium at the Institute for Biophysics followed by a reception for VIP guests.



Peter Shepherd (Chair of the Editorial Board of the *Biochemical Journal*) presents Tao Xu (the Journal's Vice-Chair, Asia-Pacific) with a plaque to commemorate the opening of the China Editorial Office in May 2011.

Portland Press staff

The achievements of Portland Press would not have been possible without the dedication and expertise of its staff in the Editorial, IT and Marketing Departments and in Portland Customer Services, many of whom are long-serving. Members of the Editorial Boards, authors, clients and the Portland Press Board have spoken unfailingly about the professionalism and competence of the staff; “The most professional group of people I’ve worked with”, as one ex-Chair of the *Biochemical Journal* Editorial Board put it.



Portland Press staff based in London (top) and Colchester (bottom) in November 2011.

Appendix

What were the most important papers published in the *Biochemical Journal* between 1986 and 2011?

Ian Dransfield

Identification of the most influential papers published in the *Biochemical Journal* in the last 25 years would appear to be a relatively straightforward task. However, changing trends in publication during this time frame make it more difficult to compare papers published over the years. In addition, the influence of biochemistry as a discipline has altered as the emphasis of worldwide research effort has shifted towards multi-disciplinary approaches to tackling biological problems.

It is clear that the science of biochemistry was dominant in terms of cutting-edge research that was being published at the beginning of the 1970s. In the last 25 years, there has been increasing emphasis on the biochemistry underlying cellular and whole animal physiology and also biomedical research. In addition, there has been a proliferation of the number of titles and articles that are published. When Eugene Garfield wrote his seminal analysis of the criteria for measurement of the impact of scientific publishing in 1972 [1] the *Biochemical Journal* was ranked 74th overall with an Impact Factor (IF) of 3.060. In terms of the frequency of citations, the *Biochemical Journal* was ranked as the 10th most cited journal. The journal with the highest IF in Garfield's analysis was *Advances in Protein Chemistry* (IF 23.0) and the journal ranking 152nd had an IF of 1.948. The range of IFs is now much greater and in the 2010 Journal Citation Reports (JCR), the journal with the highest impact is *CA-A Cancer Journal for Clinicians* (IF 94.333), while the journal ranking 152nd has an IF of 9.743. According to the 2010 ISI database, the *Biochemical Journal* is now ranked 493rd overall, with an IF of 5.016. It remains a highly cited journal, now ranking 81st in the list of journals with the highest number of total citations.

In addition to IF, there are a number of other metrics that may shed some light on the papers that have been published in the *Biochemical Journal*. The Cited Half-Life (which reveals the median age of articles that were cited in a particular JCR year) for the *Biochemical Journal* is > 10. Thus, papers published between 2000 and 2010 account for 50% of total citations to the *Biochemical Journal* in 2010, perhaps providing an indication of the cited longevity of published papers when compared with other journals with a similar IF like *Journal of Biological Chemistry* (Cited Half-Life 8.8), *British Journal of Pharmacology* (Cited Half-Life 7.8) and *Journal of Cell Science* (Cited Half-Life 6.9). Another useful comparator is the Immediacy Index, which provides an indication of how quickly published articles are cited and thus the reporting of "cutting-edge" science. Again, the *Biochemical Journal* compares well with competitor journals, having an Immediacy Index of 0.842.

There have been some papers published in the *Biochemical Journal* that have received enormous numbers of citations. At the top of the list are methodological papers. Indeed, the top 10 cited papers all relate to methods that are widely used in research. For example, Burton's 1956 paper entitled 'A study of the conditions and mechanism of the diphenylamine reaction for the colorimetric estimation of deoxy-ribonucleic acid' [2] which has 16,990 citations. Similarly, Greenwood and Hunter's paper from 1963 on 'Preparation of ¹³¹I-labelled human growth hormone of high specific radioactivity' [3] has received more than 10,181 citations. There are also highly cited papers published in the Journal that document major advances in our understanding of biological processes. For example Berridge's 1983 paper relating to signal transduction mechanisms, 'Changes in levels of inositol phosphates after agonist-dependent hydrolysis of membrane phosphoinositides' [4] (2,192 citations) and Sanger's 1949 paper on the 'free amino groups of insulin' [5] (2,180 citations).

The publication of review articles in the *Biochemical Journal* has a key role in the dissemination of scientific knowledge. The top ten reviews from the last 25 years have been cited more than 13,500 times between them, representing an average of >1300 cites per article. Some of these articles have been published relatively recently, and therefore have very high average citations per year. For example, 'Caspases: the executioners of apoptosis' [6] by Gerald Cohen has been cited more than 180 times per year. Similarly Knowle's review on 'Nitric oxide synthases: structure, function and inhibition' [7] has been cited in the region of 130 times per year since publication. Although the designation of review article should be relatively straightforward, two seminal articles from the group of Philip Cohen which provide a comprehensive analysis of inhibitors of signalling intermediates have also been heavily cited. These papers by Davies et al. 'Specificity and mechanism of action of some commonly used protein kinase inhibitors' [8] (2,704 citations) and Bain et al. 'The specificities of protein kinase inhibitors: an update' [9] (745 citations) stand out from other primary research articles. In a similar manner, Henrissat's articles on the use of amino-acid sequence similarities to classify glycosyl hydrolases [10,11] with 1,680 and 1,335 citations respectively also rank alongside the best reviews in terms of impact.

Looking at the five most highly cited *Biochemical Journal* papers (not including review articles) for each year reveals that papers relating to signal transduction predominate. As the absolute numbers of citations will tend to increase with age of publication, comparison between years is somewhat difficult as illustrated in Figure A1.

However, there have been some notable papers in terms of their impact upon their field. In particular, the paper from Bialojan and Takai in 1988 on the mechanism and action of okadaic acid [12] which has over 1300 citations. Similarly, the description of the mechanism of action of wortmannin and its effect on neutrophil responses by Arcaro and Wymann [13] and the impact of wortmannin on mitogen-activated protein kinase pathway in regulation of insulin growth factor-1 signalling by Cross et al. [14] have also been very influential. Other papers reporting the mechanism of action of inhibitors of signalling pathway intermediates include Merritt's paper on Ca^{2+} channel inhibition by SKF96356 [15] and a paper describing the lack of effect of pertussis toxin on Ca^{2+} mobilization and phosphoinositide signalling following muscarinic receptor stimulation by Masters et al. [16].

A significant number of important papers published in the *Biochemical Journal* report novel mechanisms of action of signalling intermediates. Irvine and Moor's report in 1986 [17] relating to the

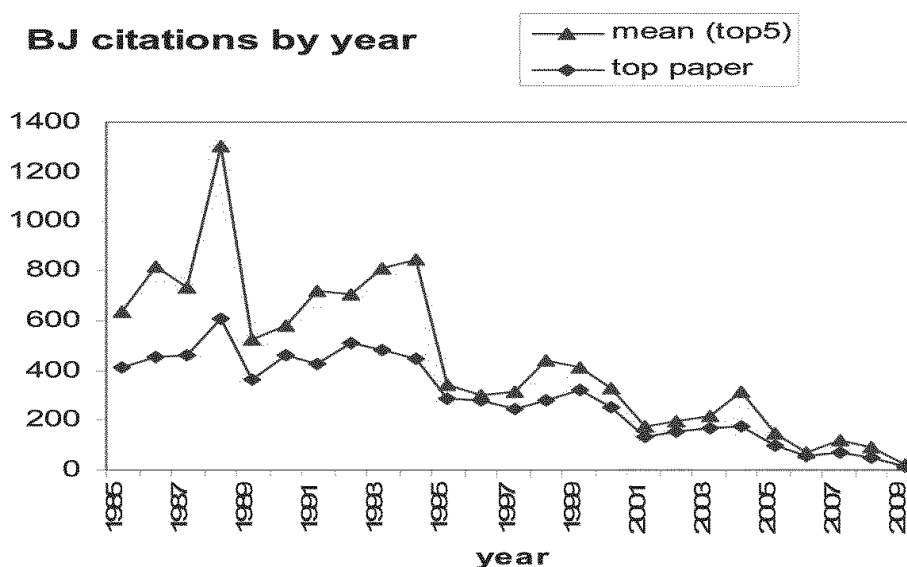


Figure A1. Citation trends for *Biochemical Journal* articles over the period 1995–2009.

requirement for extracellular calcium for the activation of sea-urchin eggs following micro-injection of 1,3,4,5-tetrakisphosphate is a good example. Indeed, a series of papers from Robin Irvine relating to the metabolism of inositol lipids, in particular inositol 1,3,4,5-tetrakisphosphate, in the mid-1980s represented key advances in our understanding of signal transduction processes in mammalian cells [18-20]. New mechanisms relating to regulation of signal transduction include the report from Young et al. [21] documenting the role of increased proteolytic degradation of protein kinase C as a mechanism for down-regulation. In addition, the identification of key new pathways such as the mammalian target of rapamycin being a substrate for protein kinase B (by Navé et al.) have had a major impact on contemporary research [22].

In addition to signal transduction processes, molecular cloning and sequence analysis has allowed identification of novel proteins or new protein family members leading to papers that are often highly cited as a result, for example the report of Meyer et al. on a new class of glutathione transferases [23] and the cloning of human glutathione transferase θ in 1994 by Pemble et al. [24]. These approaches can also reveal the relationships of protein families to other molecules, as in the paper by Price et al. reporting four new monocarboxylate transporter homologues [25]. The molecular cloning of human stromelysin and collagenase [26] and the characterization of the role of stromelysin in the activation of pro-collagenase [27] represent landmark papers in the study of protease function. The identification of the different extracellular matrix substrates for the matrix metalloproteases was also reported [28], as was the important observation that transforming growth factor β was released following matrix metalloprotease-mediated degradation of decorin [29]. Examination of functional aspects of proteins containing specific sequence motifs can also provide important insight, for example Dowler's paper on plekstrin-homology-domain-containing proteins and their binding to phosphoinositides [30].

Novel mechanisms associated with programmed cell death and their contribution to disease processes have been the focus of some very exciting papers published in the *Biochemical Journal*. For example, Gerald Cohen's report of apoptosis in the absence of intranucleosomal DNA fragmentation by endonucleases [31] and the role of mitochondrial permeability transition to lethal injury by Nieminen et al. [32]. Detailed investigation of the role of thiol groups present on the adenine nucleotide translocase by McStay et al. added to our understanding of the mechanism of the mitochondrial permeability transition pore [33]. Papers defining the role of caspases and calpains in neuronal apoptosis [34] and the influence of the MAPK pathway in controlling the cellular response to stress [35] demonstrated how analyses of signalling and proteolytic pathways can have a significant impact on our understanding of cellular process. There have also been important contributions detailing the molecular mechanism of cytochrome *c* release from mitochondria during apoptosis, e.g. Antonsson et al.'s 2000 paper [36] and the description of the mechanism of action of Z-VAD.FMK in blockade of CPP32 degradation by Slee et al. [37].

The production and release of hydroxyl radicals has been examined in a number of papers. In 1989, McCall et al. reported the mechanisms of production of nitric oxide from neutrophils and the potential for interaction with superoxide anions [38]. A few years later a report of hydroxyl radical generation when nitric oxide and superoxide were released simultaneously was published [39], as was a report identifying a role for the GTPase Rac1 in reactive oxygen species generation [40]. The mechanisms by which mitochondria generate and release superoxide anions was subsequently defined by Han et al. [41], and Kushnareva et al. [42] elucidated the role of complex I in reactive oxygen species generation. Control of complex I S-nitrosylation was also the subject of a paper by Burwell et al. [43] that is likely to represent an important advance in our understanding of mitochondrial function and ATP generation. The impact of free radicals on cellular function, e.g. fibroblast proliferation [44], was of key interest, as was their contribution to development of diseases such as atherosclerosis [45]. The mechanisms of development of disease have also been the subject of key papers published in the *Biochemical Journal*. In 1988, Hunt and colleagues published a manuscript describing the role of glucose autooxidation in protein modifications

that contribute to diabetes mellitus and aging [46]. In the early 1990s, there was considerable interest in the cyclo-oxygenase enzymes that regulate prostaglandin and thromboxane generation. The structure of the cyclo-oxygenase gene was published in the *Biochemical Journal* in 1994 [47] and the following year, Gierse et al. published a study of the constitutive and inducible forms of the enzyme [48].

Predicting future classics from more recent papers is more difficult. The paper by Garcia-Martinez and Alessi relating to the mechanism of action of mTOR complex 2 [49], the report by the same group of a specific inhibitor of mTOR signalling [50] and Barnett and colleagues' paper on Akt isoenzyme-specific inhibitors [51] are likely to be influential papers in the field of signal transduction. Papers relating to signalling mechanisms that will undoubtedly be influential in the future include that by Sanders et al. defining the mechanisms of AMP activation of the AMP-activated protein kinase cascade [52] and Fredé's report defining the role of HIF-1 activation by lipopolysaccharide in human monocytes [53]. The mechanisms relating to disease pathogenesis remain an important focus of research, for example characterization of kinase activity of LRRK2 mutants found in Parkinson's disease [54] and the impact of mutations in WNK1 and WNK4 in Gordon's hypertension syndrome as described by Vitari et al. [55]. New reagents for the study of important cellular processes are also likely to be the subject of *Biochemical Journal* papers that will be important in the future; for example Khan's analysis of the specificity of histone deacetylase inhibitors [56]. Furthermore, technological advances, such as the description of far-red fluorescent tags for use in imaging by Shcherbo et al. [57], may also become future citation classics.

In summary, the *Biochemical Journal* has a long history in the dissemination of key advances in the life sciences and continues to be an important conduit for science communication. Papers elucidating the mechanisms of cellular and molecular biological mechanisms will continue to represent a major focus for the future.

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