

The physionome: A piece of the bionome

The bionome projects

We can classify a part of the world of biological science research into a set of large scale projects about which one can conceptualize, even though realization may take decades. These comprise the *bionome*. Following the order of complexity, and in many ways the hierarchical order of explanation, one starts with the gene and ends up with the earth, from genome to geonome. Defining the nature of such projects, current and future, helps to place them in their socioscientific and political context.

Given the genetic structure of all the species on earth, one would not have much information that helps with the day to day problems of determining how an individual is functioning, or how that function might be improved with pharmaceutical assistance. Knowledge of the genome, however, allows understanding and is already leading to cures. The politics or sociology of science has therefore deemed it appropriate to learn the structure of at least the human genome. From that we may conceptualize the next projects that are needed to bring us closer to the realities of life and function and dysfunction. The sequence, from this point of view, is first the gene, then the structure that evolves from the genes' instructions, then animal or plant function. For animals, the next stage is the function of the mind, the psyche, of the individual and then of the group. It is the group behavior, finally, that spells the fate of our favorite planet.

The following seven paragraphs are from Bassingthwaighte, *Acta Stereologica* 11 (Suppl. 1), 305-319, 1992. Our logic in presenting such a long quote is that the original is unlikely to have been seen by this group of readers.

Humans have but 100,000 genes made up from about 10^9 base pairs. The body has about 250 different cell types, and each cell type has a multitude of enzymes and structural proteins. The number of cells in the body is beyond counting. The number of structural elements in a small organ exceeds the number of genes; the heart has about 10 million capillary tissue units, each composed of endothelial cells, myocytes, fibroblasts and neurons. The lung has even more. Consequently, the genes, which form the

instruction set, must command the growth of cells and structures most parsimoniously, and yet end up with functioning structures that last for decades. They even contain the instructions for their own repair!

From genome to geonome

The genome, the master instruction set, contains the list of ingredients, and the details of how to make the chemicals of our body. But how does this instruction set lead to the composite whole? What marvels of interactions allow growth, the formation of structural and functional units? The genotype gives rise to the phenotype, each one a different representation of the morphonome. The morphonome may be regarded as the set of measures of an individual of a species which gives a complete description of the structure of that individual. It includes the structure of the genome, the proteins, substrates, hormones, membranes, channels, organelles, cells, tissues, organs, and the composite body of the organism. The morphonome describes all the constituents of the body, and their spatial relationships to one another, and so defines the basis of life. Its reflections are found in the patterns of the phylogenetic tree. But it is not life, and in the Frankensteinian sense, the morphonome needs to be brought to life.

The description of life is the "physionome," the physiological dynamics of the normal intact organism, from cell to sentient being. Cell-to-cell information exchange (via neural, hormonal, electrical mechanisms) governs biological function. Function affects phenotypic expression, and vice versa, so the morphonome is influenced by the physionome through growth, injury, training, and so on. Biological systems are regulated via multiple enzymic, humoral and neural controllers. Fractals and chaos come together in the expression of the morphonome and the physionome: we might generalize to imply that the morphonome is fractal, showing self-similarity at many levels, while the physionomic functions show self-similarity over space and time, the often chaotic

continued on page 2

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Contents

The physionome: A piece of the bionome....	1
Anonymous ftp at NSR....	2
Software used at NSR....	2
New MMID4 and MSID4....	3
SIMCON version 2.8.1....	3
Ask Dr. SIMCON....	4

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"The physionome" from page 1

processes occurring on a fractal substrate of structure.

The physionome encompasses molecular dynamics, the energetics of conformational change, enzyme regulation, and the regulation of phenotypic expression by cellular function or influences from neighboring cells. While most cells have the same biochemical capabilities, phenotypic expression results in great differences between different cell types. Even a relatively simple process such as cell ion regulation is governed by a large set of interacting processes which together perform remarkably precise homeodynamics. We use homeodynamics here to indicate that probably no cell constituent is really held at a constant (homeostatic) level, but that fluctuations are the rule. Integrated organ function is not a miracle, but it is a marvel of integrated chemical, mechanical, and electrical regulation. Without these we would not have "being" of a sentient form, or communication where locomotion, the activation of muscle, is the brain's outlet to the world.

Functional physiology allows the development of a functional psyche, and there is good reason to look upon the psychonome as having its own structural fractal properties and chaotic dynamics. The psychonome is the quantitative description of the psychological dynamics of the intact organism within a normal environment. These may be illustrated by the interactions of

sensory and motor functions with mood and energy levels, by the depression of disease or weakness, by the demands of the physical world's coldness or heat or raw power over us.

In groups our psyches interact to form the socionome, the behavior of groups, and the nature of the interactions between groups or societies, races, or nations. While this area of study has been closer to philosophy than to science, because measurement is so difficult, the socionome is now being more closely defined. It too has its fractal characteristics.

The geonome, the quantitative description of planet earth's form and function, is the target of a huge amount of study. The topics range from the slow processes of plate tectonics to the more rapid processes of ozone layer depletion and of weather patterns. Though man is but one of many species, our inability to live in harmony with nature and our innate desire to exploit earth's riches to the full is resulting in the destruction of species of animals and plants and the degradation of man's habitat. Global warming may be changing the natural fluctuation of the earth's temperature, the waxing and waning of ice ages. The chaotic oscillations in population densities induced by famine and pestilence must have their reflections now in the fluctuations in the state of the geonome. Nevertheless, as with deletions in the gene, some fluctuations will lead to extinctions.



James B. Bassingthwaight

Software used at NSR

Commercial and freeware software products available for internal use at NSR include graphical user interfaces, mathematics and statistics packages, image analysis tools, and document/graphics preparation software.

Graphical user interfaces

We do not often use the OpenLook window system, Sun's user interface based on the X11 window system. Our all-purpose user interface is a generic X11, revision 5, (X11R5) system with all of the latest patches. Motif 1.2.1 is also available, and is built as an enhancement to X11R5. OpenWindows 3.0, X11R4, and even SunView, Sun's pre-X11 window system, are still present but will eventually disappear.

Mathematical and statistical packages

NSR has licensed several commercial products for doing mathematics and statistics. Matlab 4.0, a programmable language for mathematics, is particularly strong for matrix calculations and for prototyping algorithms. Splus 2.3 is a package with similar scope, but is oriented more toward statistical analysis. Symbolic mathematics can be done with the Maple

system, using the recently released version V.2. All three products have extensive support for graphics under the X11 window system.

Image analysis tools

For image analysis we use Analyze 6.0 and Vida 1.1. Both packages are being developed to provide functions needed for positron emission tomography projects.

Document and graphics preparation software

Manuscript preparation at the Simulation Resource is now done with several popular commercial packages, but primarily FrameMaker 3.0. Other products we use include CorelDraw 1.3, the Island 3.0 suite (Presents, Chart, Graphics, Draw, and Paint), and eXclaim 1.1, a spread-sheet program. Eric Lawson, our publications specialist, can tell you more about these programs and how to access them.

A growing collection of freeware is installed at NSR. Some of this software is very good, and can be maintained from source code. For example, we frequently use freeware previewers to

continued on page 3

Anonymous ftp at NSR

You may get files from NSR by using anonymous ftp. If you are using a UNIX system, use the following steps to get the "Readme" file first, then read it carefully for detailed instructions. Macintosh and PC users may use similar procedures specific to their system and communication software.

1. Enter `ftp`
`nsr.bioeng.washington.edu` at the **system prompt**.
2. Enter `anonymous` at the **resulting Name: prompt**.
3. Enter a complete electronic mail address at the **Password: prompt**.
4. Enter `get Readme` at the **ftp> prompt**.
5. Enter `quit` to return to your system.

The "Readme" file is a text file that can be read with your usual text editor

"Software used" from page 2

look at PostScript, TeX, and troff documents before printing them. We use several freeware graphing programs, among them ACE/gr, 3DPlot (pdraw), Contour and gnuplot. The pbm-plus suite of image filters allows us to convert images from one type to another, and is especially useful in conjunction with xv, an image viewing program which handles several formats common on Macintosh computers.

Other freeware, such as Khoros (an image processing toolkit) and Tk/Tcl (an embedded programming language with X11 graphics), can be made available quickly if the need arises. This software is freely distributable in source or binary form. You can obtain the packages from us or directly from ftp servers on the Internet. If you need help acquiring freeware, or help in locating an ftp server, contact us. 

Larry Weissman

SIMCON Version 2.8.1

SIMCON (Version 2.8.1) was installed on June 11. This summary of the release notice details major enhancements, changes and bug fixes. The newly revised *SIMCON User Guide* documents the new features and changes. PostScript versions of the complete notice and the new user guide can be downloaded from NSR.

SIMCON 2.8.0 summary

Enhancements

- E01. Added a function generator, cinput.
- E02. Added an additional optimizer, simplex.
- E03. Enabled saving of optimization, sensitivity, and residual runs.
- E04. Enabled viewing of results of residual runs.
- E05. Weighted sensitivities and optimization data in the same way.
- E06. Put run numbers on simulation plots.
- E07. Enabled optimization of up to eight parameters simultaneously.
- E08. Enabled optimization of up to four curves simultaneously.
- E09. Enabled sensitivity analysis initiation from all menus and the parameter editor.
- E10. Added input function and residual control submenus.
- E11. Enabled specification of the number of parameters to print to the simcon.par file.

Changes

- C01. Reorganized the parameter array.
- C02. Standardized output file headers.
- C03. Enabled termination of tabular listings with the characters x and s.
- C04. Implemented CV calculation before evaluation of the completion section of the model (SIMEND).
- C05. Implemented writing of the optimization report to a viewable temporary file.
- C06. Added more file identification.
- C07. Implemented writing of simcon.par and simcon.out in the same way when loops are on.
- C08. Implemented saving of run parameters in database (binary) format.
- C09. Implemented consistent scaling of reference data.

Bug fixes

- B01. Fixed crashing when sensitivity runs with too many points are calculated.
- B02. Implemented validation of relevant control parameters before an optimization, sensitivity or residual run starts.
- B03. Implemented unique date stamping of sensitivity runs.
- B04. Corrected the configuration control parameter menu title.
- B05. Fixed hanging of model when a save is attempted after killing a run.
- B06. Corrected sensitivity runs initiated immediately after starting a program.
- B07. Added a diagnostic message generated by invalid reference data index optimization.
- B08. Corrected hardcopy plot loop increment labels.
- B09. Corrected updating of Version 1 database files.
- B10. Fixed CV calculation with a reference data scale factor not equal to 1.0.
- B11. Fixed crashing when CV is calculated with zero equivalent reference data.
- B12. Fixed semilog plot scaling.
- B13. Made terminology in the database manipulation menu match the database structure.
- B14. Added data index submenu access to Help.

Compatibility with previous release

The application and use of the reference data scaling factor within SIMCON has been altered. (See item C9.) Application of the scaling factor by models should be removed, because the data are now scaled before they are stored.

Several changes have been made in the parameter array structure. However, the interface will detect parameter files, both from the database and files in simcon.par format, that are not in the new format and, upon confirmation from the user, will automatically convert them to the new format. The program *usimdat* is provided to convert an entire database. See the *usimdat* manual page for details. 

Rick King

New MMID4 and MSID4

New versions of the MMID4 (Version 2.1) and MSID4 (Version 2.1) programs are installed at NSR. The major changes in these versions relate to calculations of flow heterogeneity (see the last newsletter). Some irregularities in the deconvolution are also fixed.

The FORTRAN code for the programs has been extensively modified and modularized. While this will not directly affect users of the model, it will ease future maintenance by expediting bug fixes and the incorporation of requested enhancements. It will also make the code more understandable to users who want to customize applications of the programs.

After being modified and augmented to include a reference section, the new *MMID4 User Guide* is available. A PostScript version of the user guide can be downloaded from NSR (see ftp procedure in the sidebar on the facing page).

Dr. SIMCON

Dear Dr. SIMCON,

At the end of a simulation run, I ask for a hardcopy of the plot and nothing ever comes out on the printer. What's going on here?

Graphless in Seattle

Dear Graphless,

A few things could be causing your problem. First check the value of the hardcopy controller, p(139). If it's set to 0, you won't get hardcopy no matter how hard you try. Set p(139) to 1 to send the graph to the LaserWriter. Setting it to 2 will send the plot to the file `simcon.pos`, a file that can be printed later.

If this doesn't fix the problem, the plot may have so many points it causes an overflow in the memory of the LaserWriter. The solution is to use the plot period, p(142), to plot fewer points and see what happens then. The number of points that can be handled depends on the amount of memory in your printer.

If you still don't get a hardcopy, your UNIX environment may be set up incorrectly. If you have multiple LaserWriters, the plot may be going to the wrong one. Possibly it's being sent to the bit bucket (`/dev/null`). I recommend that you check with your system administrator on this one.

Dr. SIMCON

Dear Dr. SIMCON,

Lately, every time I use a new parameter file or import parameters from a file that I archived, I get a message about the parameters needing to be updated. What should I do?

Behind the times

Dear Behind,

With the installation of SIMCON version 2.8, the order of the control parameters has been altered and new control parameters have been added. If you try to use a file with the old layout, SIMCON tells you that the parameters need to be updated and asks for permission to do so. (Pretty polite, eh.) Normally you should let SIMCON go ahead and update the parameters. You can update your whole SIMCON database by using the program `usimdat`. If you have already updated some of the parameter files, you can still use `usimdat`. It will only update the files that need it.

Dr. SIMCON

Dear Doctor,

I've just done a simulation run, and now I want to save the run and get a hardcopy of the plot. What's the quick way to do so?

Rushed

Dear Rushed,

Easy question. No quick way exists. You have to save the run, run the model again, and then request a hardcopy. (Like life, SIMCON can only strive for perfection.)

Dr. SIMCON

Dear Dr. SIMCON,

With SIMCON 2.8, when I save a run the parameter file is now in binary, and I can't print the file or use an editor to look at the values. Help me out here.

Confused

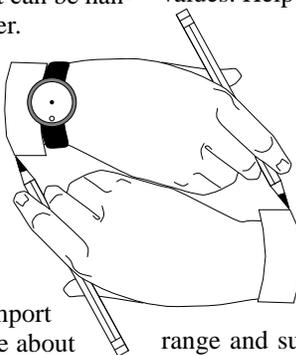
Dear Confused,

You're correct. You cannot use an editor on these files, since they are meant to be an archive, and you don't *really* want to change the values anyway. We haven't left you totally in the lurch. The new `simnlist` program will read binary files and print out the values with their names. There are also new `simnlist` switches that allow you to do things such as only print parameters in a specified

range and suppress printing of control parameters or parameters without names. See the `simnlist` manual page for details.

P.S. There were several reasons for the shift to binary files. The main reason is that they preserve the full accuracy of the data rather than truncating at some preset number of decimal places. Also they are more compact (~ 1/4 the size of text files) and, since they cannot be edited, are not liable to be inadvertently modified. Finally, even though they are not text files, they are still portable to platforms other than Sun workstations.

Dr. SIMCON



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