BioThermoKinetics of the Living Cell

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Biothermokinetics, Metabolic Control Analysis, metabolic engineering and the World Wide Web Rapid dissemination over the internet

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THE PAST

In the 1980s universities all over the world became connected to a variety of computer networks. These networks (e.g. BITNET and JANET) were connected by a very small number of gateways which meant that communications between networks had to be done via a message-queuing protocol - quickly baptised "electronic mail" or "email". For some time academics thought of the benefits of computer networking only in terms of being able to send messages between each other using this medium which was cheap and (sometimes) fast. However, email could be used in more ways than normal ("snail") mail, since mailing lists provided a means of broadcasting a message to a large number of addresses. Mailing lists are a good way of providing a discussion forum where people with common interests can ask questions or discuss a subject collectively. To this end, Hans Westerhoff created a mailing list for the BTK study group in approximately 1988, hosted at a BITNET server in Israel.

By the turn of this decade, the Internet became the big thing. The idea was to connect the various computers to a single network such that real-time protocols could be used as well as queuing ones. Not all universities and laboratories were connected to the internet immediately, so it was more a gradual conversion. The Internet provides more communication means than just email: Usenet News is a protocol for discussion fora, and can be significantly more efficient than mailing lists; Telnet is a protocol for logging on to a computer remotely - indeed this is the preferred means of accessing supercomputers; FTP is a protocol for transferring files of any type (including programs and data); IRC and MUD are protocols that implement a set of communication channels, in which one person types to a group of others in real time; Gopher is a client-server protocol for information transfer - users connect to servers with a client program, and the servers then allow users to read various pages of text or, in a limited way, graphics; the World-Wide-Web (WWW or simply the Web) is also a client-server protocol for mostly the same purpose as Gopher. but in which graphics are much more prominent and easy to view and the text can contain links to other pages (hypertext). It is the Web that contributes to the majority of information traffic on the Internet and which has been widely popularised.

At the 1992 BTK meeting in Bombannes it was decided to convert the then little-used BTK mailing list (still based on a BITNET computer) into an Internet mailing list [1] and usenet newsgroup [2]. This has had periods of intense discussion followed by others of silence; however its readership seems to be high (as judged by the number of users to respond to electronic announcements of Web sites) and attracts people who were not members of the BTK group. The group of David Fell has also implemented an FTP server

[3, 4] from which programs for metabolic simulation and bibliography lists can be downloaded. Also available from their server is the text of the proceedings of the 1994 meeting in Schröcken.

THE PRESENT

In an era in which scientists are increasingly being asked by their financial sponsors to ensure dissemination of their work, we consider that the Web provides a wonderful means of proving tutorials, lists (and indeed text and figures) of publications and other information about one's activities. Thus, in late 1993 we set up a Web server with information about some of the research done in our laboratory [5]. At that time there were already many other biological sciences Web servers, but none from the BTK study group. In May 1995 we added to our server a review of Metabolic Control Analysis (MCA), entitled "MCA Web" [6]. This was not intended to be a thorough review of the field, but rather a short one that nevertheless provided the most basic concepts and references to the literature. We foresaw this review as the origin of a dynamic process that would gather momentum once other groups realised how the Web can attract the attention of other researchers from related fields, and (maybe more important) students. The MCA Web is composed of the following pages: a "home" page that contains an index of the other pages and links to all the other sites know to us that are related to MCA; one page describing the control-coefficients and their relation to the notion of rate-limiting step; another describing the enzyme elasticity coefficients and their relation to enzyme kinetics; a page describing the connectivity relations; a page with the description of the response coefficients; one other covering how branches, cycles and enzyme-enzyme interactions can be dealt with MCA; one page on the various matrix methods; one about experimental methodologies; one about software for MCA and a final one with references.

The classical way in which one views pages on the Web is by following links in pages that have already been displayed on one's client (browser). This means that there is a Web of links formed between different texts. For a page to have large exposure it needs to be referenced from as many others as possible. More importantly, it needs to be referenced by a large number of pages that contain related information. There is no point in having links to the MCA Web from pages about motorcycling as there is a rather small probability that people looking for information about motorcycles would also be interested in MCA (even though there must be some!). On the contrary, a large proportion of people interested in biotechnology is surely (or at least hopefully) also interested in MCA, so it is very useful to have links to the MCA Web from biotech pages. Since we created the MCA Web, we have been contacting the managers of other Web servers with related material to add links to our server. Of course, if we now add links in MCA Web to other pages closely related to ours (e.g. other MCA pages) these also get the added exposure by a Web effect.

More recently the number of pages and servers on the Web has increased so much (it is still in exponential growth) that it became quite difficult to find any information of interest just by jumping from page to page (a practice known as *surfing*). The first solution to this problem came about with servers that provide an indexing service. These servers have programs that *surf* the Web in an automated way, creating an index of the words found in the pages. One can then connect to one of these sites, the most popular of which are Alta Vista [7] and Lycos [8], and search for subjects. This method of using the Web is complementary to *surfing* since one is less likely to find something that one did not look for in this way (even though our experience shows this to be a much better way of finding

useful information than the use of libraries). An additional benefit of these servers is that searches may be made using Boolean operators (AND, NOT, OR), and some intelligence in ranking the hits terms of the strength of a match is beginning to become available

One useful feature of the Web is that one can set up a means of counting the number of times each page has been loaded by a client program. We have implemented this in our server, and table 1 contains data for the MCA Web from its creation until the end of April 1996, approximately one year after it was created. We can see that apart from the home page (which is the entry point) most people seem to be interested in the page with software.

Table 1: Accesses to the MCA Web discriminated by page for the period from its creation until 30 April 1996. Every time a page is retrieved counts as one access.

05/95	06/95	07/95	08/95	09/95	10/95	11/95	12/95	01/96	02/96	03/96	04/96	totals
49	426	194	180	159	224	287	193	309	326	162	191	2700
7	81	26	17	22	30	46	18	52	44	22	35	400
6	39	18	8	14	26	19	15	32	35	17	34	263
8	58	13	11	14	29	21	15	32	42	23	27	293
4	31	6	3	12	15	12	15	25	25	13	19	180
3	51	12	11	15	21	28	18	33	47	18	23	280
1	43	13	5	12	14	22	16	28	25	18	21	218
0	57	17	8	12	21	17	15	26	31	25	28	257
0	81	25	16	19	30	62	54	77	106	59	68	597
0	92	24	12	12	31	32	26	36	40	32	31	368
78	959	348	271	291	441	546	385	650	721	389	477	5556
	49 7 6 8 4 3 1 0 0	49 426 7 81 6 39 8 58 4 31 3 51 1 43 0 57 0 81 0 92	49 426 194 7 81 26 6 39 18 8 58 13 4 31 6 3 51 12 1 43 13 0 57 17 0 81 25 0 92 24	49 426 194 180 7 81 26 17 6 39 18 8 8 58 13 11 4 31 6 3 3 51 12 11 1 43 13 5 0 57 17 8 0 81 25 16 0 92 24 12	49 426 194 180 159 7 81 26 17 22 6 39 18 8 14 8 58 13 11 14 4 31 6 3 12 3 51 12 11 15 1 43 13 5 12 0 57 17 8 12 0 81 25 16 19 0 92 24 12 12	49 426 194 180 159 224 7 81 26 17 22 30 6 39 18 8 14 26 8 58 13 11 14 29 4 31 6 3 12 15 3 51 12 11 15 21 1 43 13 5 12 14 0 57 17 8 12 21 0 81 25 16 19 30 0 92 24 12 12 31	49 426 194 180 159 224 287 7 81 26 17 22 30 46 6 39 18 8 14 26 19 8 58 13 11 14 29 21 4 31 6 3 12 15 12 12 15 12 12 13 15 12 12 11 15 21 28 11 43 13 5 12 14 22 21 17 0 81 25 16 19 30 62 0 92 24 12 12 31 32	49 426 194 180 159 224 287 193 7 81 26 17 22 30 46 18 6 39 18 8 14 26 19 15 8 58 13 11 14 29 21 15 4 31 6 3 12 15 12 15 3 51 12 11 15 21 28 18 1 43 13 5 12 14 22 16 0 57 17 8 12 21 17 15 0 81 25 16 19 30 62 54 0 92 24 12 12 31 32 26	49 426 194 180 159 224 287 193 309 7 81 26 17 22 30 46 18 52 6 39 18 8 14 26 19 15 32 8 58 13 11 14 29 21 15 32 4 31 6 3 12 15 12 15 25 3 51 12 11 15 21 28 18 33 1 43 13 5 12 14 22 16 28 0 57 17 8 12 21 17 15 26 0 81 25 16 19 30 62 54 77 0 92 24 12 12 31 32 26 36	49 426 194 180 159 224 287 193 309 326 7 81 26 17 22 30 46 18 52 44 6 39 18 8 14 26 19 15 32 35 8 58 13 11 14 29 21 15 32 42 4 31 6 3 12 15 12 15 25 25 3 51 12 11 15 21 28 18 33 47 1 43 13 5 12 14 22 16 28 25 0 57 17 8 12 21 17 15 26 31 0 81 25 16 19 30 62 54 77 106 0 92 24	49 426 194 180 159 224 287 193 309 326 162 7 81 26 17 22 30 46 18 52 44 22 6 39 18 8 14 26 19 15 32 35 17 8 58 13 11 14 29 21 15 32 42 23 4 31 6 3 12 15 12 15 25 25 13 3 51 12 11 15 21 28 18 33 47 18 1 43 13 5 12 14 22 16 28 25 18 0 57 17 8 12 21 17 15 26 31 25 0 81 25 16 19 30	49 426 194 180 159 224 287 193 309 326 162 191 7 81 26 17 22 30 46 18 52 44 22 35 6 39 18 8 14 26 19 15 32 35 17 34 8 58 13 11 14 29 21 15 32 42 23 27 4 31 6 3 12 15 12 15 25 25 13 19 3 51 12 11 15 21 28 18 33 47 18 23 1 43 13 5 12 14 22 16 28 25 18 21 0 57 17 8 12 21 17 15 26 31 25

We were also asked by the organisers of this meeting to put up a page with the second announcement of the meeting. This page [9] has been accessed in excess of 300 times since it was created and we hope that it has attracted to the meeting people who otherwise would be unaware of its existence.

THE FUTURE

The MCA Web is a *live* hypertext. Some more pages are planned to be added and the existing ones are always ready to be altered. This is one great advantage of electronic publication over the classic type, one can evolve the information provided and so make it up to date. The effort required to alter the contents of a page are as great as writing one email message, for those that have access to a server.

Since the BTK group has had no presence on the Web (at least as a group, rather than some of its individual members) we have created a page that has acted as an unofficial home page for the BTK study group [10]. We hope to be able to discuss the existence of an official Web page for the group and would like the other members to come forward with their own suggestions at this meeting.

ACKNOWLEDGEMENT

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REFERENCES

- [1] the email address of posts to this list is btk-mca@dl.ac.uk; to obtain the detail on how to subscribe (free) send an email message with "help" to biosci@daresbury.ac.uk
- [2] bionet.metabolic-reg in most usenet newsgroups servers
- [3] Woods, J.H. & Fell, D.A. (1994) Modern Trends in Biothermokinetics 3, (Gnaiger E., Gellerich, F.N & Wyss, M eds) Innsbruck , Innsbruck University Press, pp. 311-312
- [4] ftp to bmsdarwin.brookes.ac.uk, log in as 'anonymous'
- [5] http://gepasi.dbs.aber.ac.uk/home.htm
- [6] http://gepasi.dbs.aber.ac.uk/metab/mca_home.htm
- [7] http://altavista.digital.com/
- [8] http://www.lycos.com/
- [9] http://gepasi.dbs.aber.ac.uk/btk/leuven.htm
- [10] http://gepasi.dbs.aber.ac.uk/btk/home.htm