

PANEL MEMBERSHIP

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3. Dr John Diffley, Cancer Research UK London Research Institute
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6. Professor Karl Oparka, Institute of Molecular Plant Sciences, University of Edinburgh
7. Professor Bert Poolman, Department of Biochemistry, University of Groningen, Netherlands
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ACKNOWLEDGEMENTS

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EVALUATION CONTEXT AND METHODOLOGY

Responsive mode funding in BBSRC

1. Responsive mode grant applications are welcomed from eligible researchers at UK universities, BBSRC-sponsored Research Institutes, and a number of other Research Institutes. All responsive mode applications accepted by BBSRC are subject to peer review through the seven Research Committees. Despite increases in the amount of funding available, competition for responsive mode grants has been particularly intense in recent years, with approximately 25% of applications funded in recent rounds.
2. BBSRC operates a number of research grants schemes within responsive mode, aimed at fostering collaboration with industry (e.g. Industrial Partnership Awards), and at assisting researchers at an early stage in their careers to obtain their first research grant (the New Investigator Scheme).
3. All Principal Investigators (PIs) on grants are required to submit a final scientific report within three months of completion of the grant. They are asked to report on progress against scientific objectives, and to list publications and other outputs arising directly from the research supported by the grant. Final reports are peer reviewed and graded by two current or former Committee members, or by other specialist advisers.

Evaluation objectives and methodology

4. This evaluation covered research supported in responsive mode through BBSRC's Biochemistry and Cell Biology Committee (BCB) since the Committee's inception in 1994. This includes research conducted at universities and responsive mode grants to BBSRC-sponsored Research Institutes. The research supported through Core Strategic Grants to the Institutes is evaluated every four years in BBSRC's Institute Assessment Exercise. Thus, although some of this research falls within BCB's remit, it was **not** included in this evaluation.
5. The objectives of the evaluation were to:
 - Assess the quality and international standing of research funded through BCB;
 - Identify the major outputs and, where possible, outcomes of BCB's responsive portfolio over the past 10 years;
 - Identify strengths, weaknesses and gaps in the scheme, the way it is structured, the influence of initiatives and priority areas on the way that the scheme has developed, and the way in which it is administered;
 - In consultation with the research community and other relevant funding bodies (government and non-government), assess whether BCB is currently funding the most appropriate areas of UK bioscience; and
 - Identify ways to build on successes, and ways to address identified gaps and issues.
6. The evaluation comprised a number of surveys, followed by a review of findings. The work was co-ordinated by BBSRC's Evaluation and Policy Unit, in consultation with the Biochemistry and Cell Biology Branch. A logic chart was used to guide the design of the evaluation (Figure 1, at the end of this

Appendix). This chart represents diagrammatically the objectives and desired impacts of BBSRC's responsive mode, and places the scheme in its wider context, showing its links to the longer-term aims of the organisation.

Surveys

7. Information was gathered from a range of sources:

- **Completed grantholders:** 297 BCB responsive mode grants were completed and graded from September 1994 (when the Committee began operation) to the end of 2004. A structured sample of 50% of these was taken, comprising **145** grants drawn from all of the 10 years of the Committee's operation and covering the full range of final report grades. A questionnaire (Appendix 3) covering a range of topics including success of the grant, outputs, outcomes, views on the coverage of the portfolio, and views on the operation of the Committee was sent to the Principal Investigators (PIs) of the sample grants.

103 responses were received (a 70% response rate), representing **35%** of all the completed and graded BCB responsive mode grants. The grants for which questionnaires were returned are listed at Appendix 4. The sample was considered to be representative in terms of quality because the distribution of final report grades was almost identical to the overall distribution of grades.

- **Current grantholders:** Similarly, a structured sample of 40% of current BCB responsive mode grants that had been active for more than a year was taken, and a questionnaire sent to each PI. **70** responses were received (72% response rate), representing **24%** of all current ASC responsive mode grants started between 2001 and 2004. Again, the sample was random with respect to the science, but fairly representative of the whole in terms of years in which the grants had been started. The grants for which questionnaires were returned are listed at Appendix 4.
- **Committee members:** **19** current and past Committee members (66% of members serving over the last five years) were interviewed by telephone (Appendix 3) on topics such as coverage of the portfolio, BCB's achievements, and views on the Committee and BBSRC's administration.
- **Other relevant UK funding bodies:** A separate questionnaire (Appendix 3) was sent to other funding bodies with an interest in BCB research in the UK, namely: the British Heart Foundation, Cancer Research UK, the Engineering and Physical Sciences Research Council (EPSRC), Help the Aged, the Medical Research Council (MRC), the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), and the Wellcome Trust. The questionnaire covered potential overlap or gaps between remits, research priorities in biochemistry and cell biology, and views on the appropriate niches for the two organisations.
- **BBSRC data:** Relevant data were collated, including the final reports submitted by the sample PIs, and information from BBSRC's grants databases.

8. Unsuccessful applicants were not included in the surveys because the focus of the evaluation was on the science supported through BCB; moreover because the majority of BBSRC's grantholders have had applications rejected as well as funded, these grantholders were likely to include issues relating to unsuccessful applications in their responses. The comments included in the questionnaires showed this to be the case.

Review of findings

9. A Review Panel was convened to consider the survey results. This independent Panel was made up of scientists not closely involved with BBSRC, but who between them had expertise across BCB's remit (see Appendix 1 for Panel membership). The Panel included one member from industry and one international member, and met for two one-day sessions in June and July 2006.
10. The Panel was asked to provide an independent scientific evaluation of the data presented, and to base its analysis on:
- The final reports of the sample grants for which the PI had returned a questionnaire. Each Panel member reviewed a subset of the sample final reports broadly within their area of expertise; and
 - The findings of the surveys. The survey data presented to the Panel are summarised at Appendix 6.
11. The Panel's analysis was guided by a number of questions covering the different objectives of responsive mode, as represented in the logic chart. To facilitate the analysis, the subject matter was divided into five subject areas:

- | |
|---|
| <ol style="list-style-type: none">1. Research quality and research outputs2. Balance and coverage of the portfolio3. Interaction with industry4. Public engagement5. Ultimate impacts |
|---|

12. The Panel's report focuses particularly on the scientific aspects of the Panel's findings. A number of general issues related to BBSRC's programmes and grant administration processes arose in the surveys and during the Panel meetings. These findings will be presented to the appropriate BBSRC body in combination with the results of other current responsive mode portfolio evaluations.

Constraints

13. The survey data presented in this report relate to the samples described above. The samples of completed and current grants represent a random cross-section of the science supported through BCB and, due to the excellent response rate, cover 35% of completed grants and 24% of current grants. Nevertheless, it should be borne in mind that they are samples, a point which is especially pertinent to the analysis of portfolio coverage.

The Biochemistry and Cell Biology Committee

14. BBSRC's Biochemistry and Cell Biology Committee (BCB) was established in 1994 following the creation of BBSRC from a re-organisation of the Research Councils. The Committee's first responsive mode round took place in September 1994. The table below contains summary data on the BBSRC's responsive mode funding through BCB over the past five years.

BCB responsive mode spend and number of grants 2001-2005

| Year | 2001/02 | 2002/03 | 2003/04 | 2004/05 | 2005/06 [§] |
|---|---------|---------|---------|---------|----------------------|
| BCB spend - responsive mode (£ million) | 12.6 | 15.3 | 18.1 | 20.0 | 20.5 |
| BCB spend – total* (£ million) | 26.3 | 33.4 | 39.5 | 42.2 | 46.8 ⁺ |
| No. BCB responsive mode grants awarded | 98 | 96 | 83 | 83 | 92 |

* Including initiatives, studentships, Core Strategic Grants to Institutes, other types of grant

[§] The 05/06 figures are affected by the move to Full Economic Costing in September 05

⁺ Estimate

15. The Committee's stated aim is 'to support and foster basic research of the highest quality at the cellular and molecular level'. The science funded by the BCB under responsive mode is defined by its remit, which is the overarching definition of the scientific responsibility of the Committee and is not generally subject to change or modification. The current remit of the BCB is:

The Biochemistry and Cell Biology (BCB) Committee aims to support and foster basic research at the cellular and molecular level. The scientific remit covers work on micro-organisms, plants and animals. Areas of research supported extend from studies on individual proteins and enzymes through the structure and function of the cell, to cell-cell interactions. The Committee recognises that its remit covers scientific areas that are of considerable interest to the pharmaceutical, biotechnology and agricultural industries and is happy to consider applications with clear strategic relevance to the BBSRC. However, the study of specific human diseases and the disease process is excluded unless unique information that will enhance understanding of basic biological processes will emerge. The BBSRC will not accept applications that are primarily medically motivated.

16. BCB's remit is very broad and the Committee has developed a themed description of its main activities. These Themes are intended to be illustrative not exclusive.

- **Fundamentals of Cell Biology and Biochemistry** - including studies on:
 - intracellular signalling
 - enzymes
 - metabolism and bioenergetics
 - the cell cycle
 - molecular motors
 - cell growth
 - senescence and death
 - regulation of gene transcription and translation

- protein transport and targeting, including plant-specific protein trafficking pathways
- intracellular biochemistry.
- **Cell-cell interactions** - including: cell-cell and cell-matrix interactions; cell motility; cell surface receptors and signal transduction including transporters and ion channels.
- **Specialised Cell Function** - including: cell differentiation; molecular immunology; cellular and molecular neuroscience specialised microbial and plant cell function.

17. Fundamentals of Cell Biology and Biochemistry is currently the largest Theme by spend:

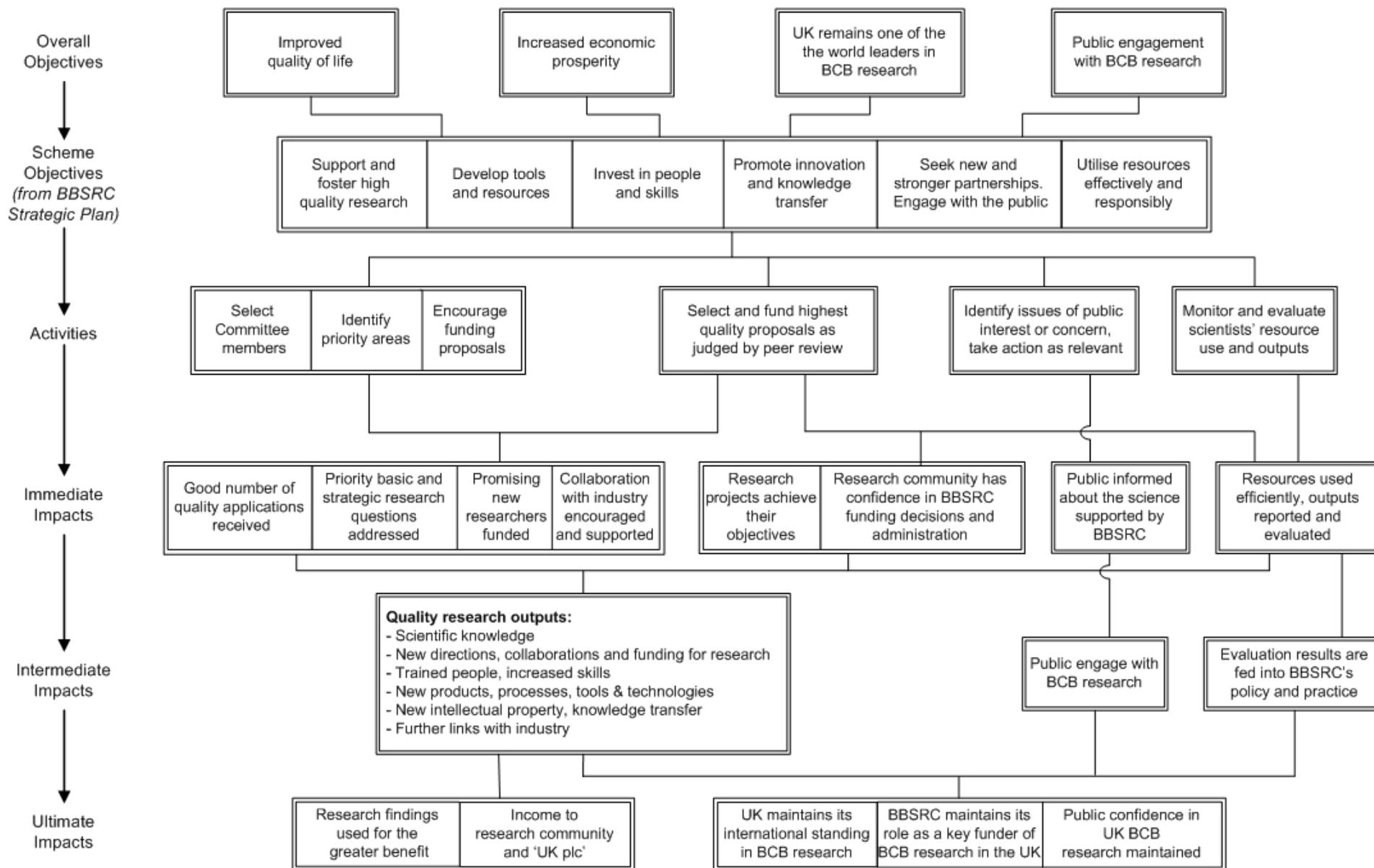
BCB responsive mode grants live on 1 January 2006 by Theme

| Theme | Spend |
|---|-------------------|
| Fundamentals of Cell Biology and Biochemistry | £43 million (69%) |
| Specialised cell function | £17 million (27%) |
| Cell-cell interactions | £2.4 million (4%) |

18. Within BCB's remit there are specific areas of science, called Priority Areas, which are areas where the Committee particularly wishes to encourage applications, for example to address important gaps in the Committee's portfolio or to promote new/developing areas of science. Priority areas are modified and/or removed over time as their objectives are achieved. BCB currently has four Priority Areas: Chemical biology; Functional analysis of multiprotein complexes; Biochemistry and cell biology of nuclear transfer, stem cell signalling and control of differentiation; and Integrated cellular systems in vitro.

19. BBSRC also identifies a number of Cross-Committee Priority Areas in areas of relevance to more than one Committee. Applications under any of these Priority Areas may potentially fall within BCB's remit: Cognitive systems; Biology of the transmissible spongiform encephalopathies; Developing alternative methods to replace, reduce and refine animal experiments; and Drug resistance and alternatives to chemotherapeutics.

Logic Chart for Biochemistry and Cell Biology Committee Responsive Mode Funding



QUESTIONNAIRES

1. Completed grants (current grantholders were sent a very similar questionnaire)
2. Committee members
3. Other funders

**Biochemistry and Cell Biology Portfolio Evaluation 2005
Survey of Completed Grants**

*Please fill in as much of this questionnaire as you can, and return it (by email if possible) by **9th February**. Contact details are at the end of the questionnaire. An electronic version of this questionnaire will be sent to you in the next few days. If completing by hand, please feel free to continue your answers on a separate sheet.*

Name:

Grant No:

Grant Title:

Research

1. Was the project supported by this grant successful in meeting its objectives?
(please tick one and comment if you wish)

| 4 (very successful) | 3 | 2 | 1 (not successful) |
|-------------------------------|----------|----------|------------------------------|
| | | | |

If you ticked 1 or 2, were the reasons for this related to:-

| | |
|---|--|
| Staff e.g. shortages, staff leaving | |
| Experimental/methodological/technical reasons | |
| Lack of resources, e.g. funding, equipment | |
| Unrealistic objectives | |
| Incorrect/inappropriate hypothesis | |

Comments:

2. Did the project have industrial involvement at the outset?

| | |
|---|--|
| IPA (Industrial Partnership Award) | |
| Link Programme | |
| Other e.g. funding, equipment, collaboration (<i>please give details</i>) | |

Comments/details:

3. When applying for the grant did you need to alter the direction of this research to fit within the remit of the BCB Committee? (please tick one and comment if you wish)

| | | | |
|--------------------------|----------|----------|--|
| 4 (not at all) | 3 | 2 | 1 (fundamentally changed the nature of the research) |
| | | | |

Comments:

4. Was it difficult to recruit staff to undertake this research? For example did you have to delay the start of the research until you found someone suitable?

YES / NO

Comments:

5. Did this grant support your wider research aims? (please tick one or more boxes and comment if you wish)

| | |
|---|--|
| Enabled extension of research into new areas | |
| Provided funding for activities that other bodies would not fund (e.g. 'blue skies' research) | |
| Strengthened the skill base of the group (e.g. techniques, cross-disciplinary skills) | |
| Generated income from patents, spin out companies, etc to support further research | |
| Helped to publicise the importance of your field of research | |
| Strengthened the standing of your research group in the field | |
| Contributed to the development of tools and technologies | |
| Supported new/stronger collaboration with industry | |
| Other (please specify) | |
| Did not support my wider research aims | |

Comments:

Research outputs - Publications

6. Have you adopted a publishing strategy for your research? (please tick one and comment if you wish)

| | |
|--|--|
| Target the highest profile general journals (e.g. Nature, Science) | |
| Target the most appropriate journals for my area of science | |
| Target journals where I can get my results published quickly | |
| Target conference proceedings | |
| Other (please specify) | |

Comments:

7. Is your publishing strategy influenced by having to produce a final scientific report for BBSRC within 3 months of completion?

YES / NO

Comments:

8. Please provide details of all publications and/or major conference papers arising as a direct result of this grant, and indicate where they have co-authors from industry or from overseas

Research outputs – People

9. Please provide details of staff employed on the grant, and their first destination after completion of their employment (*Grade/position; Period of appointment; First destination*)

Research outputs – Further funding

10. Have you received further funds from BCB to continue or develop the work funded by this grant?

YES / NO

If yes, please provide details (*Grant ref no.; Value (£); Start/end dates*)

If no, why not? (please tick one or more and comment if you wish)

| | |
|---|--|
| The area of science was not covered by the BCB remit | |
| Funding is more accessible from other sources (other BBSRC Committees, other Research Councils, other funding bodies) – <i>please specify</i> | |
| Applied to BCB but proposal was not funded | |
| My research priorities have changed | |
| Other (<i>please specify</i>) | |

Comments:

11. Have you received a follow on grant related to this BCB grant from another funding body?

YES / NO

If yes, please provide details (*Funding body; Value (£); Start/end dates*)

Research outputs - Exploitation

12. Did/could any new products, processes, tools or technologies result from this grant? For example, reagents, tools, software or methodology?

YES / NO

If yes, please provide details

13. Have you or your colleagues applied, or are you likely to apply, for any patents, licenses or other form of intellectual property rights as a result of the research supported by this grant?

YES / NO

If yes, has the patent been licensed to other companies? YES / NO

If yes, has the licence yielded any income? (please give details with dates e.g. £100,000 from 2000-2002)

14. Have you or your colleagues established any Spin-out companies from the research supported by this grant?

YES / NO

If yes, please provide details (*Company name; Area of activity; Date established; Trading/dormant; Annual turnover; Staff no.s*)

Other outcomes

15. Did any other outcomes arise from the research supported by this grant? (please tick one or more and provide details where appropriate)

| | | |
|--|---|--|
| New ideas/avenues for research | | |
| New or improved academic contacts - <i>if cross-disciplinary, please specify which discipline</i> | UK | |
| | Overseas | |
| New or improved industrial contacts - <i>please specify type of industry</i> | UK | |
| | Overseas | |
| New formal academic research collaboration (e.g. joint publication, joint funding application) | UK | |
| | Overseas | |
| New formal industrial research collaboration (e.g. joint publication, joint funding application) - <i>please specify type of industry, nature of collaboration</i> | UK | |
| | Overseas | |
| Contribution to the reduction, refinement and replacement of animals in experiments | | |
| Contributions to public awareness or science in society debates | Publicity in the general non-scientific media | |
| | Schools activities | |
| | Public dialogue | |
| | Other (<i>please give details</i>) | |
| Other (<i>please specify</i>) | | |

Comments/details:

General

16. What is your area of expertise? (tick one or more classification)

| | | | | | |
|------------------------|--|----------------|--|--------------------|--|
| 1. Animal cell culture | | 10. Cell walls | | 19. Nucleic Acids | |
| 2. Biocatalysis | | 11. Design and | | 20. Photosynthesis | |

| | | | | |
|--|--|---|------------------------------------|--|
| | | modelling of biomolecules | (plants, algae etc) | |
| 3. Bioenergetics | | 12. Dietary fibre, complex polysaccharides | 21. Plant biochemistry | |
| 4. Biomimetics | | 13. Enzymology | 22. Protein synthesis | |
| 5. Biomolecular structure/function | | 14. Fixation of nitrogen | 23. Proteins and peptides | |
| 6. Biopolymers | | 15. Intercellular transport and signalling | 24. Vitamins, provitamins and food | |
| 7. Biotransformation | | 16. Intracellular transport and signalling | 25. Tissue culture | |
| 8. Carbohydrates, sugars, simple polysaccharides | | 17. Lipids, steroids | Other (<i>please specify</i>) | |
| 9. Cell biology | | 18. Membranes; structure, functions and processes | | |

17. Do you think your area of expertise is well supported by the BCB Committee?
(please tick one and comment if you wish)

| | | | |
|-------------------------|----------|----------|-------------------------------|
| 4 (very well) | 3 | 2 | 1 (not at all well) |
| | | | |

Comments:

18. The BCB Committee's aim is "to support and foster basic research of the highest quality at the cellular and molecular level". Do you think that the Committee is achieving this aim? Are there any exciting areas that it should be covering but isn't? (for the current portfolio see www.bbsrc.ac.uk/science/areas/bcb.html). Please tick one and comment if you wish

| | | | |
|-------------------------|----------|----------|--------------------------|
| 4 (very well) | 3 | 2 | 1 (not at all) |
| | | | |

Comments:

19. Do you have any comments on the operation of the BCB Committee (e.g. remit, themes and priority areas) ?

20. Do you have any comments on the grant application/administration process?

21. Have you acted as a referee for a BBSRC grant? YES / NO

Do you have any comments on the refereeing process (e.g. quality, helpfulness of referees' comments)? How can BBSRC increase the number and quality of referees' comments?

22. Do you have any other comments relevant to this evaluation?

Please return by email or post to Fiona Hindley by 9th February

Biochemistry and Cell Biology Portfolio Evaluation 2005 Survey of Current and Past Committee Members

(by semi-structured phone interview, with introductory email sent beforehand)

Name:

Organisation:

Date started:

Date ended:

For past members, please answer the questions relating to Committee as it was when you served on it, not as it is now

BCB Portfolio

1. What are your views on the coverage of the portfolio? What's missing? What's good? [Industrial members – are we missing areas that industry think we should be funding?]
2. Who applies to BCB and who doesn't (in terms of disciplines)? Who is funded by the Committee? Who are we missing? E.g. non-biol departments
3. Does the portfolio overlap with other BBSRC Committees? (Does overlap matter?)
4. How does the portfolio compare with other UK BCB funders? Overlap? Gaps?
5. What do you think of the themes and Priority Areas? Pros, cons, how to improve
6. What impact do Priority Areas have on your assessment of applications? Do they influence your judgement at all?
7. What areas/opportunities may we have missed in the past? Why did we miss them?

Achievements

8. BCB's stated aim is "to support and foster basic research of the highest quality at the cellular and molecular level". Do you think that it is achieving this aim? (4-1 scale)
9. How good is the science that BCB funds? (4-1 scale)
10. What are BCB's key achievements over the past 10 years? Or, in other words, what difference has BCB made? (specific examples of high profile/important achievements where possible)
11. What does BCB research achieve? i.e. who are the end users? how are the results of the BCB-supported research used? What new avenues has it opened up? Please give examples
12. Has the research portfolio supported by BCB contributed to the 'public good' e.g. quality of life, wealth creation? (4-1 scale)

Wealth creation

Public engagement with BCB/bioscience

Quality of life

Reducing the use of animals in experiments

Industry

13. Please comment on the relationship between BBSRC supported BCB research and industry. Is it getting better or worse? What would the ideal be? (indicate that very few grants had industrial funding at outset)

Process and Management

14. What do you think about the way Committee meetings are structured? How could they be improved?

15. Does the BCB Committee work well as a team in reaching conclusions?

16. Do you have any comments on the fact that some two thirds of grants are not discussed at the meetings due to lack of time. Does it matter? If so, how could this be improved?

17. What do you think of the state of refereeing? How does it compare with the past? What is the ideal number of referees responses?

18. Do you have any other comments on the Committee or grant appraisal process? (strengths and weaknesses)

19. What do you think of the final report grade system? How could it be improved?

20. What are your views on BBSRC's management of the grant appraisal process and management of the Committee?

Other

21. What do you think are the most important functions of the Committee? Do you have any comments on its role within BBSRC as a whole?

22. Do you have any other comments?

Biochemistry and Cell Biology Portfolio Evaluation 2006 Survey of UK Funders

Please answer as many questions as you can, and return to Fiona Goff, preferably by email, by **1st March**. If completing by hand, please feel free to continue your answers on a separate sheet.

Fiona Goff, Research Evaluation Manager
fiona.goff@bbsrc.ac.uk
BBSRC, Polaris House, North Star Avenue, Swindon SN2 1UH
Tel 01793 414678, Fax 01793 414674

Name:
Job title:
Organisation:

Remit (please refer to enclosed background information)

1. How does the Biochemistry and Cell Biology (BCB) Committee's remit compare with your remit in this scientific area? E.g. areas of overlap, gaps
2. What do you think of the BCB's remit and themes as described in the enclosed document? Does this remit adequately cover what you understand to be BBSRC's responsibilities in the BCB area?
3. Do our current priorities (see enclosed document) reflect your perception of the key research needs (as they relate to BBSRC's remit) in the area?
4. Are the boundaries between our two organisation's remits and responsibilities in this area clearly defined? Do you have any concerns about the clarity of the interface?

Coverage and resources

5. Are there any areas within (or potentially within) BCB's remit that you receive many proposals for but cannot fund?
6. Are there areas relevant to your organisation within BCB's remit that need more support in the UK? Conversely, are there areas where support is less crucial? E.g. where there are many potential funders or where you feel the science is less important to the UK
7. If you have the data to hand, what was your annual budget in the BCB area (or sub area), and/or how many grants did you support in the last financial year?

| Area | Budget | | No. grants | |
|------|--------|------|------------|---------|
| | Amount | Year | No. | Year(s) |
| | | | | |
| | | | | |

Funding processes

8. At present, the majority of BBSRC's responsive mode grants involve academic research and are 3 years in length, supporting one postdoctoral Research Assistant. Is this typical of the type of funding provided by your organisation? Do you have any comments on this?
9. How could funding organisations work together to better serve the BCB research community? Are there any barriers to joint working between your organisation and BBSRC in this area?
10. Do you have any other comments relevant to this evaluation?

Thank you, your contribution is much appreciated.

LIST OF SAMPLE GRANTS

Completed grants

1. A functional approach to the study of a novel GABA receptor subunit
2. A molecular analysis of ribosomal frameshifting
3. A new function for the peptide signal, systemin
4. A proteomics based approach applied to the definition of IgE- receptor mediated signalling pathways in mast cells
5. A putative mammalian aspartic proteinase involved in apoptosis
6. A structure-function study of the class II phosphoinositide 3- kinase isozymes
7. Activities and regulation of beta spectrins
8. AMP/Snf1-related protein kinases in higher plants: key players in the response to nutritional and environmental stress?
9. Analysis of a new CD23 receptor in a human B lymphoid cell line
10. Analysis of the mechanism of TIMP-MMP interactions and strategies for the development of 'designer' TIMPs
11. Analysis of the redox components, role and biosynthesis of the periplasmic nitrate reductase system of *Paracoccus denitrificans*
12. Bacterial redox proteins: lupanine hydroxylase, novel quinocytocrome C
13. Biochemical studies of native and recombinant N-methyl-D- aspartate receptors
14. Biosynthesis of mupirocin by *Pseudomonas fluorescens*
15. Cell signalling through the cytoplasmic domains of the adamalysins
16. Cell-type specific monitoring of intracellular calcium in a *Drosophila* epithelium using an aequorin transgene
17. Characterisation and identification of an E2F- specific co- repressor which regulates cell-cycle dependant transcription
18. Characterisation of hybrid GroEL molecular chaperones
19. Characterisation of key events involved in the self- incompatibility (SI) response in *Papaver rhoeas*
20. Characterising the active site of pyrophosphate: fructose 6- phosphate 1- phosphotransferase from plants
21. Components of the thylakoid protein translocation machinery
22. Constitutive activation of D2 dopamine receptors and the mechanism of inverse agonism
23. Control of nitrate reductase (NR) and sucrose-phosphate synthase by reversible phosphorylation and a novel NR inhibitor
24. Cytochrome biosynthesis in *Escherichia coli* role of the ABC transporter, CydDC
25. Determination of pathways responsible for programming macrophages in inflammation
26. Determining the function of a novel interferon stimulated gene (BEST5) expressed during bone formation
27. Development of G-protein switches to control endogenous and exogenous plant cell circuits
28. Differential PKA regulation of neuroendocrine BK channels determined by alternative splicing of pore forming subunits
29. Dissection of the enzyme activities involved in transcription and replication of the dsRNA genome of bluetongue virus
30. Does maturation-restricted expression of cytosolic phospholipase A2 direct differentiation during B cell development?
31. Downregulation of tyrosine kinase receptors
32. Dynamic aspects of the structure and function of the light harvesting complexes of photosystem II in plants

33. Effects of acute ischaemia on thalamocortical synaptic transmission in vitro
34. Elucidation of the bacterial c-type cytochrome biogenesis pathway; redox protein assembly in the periplasm
35. Elucidation of the mechanism of myosin ATPase through directed probes
36. Elucidation of the structure, function and dynamics of photosystem two
37. Endoplasmic reticulum-associated protein degradation in plant cells
38. Energy coupling and the basis of specificity of Escherichia coli topoisomerase IV
39. Expression of tubulin and mutant tubulin in transgenic maize calli
40. Flagellar ATPases: rate of in situ ATP hydrolysis measured with a new probe for phosphate
41. Fluorescence measurements on membrane protein structure and function
42. Fluorescent imaging of cGMP in cerebellar Purkinje cells during the induction of cerebellar long-term depression
43. Functional analysis of KATI and other plant K⁺ channel proteins
44. Functional characterisation of a nucleoside transporter in trypanosomes
45. Functional characterisation of BiP subdomains to unravel its function in protein synthesis, folding and quality control by the ER
46. Functional consequences of the interaction of Ryania alkaloids with the sarcoplasmic reticulum Ca²⁺-release channel
47. Functional significance of CD40 expression in hepatocytes and intrahepatic endothelium
48. Gene cloning and regulation of the protein moiety of a glycoprotein involved in cell adhesion
49. Genetic and functional characterisation of the cGMP-dependent protein kinase family
50. Genetically engineered control of the primary photosynthetic reactions of photosystem II
51. Growth regulation of RNA polymerase III transcription
52. Identification and characterisation of novel Ran-binding proteins
53. Identification and characterisation of signals for self-renewal and differentiation in haemopoietic stem cells
54. Identification and cloning of the myeloid cell surface receptor for chaperonin 60
55. Identification of genes involved in the repair of a damaged membrane protein complex
56. Identification of ligands for the Natural Killer cell C-type lectin-like receptors CD69 and NKR-P1
57. Identification of preferential substrates and regulatory proteins for MEK kinase isozymes based on protein-protein interaction
58. Importance of alternative transcripts of the mb-1 and B29 genes in B-cell biology
59. Insulin-related peptides in locusts
60. Interaction of eukaryotic chaperonin CCT with polymerising cytoskeletal components
61. Interaction of yeast calmodulin with three proteins showing Ca²⁺-sensitive calmodulin binding
62. Internal molybdenum metabolism and molybdate-dependent gene regulation in bacteria
63. Intracellular signalling in the oxidative stress response in eukaryotes
64. Intracellular targeting of secretory immunoglobulins in plants
65. Investigation of the influence of perturbations of the cAMP relay dynamics on multicellular Dictyostelium morphogenesis
66. Isolation and characterisation of apoptosis controlling genes from primate herpes viruses
67. Location and control of endomembrane calcium release channels in plants

68. Manipulating frost sensitivity and the basis of acyl specificity of acyltransferases
69. Manipulation of lignin biosynthesis by down regulation of multiple enzymes
70. Mechanistic mapping and redox regulation in NO- synthase and a related monooxygenase
71. Molecular analysis of human splicing complexes
72. Molecular characterisation of the principal peptide binding site of PD1p
73. Molecular mechanisms controlling angiogenic signalling from the sphingosine-1 phosphate receptors edg1 and edg3
74. Molecular mechanisms of modulation and regulation of the large conductance Ca²⁺-activated K⁺ channel
75. Molecular studies on a novel signal transduction pathway regulating Fcγ₃ mediated internalisation of immune complexes
76. Mutational analysis of lysosomal enzyme sorting in Dictyostelium
77. Natural resistance-associated macrophage protein (Nramp): functional effects of PKC-mediated phosphorylation and protein interactions
78. Nematode structural protein folding catalysts; structural characterisation and evaluation as targets for anti-helminthic development
79. New inhibitors and mechanism of the chloroplast cytochrome b_f complex, and an analysis of chlororespiratory enzymes
80. Pathways for the synthesis of metal sulphur clusters in living cells
81. Phosphoinositides and the transduction of light signals in duckweeds
82. Physiological and genetic analysis of Drosophila taste transduction: overlap between visual and chemosensory pathways
83. Protein targeting in plant cells
84. Proteomic analysis of the Hsp90 chaperone system
85. Purification and characterisation of Holliday junction resolving enzymes from archaea
86. Purification and molecular characterisation of NEM-sensitive phosphatidic acid phosphatase (PAP1)
87. Regulation and activity of the mitotic polo-like kinases (plks) of Xenopus and Drosophila
88. Regulation of ARF signalling by 3-phosphorylated inositol lipids
89. Regulation of cardiac KATP channel expression by oestrogens
90. Regulation of CD4 T cells by CD8 T cells in the graft versus host reaction
91. Regulation of neuronal endoplasmic reticulum calcium stores by intraluminal calcium
92. Regulation of pollen tube growth orientation by calcium dependent protein kinase (CDPK)
93. Regulation of preadipocyte differentiation by specific protein kinase C isoforms
94. Regulation of System A amino acid transport by insulin, cell stress and microtubular dysfunction
95. Regulation of the actin cytoskeleton by WASp-family proteins
96. Regulation of the size of the inositol trisphosphate-sensitive calcium stores by parathyroid hormone
97. Retinoblastoma gene homologues from plants and their role in cell growth and differentiation
98. Ribozyme-mediated cell-specific downregulation of gene expression in the adult CNS using adenovirus vectors
99. Role of endothelial MAP-kinases in supporting transendothelial migration of T-lymphocytes
100. Role of folding enzymes and molecular chaperones in the translocation, folding and assembly of procollagen in the endoplasmic reticulum
101. Role of microdomains of ATP and Ca²⁺ concentration in glucose- triggered insulin secretion

102. Role of the CRE/CREB factor in cyclic AMP and NGF signalling in neuronal cells
103. Role of the NSF-related VCP in endosomal vesicle fusion and its regulation during the cell cycle
104. Selective agonist definition of G-protein channelling
105. Signal transduction coupling photoreception by CRY1 to CHS transcription in Arabidopsis
106. Signalling pathways activated by Shc phosphorylation
107. Spectral tuning of violet- and ultraviolet- sensitive visual pigments of vertebrates
108. Sphingosine 1-phosphate and lysophosphatidate signalling in mammalian cells
109. SRP-independent protein targeting to the ER in yeast
110. Stimulus-induced oscillations in guard cell cytosolic free Ca²⁺
111. Structural and functional analysis of the specialised BRCT domain of E. coli DNA ligase
112. Structural and functional modifications of translation initiation factors eIF4A and eIF4G in foot and mouth disease virus infected cells
113. Structural and thermodynamic characterisation of the oligomerisation and DNA interactions of the histone-like nucleoid structuring protein, H-NS
114. Structure and function of Ins(1,3,4,5)P₄ binding proteins in platelets
115. Structure and function of the nicotinic acetylcholine receptor: molecular dissection of the desensitised binding sites
116. Structure and function of the quinone binding site of the photosystem 1 reaction centre
117. Structure/function of cold and pressure adapted enzymes isolated from deep sea fish
118. Structure: function analysis of RhoE and identification of its downstream targets
119. Structure-activity relationships of D-glucuronide and L-fucose membrane transport proteins
120. Structure-function studies of the CCP (sushi) modules in the metabotropic GABA receptor that define three putative subtypes
121. Studies of receptor mobility and membrane microstructure by single particle tracking and FRAP
122. Studies of the Res proteins of Bacillus subtilis and their role in cytochrome c assembly
123. Study of cytochrome oxidase biogenesis in yeast: deficiency mutations and suppressors affecting the enzyme assembly
124. The biosynthesis of polytopic integral membrane proteins
125. The function of the Drosophila class II phosphoinositide 3- kinase in signalling and development
126. The function of the extracellular domain of CD45: an in vivo genetic complementation study
127. The mechanism of action of acidic transcriptional activators
128. The membrane associated domain of the vacuolar H⁺-ATPase: assembly, structure and function
129. The molecular basis of interfacial recognition by human secreted phospholipase A₂
130. The origin of the skew in the amplitude distribution of fast miniature synaptic currents in the mammalian brain
131. The photosynthetic reaction centre of green sulphur photosynthetic bacteria
132. The regulation of phosphoenolpyruvate carboxykinase in C₄ and CAM plants
133. The role of a novel cyclin in cell growth and division
134. The role of CD31/PECAM-1 in T cell adhesion, migration and survival
135. The role of CD45 in signalling pathways mediated by GP1-linked molecules in T-cells.
136. The role of class IA phosphoinositide-3 kinases in IL-3 induced proliferation

137. The role of MAP kinase phosphatase-2 in MAP kinase signalling
138. The role of nuclear dots (ND10) in mammalian cell function and adenovirus infection
139. The role of phosphoinositide 3-kinase(s) in chemokine mediated signal transduction and chemotaxis
140. The role of the stress-activated protein kinases in mitotic cell cycle arrest
141. The structural and functional role of co-and post- translational modifications at the N-terminus of the HIV-1 Nef protein
142. Ultrastructural localisation of nicotinic receptor subtypes in rat striatum and substantia nigra
143. Use of an in vivo fluorescence assay and dominant genetics to investigate membrane traffic in Arabidopsis
144. Using protein ligands and site-directed mutants to study porin channel dynamics
145. Xyloglucan endotransglycosylase (XET) isoenzymes: diversity of action on donor and acceptor substrates

Current grants for which questionnaires were returned

1. A protein that looks like DNA! The fundamental interactions required for DNA mimicry
2. A proteomics-based approach for understanding plant microtubule organization
3. A role for Bag-1 in the regulation of differentiation and apoptosis in keratinocytes
4. An investigation into some molecular determinants of NMDA receptor-channel behaviour
5. Bicarbonate mediated signal transduction in Cyanobacteria
6. Biochemistry of Acyl CoA dependent proteins in plants: a targeted proteomics approach
7. Biochemistry of plant AcylCoA binding proteins using a targeted proteomics approach
8. BspMI; a novel system for DNA recognition and cleavage
9. Cell cycle regulation by MDM2: a combined proteomic and molecular investigation
10. Characterisation of recombination substrates and recombination repair pathways at replication forks in mammalian cells
11. Characterisation of the role in cytokinesis/cell separation of novel cytoskeletal components in budding yeast
12. Characterising the signalling mechanisms of receptor tyrosine phosphatase CRYPalpha
13. Dissecting the cell biology of plastid division
14. Dissecting the functions of Ulp1, a SUMO-1 specific protease
15. Dissection of the ATPase switch controlling papillomavirus DNA replication initiation
16. Docking and electron transfer reactions of metalloproteins studied using site-directed mutants of cytochrome c
17. Dynamics of photosynthetic membranes
18. Elucidating the key role of connexin 31 in epidermal differentiation
19. Enzymatic activity of a mono-haem c-type cytochrome. Cytochrome c' is a nitric oxide reductase
20. Formation of a multi-component complex regulates phosphatidylcholine hydrolysis, cell shape and secretion
21. Function of multidomain protein Eps 15 in Drosophila endocytosis
22. Functional roles and regulation of P-Rex, a new family of guanine-nucleotide exchange factors

23. Heregulin signalling via nitric oxide in the nervous system
24. High pressure freezing to capture endoplasmic reticulum and Golgi dynamics
25. How are NMDA receptors specifically coupled to the excitotoxic cell death pathway in cerebellar granule neurons?
26. Identification of a factor required for trafficking of a functional adrenocorticotropin receptor to the cell surface
27. Identification of the synergy receptor binding domains in snake venom disintegrins and their role in integrin recognition
28. Inhibition of beta-amyloid formation using N-methylated peptides
29. Intracellular targeting and regulation of gene expression by Exchange-Protein-Activated-by-Cyclic AMP (EPAC)
30. leptin modulation of GABA_A receptor function: a novel process for regulating hippocampal excitability
31. Lipid rafts and the spatial control of exocytosis
32. Mitochondrial energy metabolism and the differentiation and survival of neural cells
33. Modelling anhydrobiosis in mammalian cells: life without water?
34. Modulation of proton and electron transfer to the active site of nitrogenase: time-resolved EPR, ENDOR and FTIR studies
35. Molecular and cellular analyses of the role of a myosin I in actin polymerisation, cortical dynamics and cell motility
36. Molecular and chemical mechanism underlying human CYP17 catalysis
37. Molecular basis of the formation of an N-cadherin/FGF receptor signalling complex and development of peptide agonists
38. Molecular biological characterisation of neuronal nicotinic acetylcholine receptors from *Drosophila*
39. NMDA receptor-mediated dendritic protein synthesis a potential mechanism for the regulation of synaptic strength
40. Novel cap-binding proteins in yeast
41. Phosphorylation-dependent specificity in the Smad3 signalling pathway
42. Prediction, generation and assessment of high- throughput protein-protein interaction data
43. Regulation and function of PIP2 in *Drosophila* phototransduction
44. Regulation of precursor cell proliferation during B lymphocyte development
45. Regulation of protein kinase c-epsilon function in fibroblasts by a ser729 phosphatase b-cop and myosin
46. Regulation of the immunosuppressive IL-10 gene by interferons
47. Regulation of the pro-apoptotic protein Bax by cell damage signals
48. Role of Arf5 and Arf6 in regulated membrane trafficking in adipose cells
49. Role of JNK MAP kinase in the response of astrocytes to TNF alpha
50. Role of protein S-thiolation as an antioxidant defence in yeast
51. Role of the Cdc37 protein in fission yeast
52. Roles and mechanisms of action of GPI anchors and N-glycans in cellular targeting and trafficking
53. Signalling pathways regulating survival and apoptosis during early murine thymic development
54. SK-1 a protein with a novel topology
55. Specificity of RGS protein recruitment by activated G-protein- coupled receptors.
56. Structure and binding specificity of the vesicular trafficking protein SNX1
57. Structure and mechanism of oxalate decarboxylase: A novel Mn and oxygen dependent enzyme involved in pH stress response
58. Structure-function relationships in tandem pore potassium channels
59. Supramolecular organisation at immune synapses in human T cell energy and tolerance
60. Targeting of the phosphoinositide phosphatase OCRL1 to the golgi apparatus

61. The control and signalling of the Neuron-glia related cell adhesion molecule in neuronal formation
62. The function of Sec 1 proteins in exocytosis
63. The functional roles of conventional myosins during neuronal growth cone motility
64. The role of cortical microtubules in the regulation of cellulose synthesis
65. The role of envoplakin, periplakin and involucrin in keratinocyte differentiation and skin barrier function
66. The role of retinoblastoma in cell cycle control
67. The role of the Sec1p-like/Munc18c protein Vps45p in SNARE complex formation
68. The roles of Rab38 and Rab32 in melanosome biogenesis
69. The signalling and mechanism of apoptotic cell extrusion from simple epithelia
70. Transdifferentiated hepatocytes as a model for studying liver function

OTHER NOTABLE GRANTS

The Panel identified a number of other notable grants (in addition to the grants highlighted in the main report):

Fundamentals of Cell Biology and Biochemistry**Manipulation of lignin biosynthesis by down-regulation of multiple enzymes.**

Lignin is a complex carbohydrate unique to plants and plays a major role in conferring mechanical strength to stems. It is of major significance to both the forestry and paper-making industries. The biosynthetic pathway leading to lignin formation was poorly understood and thought to involve multiple biochemical steps. The PI developed a strategy by which partial sense sequences for multiple genes in the lignin pathway could be expressed (and down regulated) from a single gene promoter. The work demonstrated that the accepted pathway for lignin biosynthesis was incomplete and resulted in the elucidation of a new biochemical pathway for lignin biosynthesis, as well as the development of transgenic tobacco plants within which the composition and mechanical properties of lignin-rich cells were altered. These plants are valuable tools for future research on the structural and functional roles of lignin in plants. The group also contributed to a public exhibition, 'Weekend of Wood' at Dundee Botanic Gardens, hosted work experience placements for school children, and the PI gave a presentation to local school teachers.

Differential PKA regulation of neuroendocrine BK channels determined by alternative splicing of pore forming subunits. The work has shown that alternative pre mRNA splicing of calcium activated (BK) channels is an important determinant of regulation of BK channel activity by reversible phosphorylation. It has been shown also that the alternative splicing is regulated by PKA and protein phosphatase 2A. The work provides insight into the regulation and functional role of BK channels in excitable cells and that the dynamic regulation of BK channel splice variant expression can control the function of individual neurones or endocrine cells. The work resulted in several good quality publications.

Purification and characterisation of Holliday junction resolving enzymes from archaea. The authors characterized two endonucleases and their roles in homologous recombination processes in an acidophilic/thermophilic archaeon. For one of the endonucleases, it was demonstrated that the enzyme makes nicks in the DNA with no sequence specificity for cleavage, but the enzyme is highly specific for the continuous arms of the DNA junctions. On the basis of these findings, the authors propose a new mechanism for resolving so-called Holliday junctions in the process of DNA recombination.

The biosynthesis of polytopic integral membrane proteins. This research focused on transport of proteins into the Endoplasmic Reticulum (ER), in particular, how transmembrane domains are inserted into the ER membrane. The group showed that the Sec61 complex is required for inserting all transmembrane domains into the ER; however there are additional factors required for insertion of different transmembrane domains.

Growth regulation of RNA polymerase III transcription. This work gave insights into mechanisms responsible for the growth control of pol III transcription in murine fibroblasts. It revealed that transcription factor TFIIIB is the principal target for this control, and is repressed through direct interaction with P53 and pocket proteins RB,

p107 and p130. In terms of public engagement, an article mentioning aspects of this work was published in a Scottish daily newspaper.

Role of the NEM Sensitive Factor (NSF) -related Valosin Containing Protein (VCP) in endosomal vesicle fusion and its regulation during the cell cycle. This work demonstrated that the mammalian orthologue of yeast Vps4p (mVPS4) is involved in endosomal trafficking. However, the research was unable to demonstrate a direct role either for p97 or mVPS4 in endosomal fusion. A follow-on grant was awarded by BCB, together with a substantial award from MRC, to continue this work over the next 5 years.

Specialised Cell Function

Intracellular targeting of secretory immunoglobulins in plants. This group demonstrated that: (i) sIgA/G assembles in the plant Endoplasmic Reticulum (ER), a process mediated by Immunoglobulin binding protein (BiP); (ii) assembled but inactive antibodies reach the vacuole; (iii) a region of the heavy chain tailpiece is responsible for vacuolar sorting – this acts as a cryptic sorting signal, deletion of which results in antibody being secreted. This work spawned an international patent application on the secretion of antibodies from plants (plantibodies).

Importance of alternative transcripts of the mb-1 and B29 genes in B-cell biology. CD79 together with specific surface immunoglobulin constitutes the B cell receptor for antigen. The group showed that alternative transcripts exist in normal and malignant B cells. Although only one paper has been published from this work to date, it was in a high impact journal (Blood), and has been well cited.

Does maturation-restricted expression of cytosolic phospholipase A2 direct differentiation during B cell development? This work was highly successful and had a significant impact, as the resulting publications have been well cited. The group have also attracted considerable subsequent grant funding to pursue the issues raised by the research supported by this grant.

Functional characterisation of a nucleoside transporter in trypanosomes. This project set out to study a nucleoside transporter in trypanosomes that can be used to transport drugs. The work was very successful in terms of publications. The PI also spent time on public engagement activities. A direct effect of this and related work over the last 10 years has been to drastically reduce the tsetse belt in South-Central and East Africa, opening it up for agriculture, and thus contributing significantly to the livelihoods of local people.

Structure and function of the quinone binding site of the photosystem 1 reaction centre. This research applied a variety of spectroscopic techniques to examine the environment of quinones in the photosystem 1 reaction centre, which transfer electrons generated through the capture of energy from light. Such work is essential to gaining an understanding, at the atomic level, of the mechanisms of photosynthesis.

Functional significance of CD40 expression in hepatocytes and intrahepatic endothelium. This research showed that ligation of the cell surface protein CD40 has different effects in different cell types in the liver: apoptosis in hepatocytes, but proliferation in endothelial cells. The work highlighted the importance of studying primary cells in addition to cell lines, whose responses will not be typical of all cell types.

Ultrastructural localisation of nicotinic receptor subtypes in rat striatum and substantia nigra. This research used electron microscopy to determine the subcellular localisation of nicotinic acetylcholine receptors in the striatum and substantia nigra regions of rat brain. By resolving technical challenges, this opened the door to further studies.

Molecular studies on a novel signal transduction pathway regulating Fcγ₃RI-mediated internalisation of immune complexes. In general this grant was successful in meeting most of the objectives, and was good value for money.

Regulation of neuronal endoplasmic reticulum calcium stores by intraluminal calcium. The work was not quite as originally described, but quite similar, and seems to have been quite successful, yielding some reasonable papers.

Cell-cell Interactions

Sphingosine 1-phosphate (S1P) and lysophosphatidate signaling in mammalian cells. This study showed that the S1P receptor S1P₁ exists in a complex with the Platelet Derived Growth Factor (PDGF) receptor PDGFβ, and that they act together to increase the efficiency with which each of them can activate the extracellular signal-regulated kinase (ERK) mitogen-activated protein (MAP) kinase cascade. The group shows that this complex allows the two receptors to share a tyrosine kinase and a heterotrimeric G protein, thereby increasing efficiency of signalling. This excellent work resulted in three papers in the Journal of Biological Chemistry.

The roles of phosphoinositide 3-kinases in chemokine mediated signal transduction and chemotaxis. This study examined the role of class 1A and class 1B phosphoinositide 3-kinases (PI3Ks) in Stromal cell-derived factor (SDF-1) induced chemotaxis of Jurkat cells. The team concluded that, surprisingly, both classes of PI3K are required. The work was published in two primary papers (Journal of Immunology, and Immunology).

Influence of perturbations of the cAMP relay dynamics on multicellular *Dictyostelium* morphogenesis. This study has exploited *Dictyostelium discoideum* as a model system to understand co-ordinated cell movement in multicellular tissues. It is an excellent example of how a simple model organism can provide insight into mechanisms functioning in higher organisms, and of the benefit of coupling of biochemistry and development research. *Dictyostelium* has four cAMP receptors, which can couple to the same signal transduction pathways leading to cAMP amplification and chemotaxis. The group showed that the affinity of the receptors determines the frequency of cAMP wave initiation and the oscillation frequency. Co-operation between the cAMP receptors was observed. Mathematical models were generated to model a range of factors that contribute to migration. The work led to multiple publications, and was continued with grants from BCB and the Wellcome Trust. It also appeared to contribute to an excellent young scientist getting established.

Cell-type specific monitoring of intracellular calcium in a *Drosophila* epithelium using an aequorin transgene. The authors report the first intracellular measurements of Ca²⁺ in insects, using the calcium reporter aequorin. They identified the major routes for Ca²⁺ uptake in tubule and established that channels belonging to the trp family form the store-operated Ca²⁺ entry pathways. Finally, much of the regulation of the Ca²⁺ signalling pathway in tubules was established, and a pivotal role for a cyclic nucleotide-gated channel proposed.

Analysis of the mechanism of tissue inhibitors of matrix metalloproteinases (TIMP-MMP) interactions and strategies for the development of ‘designer’ TIMPs. This research used an elegant combination of biochemistry and cell biology to determine the role of extracellular matrix turnover, and its position in development and degradative disease processes. The research established the interactions between tissue inhibitors of metalloproteinases and the metalloproteinases itself. Mutants were designed that can now be used to determine the tissue turnover in *in vivo* models.

The role of stress-activated protein kinases in mitotic cell exit. This research showed that the stress activated kinases, p38MAPK, can mediate apoptotic cell death in cells arrested in mitosis with anti-microtubule drugs. This work also showed that anti-microtubule drugs, often used in cancer therapy, can not only induce cell death, but can also induce cell survival pathways depending on context.

Nematode structural protein folding catalysts; structural characterisation and evaluation as targets for anti-helminthic development. This work led to the structural and functional characterisation of gut-associated cyclophilin B isoforms from *C.elegans*. The role of several enzymes (*e.g.*, PPI, PDI, P4H) in nematode development was elucidated, with a particular focus on the collagenous exoskeleton. Importantly, the work highlighted key enzymes to target in future development of anti-helminthic compounds.

Regulation of the actin cytoskeleton by WASp-family proteins. In general this was successful, and there was a commercial outcome (5 new commercialised Mc Abs).

Genetic and functional characterisation of the cGMP-dependent protein kinase family. This project has attempted to define the cyclic GMP-dependent protein kinases (cGK) that regulate epithelial function in a fly (*Drosophila*) “renal” tubule model. The work identified *dg1* and *dg2* as genes encoding cGK activity; these encode proteins that are homologues of vertebrate cGKII and cGKI, respectively. Expression of *dg1* confers an epithelial phenotype (increases in fluid transport) indicating its importance in the formation of this cell type in *Drosophila*. In order to further assign function to *dg1*, *in vivo* knockdowns, by expressing truncated regulatory domains, have been generated. Such dominant-negative modifications may open up *in vivo* methods for other enzymes. Some of this work (regulation of fluid movement and intracellular Ca⁺⁺ flux) indicates that cellular location and the formation of protein complexes is key to the proper physiological function of cGK in the renal tubule.

In addition, this group also made a major contribution to the communication of science to a lay audience; the PI was involved in exhibitions at Glasgow Science Centre to schoolchildren.

Regulation of ARF signalling by 3-phosphorylated inositol lipids.

3-phosphorylated inositol lipids are implicated in important cellular events such as vesicle trafficking and plasma membrane fusion via activation of small molecular weight GTPases such as ADP-ribosylation factors (ARF); loss of regulation of PIP3 may underlie certain cancers. This project has shown that phosphatidylinositol 3,4,5-trisphosphate (PIP3) activates ARF6 through and intermediary protein ARNO. The GTPase activity of ARF6 (a molecular ON/OFF switch), which ultimately regulates the cyto-skeletal rearrangements and influences vesicle fusion, is therefore subtly regulated by an intermediary protein. In addition to adding to the understanding of the action of PIP3, the project has employed cutting edge fluorescence techniques

such as FRET, which has in part led to their greater use in the study of lipid mediated cell signalling events.

SRP-independent protein-targeting to the ER in yeast. The process of transporting a protein to the cell surface and beyond begins with the transport of the protein into the endoplasmic reticulum (ER). A ribonucleoprotein complex called Signal Recognition Particle (SRP) plays a well-documented role in targeting proteins to the ER. However, some proteins are efficiently targeted to the ER even in the absence of SRP. This grant funded work identifying a novel pathway by which a subset of secreted proteins are translocated into the ER. This involved the identification and characterisation of a novel heat shock 70-like protein, LHS1. In addition to being science of the highest quality, it also represented an example of how different modes of BBSRC funding can work together, because much of the work (including a first author EMBO J paper) was done by a BBSRC-funded PhD student.

SURVEY RESULTS AND ANALYSIS

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1. INTRODUCTION

1. This paper reports the results and analysis of the surveys conducted for the evaluation of the Biochemistry and Cell Biology (BCB) Committee responsive mode portfolio. As outlined in the main paper, the results are drawn from a surveys of current and past grantholders, current and past Committee members (serving over the last five years), and other funding organisations. Response statistics are summarised below:

| Survey | Number of responses | Response rate | % of total |
|------------------------------------|---------------------|---------------|--|
| Completed grants | 103 | 70% | 35% of all completed and graded grants |
| Current grants | 70 | 72% | 24% of all current grants underway for >1 year |
| Current and past Committee members | 19 | 13% | 66% of Committee members (last 5 years) |

2. Questionnaire responses were received from the following UK funding bodies:
 - Research Councils: the Engineering and Physical Sciences Research Council (EPSRC), and the Medical Research Council (MRC);
 - Charities: the British Heart Foundation, Cancer Research UK, Help the Aged, and the Wellcome Trust
 - The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).

A note on using the data

3. The questionnaire data presented in this report relate to the samples described above. While the samples were random from the point of view of the science involved, and representative in terms of years and final report grades, it should nevertheless be borne in mind that they are only samples.
4. Respondents were given options to tick in some of the questions, whereas other questions were open-ended. Responses to open-ended questions (where the response rate was generally lower) are indicated. Representative quotes from respondents are also included where appropriate.
5. Where relevant, the survey findings are compared with the results of the surveys conducted for the recent Animal Sciences Committee (ASC) portfolio evaluation and the ongoing Genes and Developmental Biology Committee (GDB) portfolio evaluation.

2. RESEARCH OUTPUTS AND ACHIEVEMENTS

6. This section covers outputs and achievements both of the Committee and of the research supported through the Committee.

2.1 Committee's achievements

7. **86%** of the sample Principal Investigators (PIs), and all of the sample Committee members felt that the BCB is achieving its aim "to support and foster basic research of the highest quality at the cellular and molecular level". Only **3%** of PIs responded that it is not doing at all well.
8. The majority of Committee members identified the key role of the Committee as being to support the best UK science through ensuring the most appropriate and fair allocation of BBSRC's resources; with others commenting that the Committee's most important function is to evaluate grants fairly, objectively and openly, through peer review. All of the sample members said that the Committee works very well as a team, and that there is robust discussion of difficult cases.

"Overall I was very impressed with the Committee and process."

Committee member

9. When asked to identify specific achievements of the Committee over the past five years, the most common responses from the sample Committee members were:
- Providing support in areas where there were no/few other alternatives, e.g. basic plant science, basic cell biology;
 - Maintaining support for a broad range of good quality basic BCB research across all of the kingdoms; and
 - Supporting specific area or groups.

"BCB protects and maintains scientific areas that would otherwise wither away in the UK. BCB's area tends to fall between more 'sexy' areas e.g. medical and pharmaceutical, but underpins the science on which they are based".

Committee member

10. The Committee's support for areas where there are no/few alternatives is reflected by the fact that **20%** of sampled PIs said that the grant had provided funding for activities that other bodies would not fund.
11. Other identified achievements were that the Committee's broad remit encourages interdisciplinary applications; that it maintains support across all of the Kingdoms; that it maintained its support for the area at times when other funders had to make major funding cuts; and that the Committee makes the effort to identify people who are outstanding in their field, or people with unique tools.
12. Several of the Committee members, and **16%** of the sample PIs who gave comments on the Committee, however, said the extent to which the Committee can achieve its aim is limited by the availability of funds, with competition now so intense that some international quality proposals cannot be funded. In addition, **14%** of the sample PIs who commented felt that the transparency of the Committee and its decisions could be improved, some

commenting that decisions appear to be affected by the balance of scientific expertise on the Committee at the time. This concern was not raised by the sample Committee members, several of whom commented that the Committee works hard to ensure that the appraisal process is fair.

2.2 Increased scientific knowledge and awareness

General

13. When asked whether the grant had supported their wider research aims, **82%** of the sample PIs said it had enabled extension of their research into new areas, and **40%** said that the grant had helped to publicise the importance of their field of research.

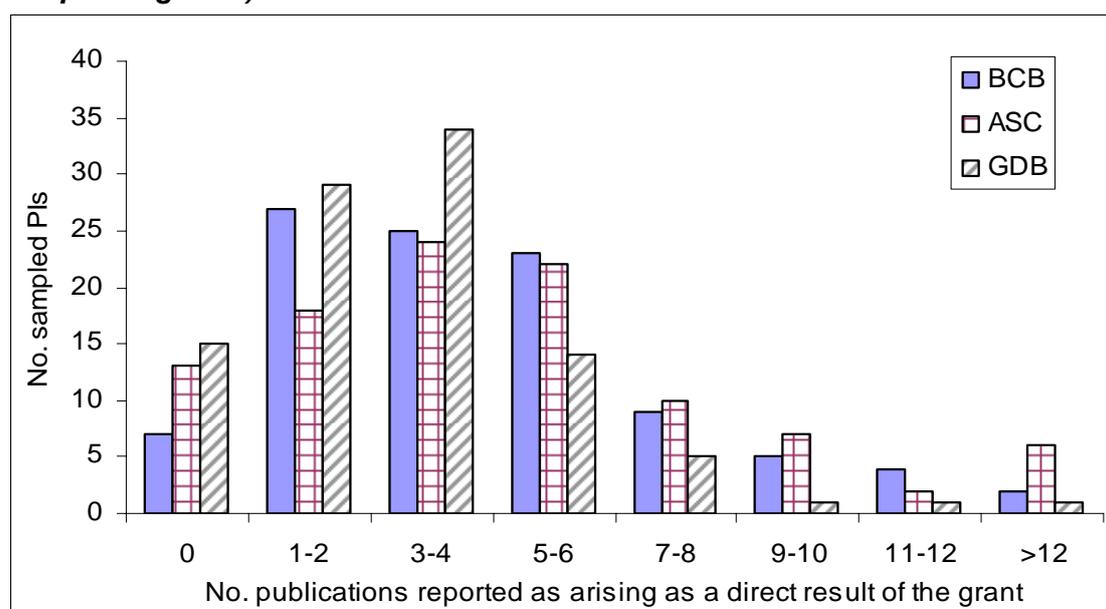
“The research undertaken with this BBSRC grant was the starting point for rather successful study and new collaborations.”

BCB Grantholder

Publications

14. PIs were asked to list publications in peer reviewed journals that had arisen as a direct result of the research supported by the grant. In total (from the 173 questionnaire responses received), **551** papers had been published in **175** peer reviewed journals. Completed grants had a median¹ of **four** publications per grant. The median for current grants, as would be expected, was much lower at **one**.
15. Figure 1 shows the distribution of numbers of reported publications per grant. To provide some context, the Figure also shows the results of the PI surveys conducted for the recent Animal Sciences (ASC) and Genes and Developmental Biology (GDB) Committees’ portfolio evaluations.

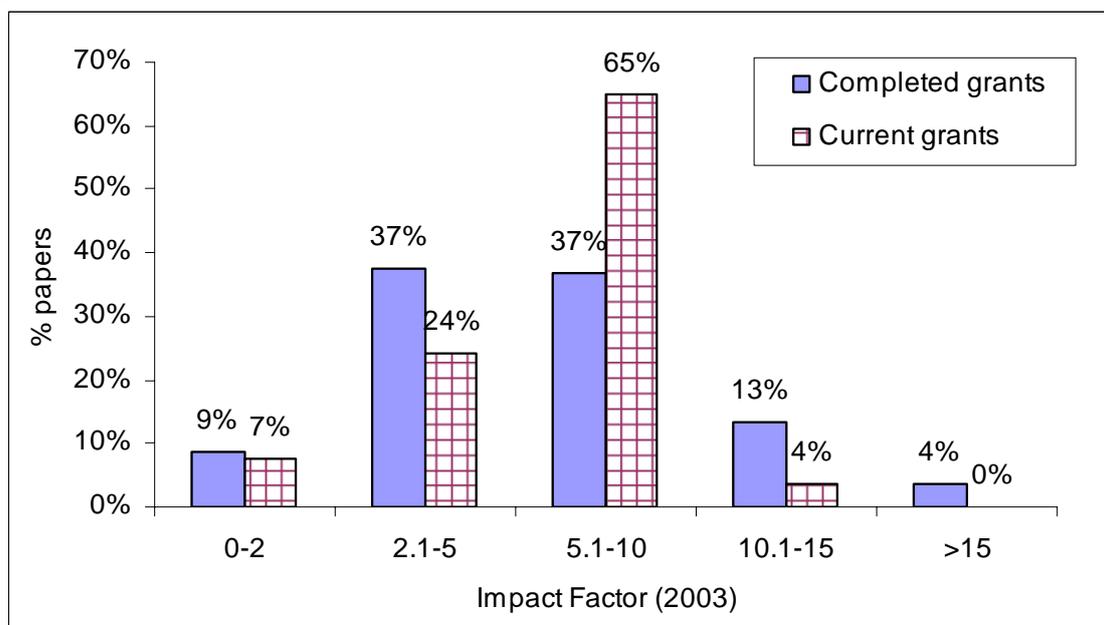
Figure 1: Numbers of reported peer reviewed publications per grant (sample completed grants)



¹ The median is used because the distribution of papers per grant is left-skewed (the majority of grants lead to the publication of 0-6 papers, but a small proportion resulted in larger numbers of papers, with a maximum of 21). The average was 4.8 for completed grants and 1.6 for current grants.

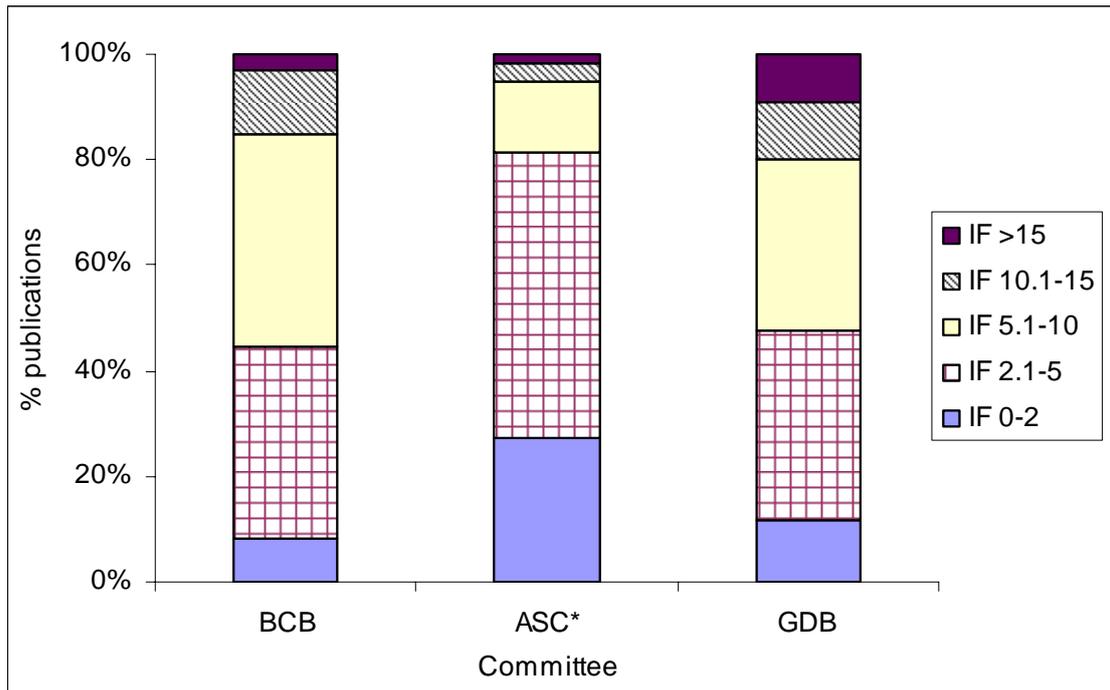
16. **15%** (82) of the papers were in journals with an Impact Factor greater than 10, including Current Biology (13 papers in total), the Plant Cell (9), EMBO Journal (9), Proceedings of the National Academy of Sciences USA (9), and the Journal of Cell Biology (6). By way of comparison, 16% and 18% of papers reported in the ASC and GDB surveys respectively were in such journals.
17. The journals most frequently reported by the sampled BCB PIs were: Journal of Biological Chemistry (64 papers), Biochemistry (22), FEBS Letters (22) and the Biochemical Journal (18).
18. Figure 2 shows the distribution of papers published by the Impact Factor of the journal they were published in. The drawbacks of Impact Factors as measures of quality are well known, so these data are presented as supplementary contextual background for the Panel's discussion, and should be interpreted with care.

Figure 2: Distribution of papers by Impact Factor of journal
(journals where >1 paper was published)



19. To provide context, Figure 3 shows the data in comparison with the results of the ASC and GDB surveys.

Figure 3: Distribution of papers by Impact Factor of journal (completed and current grants, journals where >1 paper was published)



* The relatively lower Impact Factors of the journals used by researchers supported through ASC was recognised (in the ASC Portfolio Evaluation) to be a feature of the animal science research area rather than any difference in the quality of the research.

Publishing strategy

20. PIs were asked whether they had adopted a publishing strategy for their research. Of the options given, the majority (**79%**) reported targeting the most appropriate journals for their area of science, with **26%** targeting the highest profile general journals. **20%** of the PIs choosing these two options added a comment that they adopt a pragmatic approach, targeting the top general journals for their best results, and top journals in the field for the rest. Only **2%** of the sampled PIs selected the option 'target journals where I can get my results published quickly'.

2.3 New collaborations and further funding for research

New collaborations

21. Many of the sampled PIs said that the research funded by the grant had helped to establish or strengthen academic contacts:

| Type of contact/collaboration | | Proportion of PIs |
|--|----------|-------------------|
| Base (all sample PIs) | | 173 |
| New or improved academic contacts | UK | 59% |
| | Overseas | 60% |
| New formal academic research collaboration (e.g. joint publication, joint funding application) | UK | 41% |
| | Overseas | 31% |

22. **9%** of PIs reported having established or strengthened cross-disciplinary contacts or collaborations, across a range of disciplines. This compares with 16% and 11% of sampled PIs in the ASC and GDB surveys respectively.

“The grant enabled us to develop the interface between experiments and mathematical modelling. This work has led to many further collaborations in this interface area.”

BCB grantholder

Further funding

23. **62%** of the PIs of sample completed grants had received further funding to continue or develop the work supported by the grant. **30%** had received further funding from BCB.
24. When asked why they had not secured further funding through BCB, **24%** of the sampled PIs said that funding (for the follow-on research) was more accessible from other sources, or that they already had funding from other sources. A further **18%** had applied to BCB but their proposal had not been funded, and **9%** commented that they had not applied for further funding through BCB because the area of science was not covered by BCB’s remit.
25. **15%** of the PIs had secured funding through other BBSRC Research Committees, including the Plant and Microbial Sciences (5 PIs), Animal Sciences (3), Biomolecular Sciences (3) and Genes and Developmental Biology Committees (3). This transition from BCB to other Committees is to be expected given the basic nature of much of the work funded through BCB. It also partly explains the fact that **9%** of sampled PIs commented that they had not applied to BCB for further funding because the area of science was not covered by BCB’s remit.
26. **31%** of the sampled PIs had secured one or more follow on grants related to the work from another funding body, the most common being the Wellcome Trust (17 PIs) and the EU (5).

“This work was pivotal to me being a co-applicant and the coordinator for a significant EU framework V award.”

BCB Grantholder

27. The table below shows that these figures contrast with the results of the ASC and GDB surveys. The differences between the Committees illustrate the fundamental nature of the research supported through BCB, and how some of the outcomes of this basic research lead to studies that are relevant to other Research Committees and other funders.

| | BCB | ASC | GDB |
|--|------------|------------|------------|
| Base (sample completed grants) | 103 | 102 | 100 |
| Secured follow on funding | 62% | 42% | 47% |
| Secured funding from the same Committee | 30% | 30% | 18% |
| Secured funding from other BBSRC Committees | 15% | 2% | 8% |
| Number of other BBSRC Committees reported | 5 | 1 | 3 |
| Secured funding from other funding bodies | 31% | 15% | 24% |
| “Funding is easier to obtain from other funding sources” | 24% | 7% | 9% |

| | | | |
|---|----|---|----|
| Number of other funding sources reported (including other BBSRC Committees) | 16 | 9 | 16 |
|---|----|---|----|

2.4 Trained people, increased skills

Staff employed on grants

28. When asked how the grant had supported their wider research aims, **72%** of PIs ticked the option 'strengthened the skill base of my group'.
29. PIs of completed grants were asked for details of the staff employed on their grant. **95%** had employed one RA, **1%** had employed two. **2%** of the grants had only supported a research technician position, and **2%** were equipment only grants on which no staff positions were funded.
30. Of the RAs, **93%** of the positions were RA1A, the remainder RA1B. Almost all of the RAs had been contracted full time on the grant for the period of the grant.
31. **36%** of the sampled grants supported research technicians, generally for the full 3 years but in a part time role (contracted on the grant for an average of **40%** of the time).
32. **27%** of the sample completed grants had had a change of RA during the grant. This compares with RA changes in 12% of both the sampled ASC and GDB grants. Staff issues such as this, and the impact that they have on the success of grants are discussed further in section 2.8 (paragraph 44).
33. PIs were also asked for the first destination of the staff employed on the grant:

| First destination | RA | Research technician |
|--|-----|---------------------|
| Base (no. staff for which first destination given) | 110 | 19 |
| Fixed-term in an academic institution | 43% | 16% |
| Overseas | 29% | 11% |
| Private sector, industry or commerce | 11% | 16% |
| Not employed | 4% | 11% |
| Government or other public sector | 3% | 0 |
| Further training (excl. teaching) | 3% | 26% |
| Other employment | 3% | 0 |
| Permanent in an academic institution | 2% | 21% |
| Teaching or teacher training | 2% | 0 |

34. The proportion of RAs moving into the private sector, industry or commerce is very similar to the 10% reported in both the ASC and GDB surveys.

Researchers at an early stage in their careers

35. BCB has awarded **21%** of BBSRC’s New Investigator² grants over the last five years, a slightly higher proportion than the proportion of responsive mode grants awarded by BCB overall (**18%**).

“The BBSRC New Investigator funding has helped me to establish my own group, develop international collaborations and to attract further funding in the research area”.

BCB Grantholder

36. Two proxies are used to examine the success of the sampled New Investigator grants: final report grades and number of peer reviewed publications reported in the questionnaire. By both measures, New Investigator grants appear to be slightly more successful in terms of final report grade, but less successful in terms of publications reported:

| Measure of success | New Investigator grants | Whole sample grants |
|--|-------------------------|---------------------|
| % Graded A or B (all sample grants) | 74% (n = 19) | 70% (n = 146) |
| Median no. publications reported in questionnaire (grants with returned questionnaires only) | 3 (n = 12) | 4 (n = 103) |

2.5 New products, processes, tools and technologies

37. **47%** of PIs reported new products, processes, tools or technologies that had or could result from the work supported by the grant. Given the fundamental nature of the research supported through BCB, many of these are tools and resources that will be primarily useful to other researchers, for example reagents and cell lines. This also means that many are still some way from exploitation.
38. By way of comparison, 27% and 48% of sampled PIs reported such outputs in the ASC and GDB surveys respectively.

2.6 New intellectual property, spin out companies

39. Nineteen (**11%**) of the sampled PIs reported having secured intellectual property (all in the form of patents) as a result of the work supported by the grant. A further five current PIs (**3%**) reported that they were likely to apply in the near future. Three of the patents (**2%** of the sampled PIs) had licensed their intellectual property, one of which (**1%**) had lead to the generation of income. In comparison, six PIs (4%) and seven PIs (4%) in the ASC and GDB surveys respectively reported having secured intellectual property; a further five (3%) and six (4%) respectively reported that they were likely to apply.
40. Three spin out companies (**2%** of sampled PIs) had been established from the research supported by the grant, two of which were currently trading. Another company was in the process of being set up. In comparison, 2% of PIs reported having established spin out companies in the ASC survey, and no spinout companies were reported in the GDB survey.

² The New Investigator scheme aims to assist researchers at an early stage in their careers to obtain their first research grants.

2.7 Contribution to the reduction, refinement and replacement of animals in experiments

41. **60%** of the sample Committee members felt that research supported by BCB had contributed to the '3Rs' (ticking 4 or 3 on a 4-1 scale). **37%** of the Committee members commented that the '3Rs' is a priority to the Committee, and that animal experimentation is only approved if it is well justified. **26%** added that the impact is an indirect one, as research at the cellular and molecular level can obviate the need for animals in experiments.

"The Committee was very conscious of this, and promoted work on cellular interaction to identify alternatives to animals."

Committee member

42. However, this was not reflected in the information given by the sampled PIs. When asked whether any other outcomes arose from the research supported by this grant, **6%** of PIs ticked the option 'contribution to the reduction, refinement and replacement of animals in experiments', compared to 21% and 8% of PIs sampled in the ASC and GDB surveys respectively. Note that due to differences in the way the question was asked, the BCB figure is considered to be an under-estimate³.

2.8 Success of grants

Overview

43. This section examines how well PIs were able to achieve the scientific objectives set out in their proposals, and investigates the explanations given for projects that had made slower progress.
44. There are two sources of data: final report grades, and PIs' responses to the question 'was the project supported by this grant successful in meeting its objectives?' Although the data from these two sources cannot be directly compared, the results are broadly comparable, and show that the majority of projects did achieve their objectives:
- **71%** of BCB grants completed since September 1994 scored A or B for their final reports (on a scale of A to D) ; and
 - **87%** of PIs of the sample completed grants and **78%** of PIs of sample current grants felt that their project had been or was likely to be successful (some of the current grantholders added that it was too early to tell).
45. Analysis over time of the assessment by PIs as to whether their projects were meeting their objectives perhaps indicates a slight downward trend in overall success, but this is not reflected by the final report grades.
46. PIs were given a number of options as to why their projects had been less successful, many ticked multiple options:

³ In the BCB questionnaire, contribution to the '3Rs' was included as a tick box at the end of a large table. Experience showed that these later options have a lower response rate, being 'skated over' by those answering the questionnaire in a hurry. The '3Rs' question was therefore included separately in the subsequent GDB questionnaire.

| Reason | Proportion of: | |
|---|---|-----------------|
| | PIs indicating that their grants had been less successful | all sampled PIs |
| Base | 21 | 173 |
| Experimental/methodological issues | 57% | 7% |
| Staff issues | 43% | 5% |
| The objectives of the research changed due to new information or after initial findings | 24% | 3% |
| Unrealistic objectives | 24% | 3% |
| Lack of resources e.g. funding, equipment | 14% | 2% |

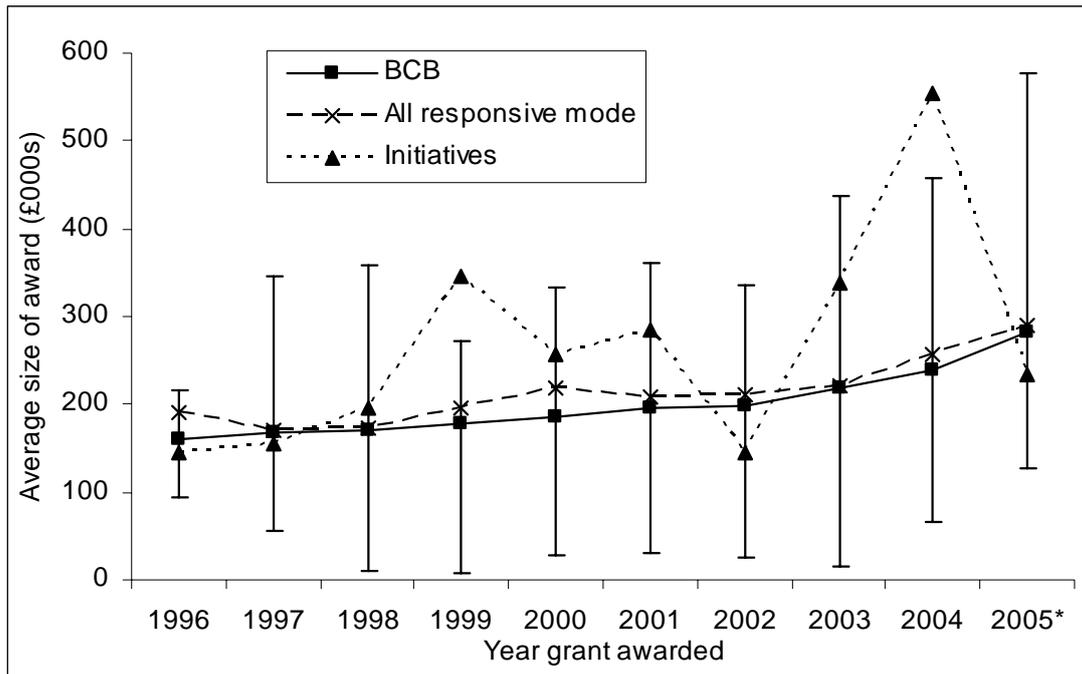
Skills and staff issues

47. When asked whether it had been difficult to recruit staff to undertake the research, **38%** of the sampled PIs said that it had. The most frequent comments given were that it was difficult to find someone with the necessary qualifications (**22%** of sampled PIs); that staff either left or temporarily stopped work during the grant, often leading to disruption, delay and the need for retraining (**13%**) and that difficulties with recruitment meant that the start of the grant had to be delayed (**11%**).
48. Although the dataset is fairly small, analysing the data by the discipline of the PI (see paragraph 62 for explanation of how PIs were divided into disciplines) shows that more than a third of PIs in the fields of cellular signaling and genetics; cell biology; and biocatalysis reported difficulties in recruiting research staff.

Size and length of grants

49. The average size of BCB responsive mode grants awarded in the spring and autumn 2005 rounds (pre-FEC) was £281,000, slightly lower than the BBSRC average of £290,000. Responsive mode grants have risen slightly in size over the past few years, rising on average by 6% per year (i.e. above inflation) (Figure 4). The trend for BCB is very similar to that for BBSRC responsive mode grants overall.
50. The low rate of increase is balanced by a much more rapid increase in the size of grants funded through BBSRC's research initiatives (also shown in Figure 4), where much of the 'novel' areas of science have been funded over recent years. Many of these initiatives have been relevant to BCB. [The initiatives data fluctuates more than for responsive mode, because the size of grants varies considerably depending on the scientific area and aims of the initiative].

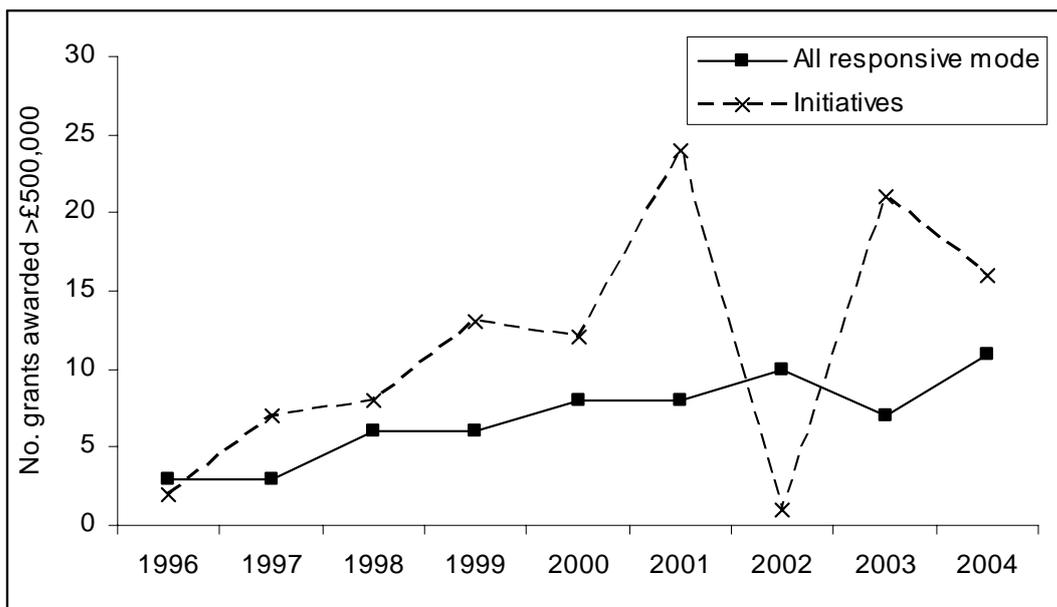
Figure 4: Size of award (all BCB responsive mode grants)



Error bars show the size of the smallest and largest BCB grants for each year

51. The BCB Committee has awarded only one large (>£500,000) responsive mode grant in the last 10 years (up to autumn 2005, pre-FEC), and this was in 2005. This represents only 1% of the large responsive mode grants awarded through responsive mode by BBSRC in the last 10 years. This finding is balanced somewhat by an increase in the numbers of large grants funded through research initiatives (Figure 5).

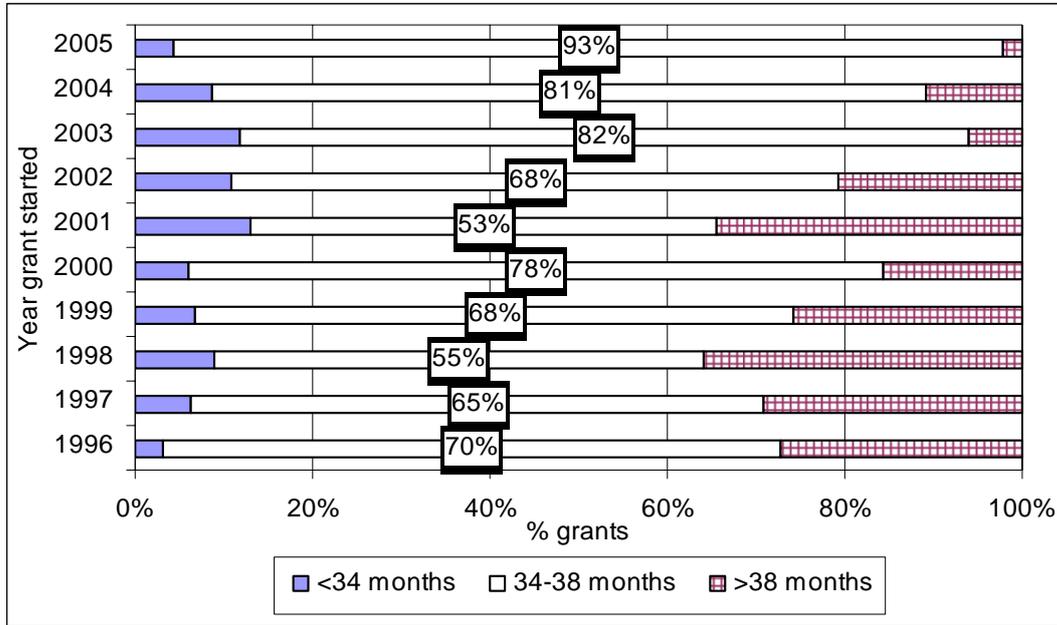
Figure 5: Numbers of large (>£500k) grants awarded through responsive mode and research initiatives



52. BBSRC has, over recent years, encouraged PIs to apply for the resources most relevant to the research (i.e. to move away from the 3-year, one

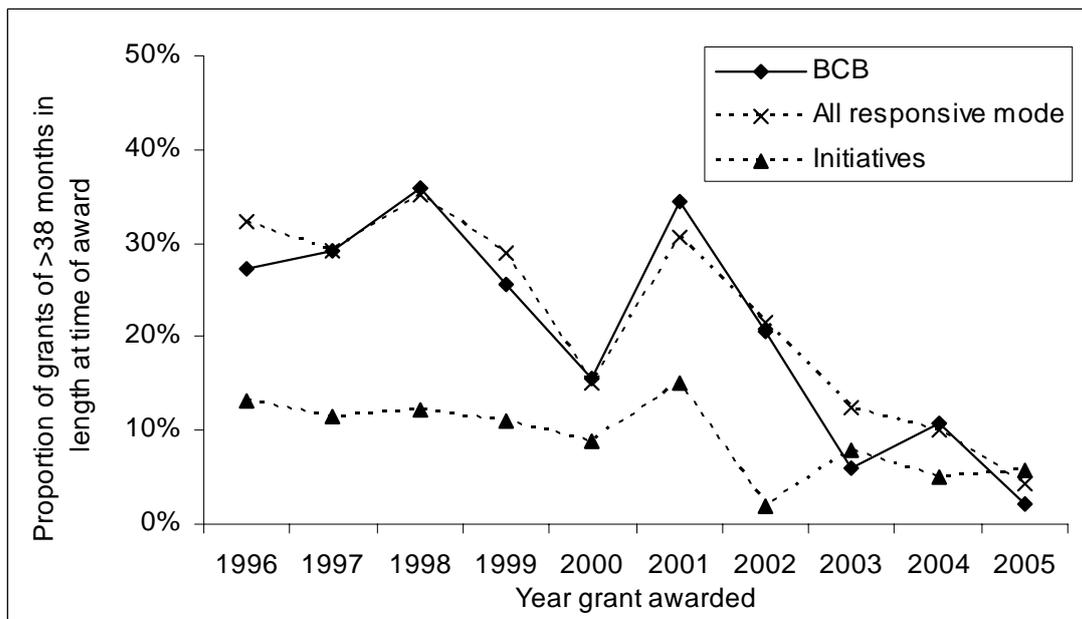
Research Assistant model). The data indicate that this is starting to work in terms of grant size, but not in grant length: despite BBSRC's encouragement to PIs, there has been a significant decline in recent years in the proportion of longer grants (Figure 6) (but no obvious trend in the proportion of short grants).

Figure 6: Approved length of all BCB responsive mode grants



53. This decline in longer grants mirrors the trend both for all responsive mode grants and research initiative grants (Figure 7).

Figure 7: Longer (>38 months) responsive mode grants as a proportion of all responsive mode grants



54 This decline in longer grants despite BBSRC's encouragement is a concern, perhaps reflecting a vicious circle of PIs applying for three year grants as they

perceive (from the high proportion of 3-year grants in previous rounds) that these grants have a greater chance of success.

55. Except for CRUK, the other UK funders surveyed confirmed that while they fund grants of a range of lengths, the majority of their grants are three years in length. EPSRC (like BBSRC) has over the past few years been encouraging PIs to submit shorter or longer applications where this is appropriate to the research involved, and report that they are slowly starting to see a change. MRC and the Wellcome Trust both also support longer term grants (e.g. programme grants), which tend to be for five years. CRUK funds in roughly equal proportions both project grants up to 3 years in length and programme grants up to 5 years through responsive mode.

2.9 The impact of receiving BBSRC grant funding over the longer term

56. This evaluation has focused on the grant as the unit of analysis because that is the unit by which BBSRC awards responsive mode funding. However, a grant is only ever one 'piece' in a 'jigsaw' of funding both over time and from different funders. 94 PIs have received more than five grants from BBSRC over the evaluation period, 25 of whom had received more than 50% of their grants through BCB.
57. The benefit of long-term support, especially in areas where funding is difficult to find from other sources, is clearly illustrated by articles recently published in BBSRC's Business Magazine about the work of three PIs who have been recipients of significant BCB funding over the past ten years: Professor Jim Barber (Imperial College), Professor Nigel Scrutton (University of Leicester), and Professor Colin Robinson (University of Warwick).

The Panel considered the following questions:

- a. Considering the data presented here, and the sample final reports, how much of the BCB portfolio is of international quality? Which aspects, if any, are not? Has the quality changed over the last 10 years?
- b. Are the scientific outputs (particularly publications) at the level expected of international quality research?
- c. Are the other outputs of the research at the level expected of international quality research in this area? Specifically:
 - trained people, increased skills;
 - new products, processes, tools & technologies;
 - intellectual property, spin out companies; and
 - contribution to the reduction, refinement and replacement of animals in experiments.
- d. Please identify the major highlights and outcomes of BCB's responsive mode portfolio over the past 10 years.
- e. Has the Committee achieved its aim "to support and foster basic research of the highest quality at the cellular and molecular level"?
- f. Are there specific areas with skills shortages amongst either RAs or research technicians? What, if anything, could BBSRC do to reduce the impact of staff issues and skills shortages on the success of grants?
- g. The data suggest that the majority of RAs are on fixed term contracts and a large proportion do not stay in the lab, is this appropriate? If not, what (if anything) could BBSRC do about this?
- h. What would be the impact of greater flexibility on the duration of grants? How could longer, larger grants be encouraged?

3. BALANCE AND COVERAGE OF THE PORTFOLIO

3.1 Remit

58. When asked a general question about the functioning of the BCB Committee, the only common message was that **25%** of the sample PIs who commented highlighted the importance of BCB's remit being broad and general to enable it to concentrate on supporting the highest quality research. In terms of comments on the remit, **6%** of the PIs who commented said that the remit is not broad enough, and **3%** that it is too broad. These comments are backed up by the fact that **96%** of PIs reported that they did not have significantly to change the direction of their research to fit their application to BCB's remit.
59. The other funders surveyed were generally satisfied that BCB's remit and its Themes are appropriate, clearly explained, and adequately cover BBSRC's responsibilities in this area. The following comments were made in relation to the remit:
- MRC stated that it is keen to strengthen the UK portfolio within BCB's remit, particularly in chemical biology and stem cell research, where MRC also has current initiatives. CRUK also mentioned the need for more support for chemical biology, noting that reviewers of such applications often perceive that the biology input is of lower quality than the chemistry;
 - EPSRC noted that it would like to see more emphasis on integrative systems research; and
 - Help the Aged requested that, following the conclusion of BBSRC's initiatives on research into ageing, ageing research become a more prominent element of BBSRC's core remit.
60. Almost all of the sample Committee members commented that BCB's remit overlaps with other BBSRC Committees, especially the Biomolecular Sciences; Animal Sciences; and Genes and Developmental Biology Committees. The overlap between remits, and the clarity of the interface between BCB and other funding bodies are discussed at paragraph 73.

3.2 Coverage

61. PIs were asked to indicate their areas of expertise against a list of 25 areas covering BCB's remit. To facilitate further analysis, these areas were then summarised (merging related smaller categories) into 10 areas:

| Discipline area | Completed | Current | Total |
|---------------------------------|-----------|---------|------------|
| Base (all sample PIs) | 103 | 70 | 173 |
| Cell biology | 57% | 60% | 58% |
| Cellular signaling and genetics | 57% | 60% | 58% |
| Biomolecular structure/function | 31% | 39% | 34% |
| Membranes | 34% | 27% | 31% |
| Biomacromolecules | 28% | 44% | 28% |
| Biocatalysis | 36% | 40% | 28% |
| Tissue culture | 24% | 40% | 25% |
| Plant Biochemistry | 25% | 14% | 14% |
| Modelling | 2% | 7% | 4% |
| Other | 18% | 9% | 14% |

Note: many respondents ticked multiple categories

62. To investigate trends in the portfolio over time, a rough analysis can be done with the above data, looking at the expertise of PIs of grants supported in each area over time. The figures show no obvious trends over time. Furthermore, when considering the balance of the portfolio, it should be borne in mind that the data indicate the self-declared expertise of the PIs, not necessarily the subject area of the grant.
63. **66%** of the sampled PIs felt that their area of expertise is well supported by the Committee, and only **7%** felt that it is not at all well supported. This lies between the results of the ASC and GDB surveys, where **56%** and **70%** of PIs respectively felt that their area is well supported by the Committee. The proportion of BCB PIs feeling well supported is higher for current PIs (**76%**) than completed PIs (**64%**). The data show a similar picture when broken down by area of expertise.
64. **58%** of the sampled Committee members commented that the portfolio of research currently supported through BCB more or less covers the Committee's remit. **53%** identified a particular area as being under-represented (in terms of research supported and applications received). Four of these related to the interface between chemistry and biology (biochemistry, chemical biology), the rest were only mentioned by one or two members each.
65. **26%** of the sampled Committee members added that in periods following changes in funding rules, there were many applications from researchers who would traditionally have applied to MRC and the Wellcome Trust.

3.3 Priority Areas

66. There is currently some debate within BBSRC and its Committees over the role of Priority Areas (PAs). PAs are intended to encourage PIs to submit applications in certain specific areas within the Committees' remits (for example to address important gaps in the portfolio or to promote new/developing areas of science), rather than to have a major influence on the peer review. Scientific excellence remains the most important criterion in the appraisal of applications. The other criteria of strategic relevance (which includes fit to PAs), prosperity & quality of life, timeliness and promise, and cost effectiveness can contribute to the final prioritisation; in practice this is

mainly used where grants of comparable scientific excellence are being prioritised.

67. PAs are changed or modified over time as their objectives are achieved. BBSRC also identifies Cross-Committee PAs in areas of relevance to more than one Committee, many of which are relevant to BCB.
68. The minor role played by PAs in the assessment process is reflected in the responses of the sample Committee members, all of whom were clear that PAs either make very little difference to their assessment of applications (**63%** of members), or are only considered when judging closely ranked applications in the borderline area (**32%**).
69. However, comments made by the sampled PIs indicate that some are not aware of this, reflected by the fact that only **4%** of the sample PIs who made comments relating to final reports (when asked a general question on the functioning of the Committee) made positive comments about PAs, whereas **25%** made negative comments. The major concerns raised were that PAs:
- Are too restrictive, and can therefore result in support going to lower quality work;
 - Reduce the funding available for basic science and new areas;
 - Can deter scientists from areas outside PAs from applying; and
 - Are often not in the most exciting areas of science. Some PIs added that science does not need this 'helping hand', as researchers will move into newly developing areas themselves.
70. In contrast, **63%** of sample Committee members felt that Priority Areas are generally a good thing, as they enable the Committee to promote areas identified as needing strengthening.

"Priority Areas were useful for encouraging areas that we thought were strategically important but where proposals were not arriving, for example interdisciplinary research."

Committee member

71. Nevertheless, **53%** of Committee members identified one or more issues associated with PAs, raising concerns similar to those voiced by PIs.

3.4 Interdisciplinarity

72. A recent exercise aimed at getting an idea of the level of interdisciplinarity in BBSRC responsive mode grants used PIs' departments as an indicator. Interdisciplinary grants were defined as those with PIs from a life sciences department and a non-life sciences department, and those with PIs based in non life-sciences departments. BCB ranked in the lower half of BBSRC's Research Committees by this measure, with **16** 'live' interdisciplinary grants (**5%** of all BBSRC interdisciplinary grants) on 1 April 2004.

3.5 Comparison with other UK funders

73. BCB's remit overlaps with a number of other UK research funders, including Government departments, other Research Councils and charities. The table below summarises the responses from other funders surveyed.

| Funder | Areas where remits overlap | Budget in overlap area (where information given) | Comments |
|--------------------------|---|---|--|
| <i>Research Councils</i> | | | |
| EPSRC | EPSRC focuses on the development of novel technologies or methodologies with potential life sciences application including Cell Biology and Biochemistry. | 05/06 responsive mode: <i>(note: data cannot simply be summed as based on keyword search so potentially many duplicates between categories)</i> Cell Biology: £2m, 12 grants Developmental biology: £2m, 8 grants | EPSRC's Life Sciences Interface Programme supports the application of physical sciences to biological research. A significant proportion of this research is supported in partnership with BBSRC (mainly through the Biomolecular Sciences; and Engineering and Biological Sciences Committees). |
| MRC | MRC focuses on human health and disease. In the context of the former, there is overlap with areas of the BCB remit. | Not provided. | MRC's support extends from fundamental biology into the study of specific human disease and disease processes, which is not covered by BCB. MRC does not support plant sciences. |
| <i>Charities</i> | | | |
| British Heart Foundation | Physiology and cell biology of the cardiovascular system (including stem cells). | Approx £8-10m/ annum, representing a mixture of project grants and PhD studentships. | The BHF estimates that approximately 20% of the research supported by BHF overlaps with BCB's remit (BCB does not support studies into the disease process or studies that are specifically medically orientated). |
| Cancer Research UK | Limited overlap with some of the research supported in CRUK Institutes. | Approximately 56% of the research grant portfolio has some overlap with the sort of basic biological research supported by the BCB and GDB committees of the BBSRC. | Applications to Cancer Research UK programme and project committees are expected to focus on areas of specific relevance to cancer. This focus on a diseased state limits the overlap with BCB's remit. |
| Help the Aged | Understanding the ageing process and senescence at the molecular/cellular level; cell differentiation; immunology; neuroscience. | 05/06: Senescence/ molecular immunology; and protein-protein interactions - £590k, 6 grants. | A large proportion of the work funded by Help the Aged, overlaps with the MRC remit. [for comparison, BBSRC estimates that it spent approximately £15.3m on Ageing and Ageing-related research in 05/06] |

| Funder | Areas where remits overlap | Budget in overlap area (where information given) | Comments |
|--------------------|---|--|--|
| Wellcome Trust | There is overlap between the BCB remit and the Trust's Molecules, Genes and Cells funding stream. | 04/05: Molecules, Genes and Cells funding stream - £55.3m. | The Trust's support extends into the study of specific human disease and disease processes, which is not covered by BCB. Also the Trust does not support plant sciences. |
| <i>Others</i> | | | |
| NC3Rs ¹ | Very little. | Not provided. | The NC3Rs remit is to fund research which advances the replacement, refinement or reduction of animal experiments. Some of these projects could be eligible for BCB funding, but the remits themselves do not overlap. |

¹ National Centre for the Replacement, Refinement and Reduction of Animals in Research

74. Many of the sample Committee members identified that BCB's remit overlaps with the remit of other organisations (particularly the Medical Research Council and the Wellcome Trust). Areas of overlap with the other Research Councils are monitored, and grant applications that are outside BBSRC's remit are redirected to the appropriate Council. Although it is possible for Research Councils to cofund research projects, BCB has had few of these cases (the majority have been through BBSRC's Biomolecular Sciences, and Engineering and Biological Systems Committees). Discussions have taken place between the BCB secretariat and the main charities supporting research relevant to BCB to ensure that the two organisations are aware of each others activities in this area.
75. The other funders and almost all of the sample Committee members felt that remit overlap does not matter, or is even a good thing, because it ensures that there are no gaps in the remit; and because the office handles overlap well: is efficient at assigning applications to the correct Committee or Research Council.
76. **16%** of Committee members highlighted negative aspects of remit overlap, that there is a risk that proposals in the 'grey areas' have a lower chance of being funded, and that it delays the process and takes up Committee time.
77. The other funders were generally satisfied that BCB's remit is well explained, and that the boundaries between the funding organisations are clearly defined. Help the Aged commented that it can be difficult to understand where BBSRC 'draws the line' between basic science and disease as this is a continuum (especially with respect to ageing).
78. However, **37%** of the sample Committee members noted that the boundary of BCB's remit is often not clear, a comment added by **6%** of the PIs who gave comments in response to a general question on the functioning of the Committee. **21%** of Committee members recommended that Committee

remit and boundaries (particularly between BBSRC Committees) need to be made clearer to the community.

3.6 International comparison

79. While it was not feasible in the context of this evaluation to generate specific international comparison data for biochemistry and cell biology, the Office of Science and Innovation recently published a number of Public Service Agreement target metrics for UK bioscience research as a whole⁴. The metrics compare the UK's performance in biosciences with other major research countries using bibliometric data from ISI National Science Indicators 2004, and show the UK to be ranked very highly for the quality of its bioscience research:
- Share of world citations: The UK ranked 2nd (behind the USA) for its share of citations in the biosciences for 1995-2004 (the data were corrected for country size);
 - Citation impact relative to world baselines in biosciences: The UK ranked 3rd (behind Switzerland and Singapore and, for the first time, ahead of the USA) in 'citation impact' (ratio of citations to publications) for biosciences for 2004; and
 - Proportion of uncited papers: The UK had the lowest proportion of uncited papers (i.e. the highest proportion of cited papers) for biosciences for 1999-2004 amongst the G8 countries.
80. BCB can also be compared internationally by comparison with the remit and portfolio coverage of the National Science Foundation (NSF) in the USA. This organisation was chosen as being from the leading country for biological research, having a grants Committee similar to BCB (Cellular Systems and Signal Transduction/Cell Regulation) with a comparable budget, and having searchable grants information on its website (it was not feasible within the available time and resources to conduct an in-depth survey, the exercise was therefore limited to readily accessible information on the websites of these organisations).
81. The NSF funds research and education in most fields of science and engineering. NSF's Cellular Systems Cluster most closely fits BCB's remit. This cluster focuses on the structure, function, and regulation of plant, animal and microbial cells, and their interactions with the environment and with one another. Areas supported include:
- The structure, function, and assembly of cellular elements (such as the cytoskeleton, membranes, organelles, intracellular compartments, intranuclear structures, and extra-cellular matrix, including eukaryotic and prokaryotic cell walls and envelopes);
 - Intracellular and trans-membrane signal transduction mechanisms and cell-cell signalling processes, including those that occur in biofilms; and
 - Cellular recognition and self defence mechanisms.

Research utilizing multidisciplinary approaches, technique development, computation and modelling, and approaches that exploit genomic information is encouraged.

⁴ PSA target metrics for the UK research base, Department of Trade and Industry, December 2005

82. The grants listed as live in the Cellular Systems Cluster on NSF's website were allocated to BCB's Themes to illustrate the nature of the science supported. **86%** of the grants (by both number and value) were within BCB's remit, the data below refer to these grants. The data show a broadly similar spread of grants and value across the three Themes:

| Theme | NSF* | | BCB | |
|---|------------------|------------|------------------|------------|
| | Total value (£m) | No. grants | Total value (£m) | No. grants |
| Fundamentals of Cell Biology and Biochemistry | 26.4 (60%) | 111 (57%) | 43.1 (69%) | 196 (70%) |
| Specialised Cell Function | 12.6 (29%) | 60 (31%) | 17.1 (27%) | 74 (26%) |
| Cell-Cell Interactions | 4.9 (11%) | 25 (13%) | 2.4 (4%) | 10 (4%) |
| Total | 43.9 | 234 | 62.6 | 280 |

* The figures refer to the 86% of NSF's Cellular Systems Cluster portfolio that is within BCB's remit

The Panel considered the following questions:

- Taking account of the data presented here, and the sample final reports, is BCB currently funding the most appropriate areas of UK biochemistry and cell biology research? (e.g. highest priority, comparison to other UK funders);
- Taking account of the data presented here and the information in Paper 3, how does BCB's portfolio reflect its remit? In your view, are there any areas which are receiving more (or less) support than they should be? Is the balance between Themes appropriate?
- Have the Priority Areas had any added benefit? What is the appropriate balance between PAs and non-PAs within the portfolio?
- Given that the Committee is proposing to revise its PAs, are any of the current PAs still important?
- Please comment on how the BCB remit compares with other UK funders in this area.

4. INTERACTION WITH INDUSTRY

4.1 Overview

83. When asked what BCB-supported research achieves, the majority of Committee members commented that it supports a bedrock of fundamental scientific knowledge that underpins future research and future commercial application. The pharmaceutical, medical and biotechnology industries were particularly highlighted. These generally longer-term impacts are discussed further at Chapter 6. This Chapter considers the interaction between BCB-supported PIs and industry during and after the grants. The sections on intellectual property and spin-out companies (Paragraphs 39 and 40) are also relevant.
84. Over half of the sample Committee members felt that there is a good relationship between BCB-supported research and industry, and that there is sufficient interaction between the two. A third felt that it is not as strong as it should be or getting worse, commenting that industry funding for basic research and collaboration with academia is declining. However, a third also noted that the fact that there is little cofunding from industry is not a problem, as the role of industry is to fund applied research, building on the basic research funded by bodies such as BBSRC. In reflection of this, a number of members commented that it is valuable having members from industry on the Committee, ensuring that industry has some input into funding decisions.
85. The three sample Committee members based in industry were generally positive about biochemistry and cell biology research in the UK. They commented that their companies collaborate closely with BBSRC, and that they are especially keen on studentships. They added that collaboration with BCB-funded research is generally fairly easy, although this does vary between institutions.

4.2 Support at outset

86. Seven PIs (4% of the sample grants) reported having co-funding or in-kind involvement in the grant at the outset. This included three CASE studentships, two grants with small in-kind support, one Industrial Partnership Award and one LINK Award. For comparison, 6% of sampled ASC PIs and 3% of GDB PIs reported industrial support at the outset of their grant.

4.3 Involvement as a result of the grant

87. Levels of involvement with industry are much higher during and as a result of grants:

| Type of contact/collaboration | | BCB | ASC |
|--|----------|-----|-----|
| Base (all sampled PIs) | | 173 | 171 |
| New or improved industrial contacts | UK | 13% | 19% |
| | Overseas | 8% | 14% |
| New formal industrial research collaboration (e.g. joint publication, joint funding application) | UK | 3% | 8% |
| | Overseas | 5% | 4% |

“The project allowed me to make significant and lasting links with agrochemical industry partners that led subsequently to two CASE studentships in my laboratory”.

“The grant led to Industrial CASE awards with GSK and Novartis”.
BCB Grantholders

88. However, the table also shows that the level of industrial contact by BCB-supported PIs is somewhat lower than reported by the sampled ASC-supported PIs (the GDB results cannot be compared due to a change in the way the question was asked).
89. The majority of PIs listing new industrial contacts or collaborations cited the biotechnology and pharmaceutical industries.

The Panel considered the following questions:

- a. Please comment on the level of interaction between BCB supported research and industry (e.g. cofunding, collaboration, take up of outputs)
- b. To what extent should BCB supported research be meeting the needs of the UK's industries?

5. PUBLIC ENGAGEMENT

90. PIs are required to conduct public engagement activities as a condition of their grant. Recent analysis by BBSRC's External Relations Unit (ERU) indicates that **75%** of recent BCB PIs were involved with public engagement activities, just lower than the average for all Committees (76%)⁵.
91. **24%** of sampled PIs reported in the questionnaire having conducted public engagement activities. In light of ERU's analysis, this is considered to be a significant underestimate (perhaps because the public engagement question was poorly answered in the questionnaire as it was at the end of a long table). However, the data are useful in giving an indication of the types of activities undertaken by PIs. The most frequent activities reported were schools activities (**15%** of sample grants); presentations to the general public including interest groups (**8%**); and popular scientific articles, contributions to books, newspaper articles (**4%**).
92. Analysis of the proportion of PIs reporting public engagement activities by year shows no obvious trend.

The Panel considered the following questions:

- a. Please comment on the level of public engagement by BCB grantholders.
- b. What are the generic issues faced by scientists working in this area relating to public engagement? What could BBSRC do to assist PIs facing these issues?*

* BBSRC runs media training courses for the researchers it funds, and is currently working on public engagement guidance which will be added to BBSRC's website.

⁵ The study used a sample of 350 final reports returned to BBSRC between June and September 2005, covering grants finishing from 2001 onwards.

6. ULTIMATE IMPACTS

93. Ultimate impacts are those that relate to BBSRC's overall objectives as an organisation, and would generally be expected to arise in the longer-term. The logic chart used to guide the evaluation identifies the following 'ultimate' impacts (relating to the objectives expressed in BBSRC's 10-year vision) that should arise from BBSRC's support for biochemistry and cell biology through responsive mode funding:
- Research findings are used for the 'public good', e.g. medical research, biotechnology, government policy;
 - Income to research community and 'UK plc', e.g. from new technologies, intellectual property;
 - The UK maintains its international standing in biochemistry and cell biology research;
 - BBSRC maintains its role as a key funder of biochemistry and cell biology research in the UK; and
 - Public confidence in UK biochemistry and cell biology research is maintained.
94. These impacts are clearly difficult to measure, and even more difficult to attribute directly to BBSRC funding. However, it is particularly important that they are evaluated because they relate to BBSRC's overall objectives: they help to answer the question 'how effectively is BBSRC doing its job?'
95. Some data relevant to the assessment of high-level impacts were collected in the surveys, and are presented below. Panel members are invited to consider this section's questions drawing on the data presented in this report, and on their knowledge and experience of biochemistry and cell biology research in the UK.

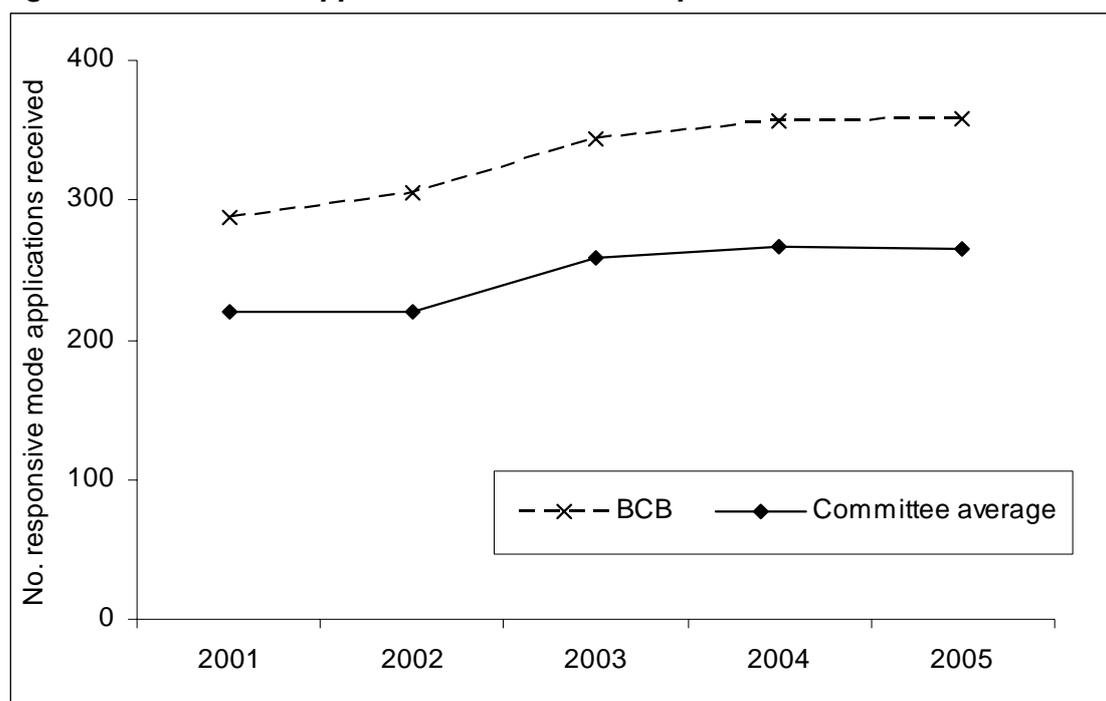
6.1 Contribution to the 'public good'

96. When asked a general question about what BCB-supported research achieves, Committee members commented that it:
- Supports a bedrock of fundamental science that underpins future research and future commercial application (sometimes a long way down the line);
 - Contributes to scientific knowledge, supporting scientists in this and other disciplines;
 - Trains scientists in the rigours of basic science (many of whom go on to work in industry); and
 - Contributes to public engagement with science, and supports science of public interest.
97. When asked in more detail about how this research contributes to wealth creation and quality of life, the majority of Committee members felt that much of the work has little direct impact as it is basic research, but that the findings form the basis on which wealth is created and quality of life is improved in the longer term, often after a very long development chain. For this reason, they stressed the importance of basic research, noting that it cannot be predicted at the outset which research will contribute to the public good.

6.2 UK ranking in biochemistry and cell biology research

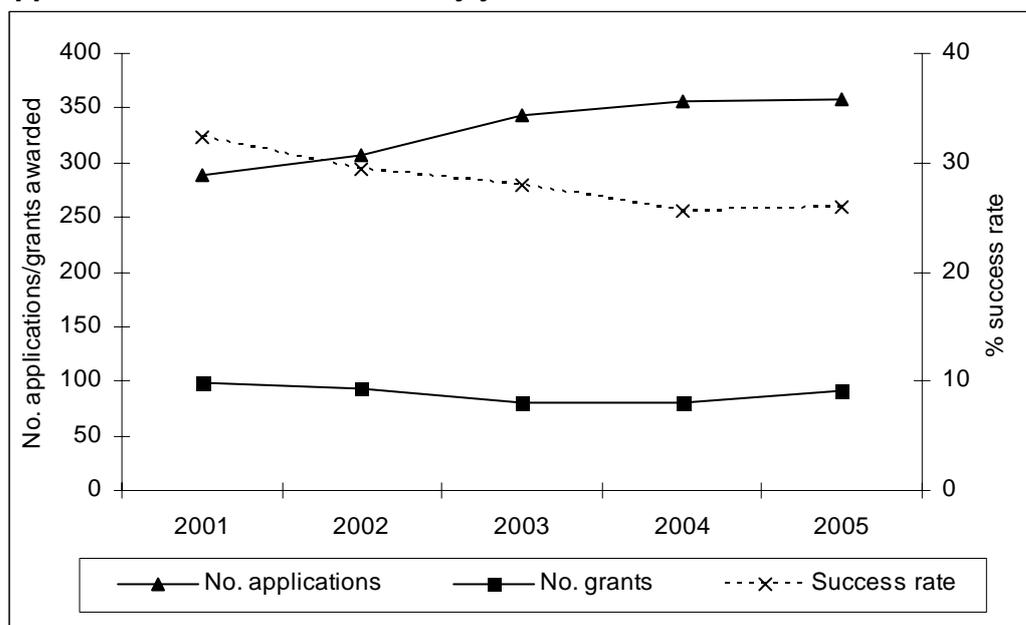
98. When asked whether the grant had supported their wider research aims, **79%** of PIs ticked the option 'strengthened the standing of my research group in the field'.
99. BBSRC's spend through BCB on responsive mode, and the number of applications that the Committee receives can be used as indicators of the level of international quality biochemistry and cell biology research in the UK. BBSRC's spending on responsive mode research through the BCB has increased over the past five years, both in value, and in proportion of overall BBSRC responsive mode spend: in FY 2000/01, **14%** of responsive mode funding was allocated through BCB (**£10 million**); in 2005/6, this had risen to **17%** and **£20 million**.
100. BCB consistently receives more applications than most of BBSRC's other Research Committees, indicating the continued strength of the UK scientific community in this area (Figure 8). The number of applications has been rising over the last ten years, and rose by **43%** during 2001-05.

Figure 8: Numbers of applications to BBSRC responsive mode



101. Despite rising funding, the increase in the number and quality of applications has had to result in a drop in the success rate, from **32%** in 2001 to **26%** in 2005 (Figure 9). The number of BCB grants awarded has remained similar over the evaluation period (Figure 9).

Figure 9: Numbers of BCB grants and responsive mode success rate for applications submitted to BCB by year



The Panel considered the following questions:

- a. To what extent is BCB research contributing to the 'public good', including human and animal health, income to 'UK plc', government policy?
- b. Is the research supported through BCB maintaining the UK's international standing in biochemistry and cell biology research, and is this likely to continue?

7. CONCLUSIONS

102 In drawing conclusions, the Panel considered the following questions:

- a. What are the major strengths, weaknesses, gaps and opportunities relating to responsive mode funding through the BCB?
- b. How could BBSRC build on successes, and address identified gaps and issues?