DIGITAL PROCESSING AND IMMUNO-REGULATORY CIRCUITS

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Although I rather doubt that semiotics per se has a lot to contribute to immunoregulatory notation and concepts, there is little question that this area requires some innovative structuring to provide a more facile framework for conceiving and discussing ideas. I have no clear-cut view of how this is to be accomplished; however, since any attempts in this direction must begin with the development of a catalog of data and concepts upon which overall theory can be based, I have tried to identify several key aspects of my own work that seem important to these deliberations.

Some time ago we introduced an immunoregulatory circuit model that offered a new approach to thinking about antibody response regulation. (1) In essence, this model proposed the existence of bistable regulatory circuits that individually control the production of particular antibody molecules or sets of molecules expressing related idiotypes. These cell interaction circuits can be thought of as analogous to the electronic binary ("flip-flop") circuits that are central to modern digital computers. They can be actively switched into either an "on" or an "off" position by auxiliary cell interactions (helper or suppressor) and will maintain that position despite minor perturbations in the immunologic environment. Nevertheless, they remain capable of being switched to the alternate position when a sufficiently strong signal is encountered.

The cells and signalling interactions that we proposed for these circuits were chosen to exemplify the properties of the circuit and were not intended as more than a rough approximation of reality. The principle, however, of a set of central regulatory circuits that acquire an initial configuration as a result of immunization (or tolerization) conditions and then tend to maintain that configuration unless immunoregulatory conditions change drastically has proven extremely useful in our subsequent work on epitope specific regulation. In essence, viewing these circuits as controlling memory B cell expression provides an explanation for the otherwise perplexing differences in antibody responses that occur when the order of immunizations with carrier molecules and hapten carrier conjugates varies. (2)

Results from a large series of studies begun with immunizations using standard carrier and hapten-carrier conjugates (3) and extending now to vaccine production studies with synthetic peptides conjugated to carrier proteins (4) have verified the existence of some kind of bistable immunoregulatory mechanism functioning in the normal immune system. This mechanism is unlikely to be mediated by the model circuits in the precise form that we proposed; however, the principle embodied in these circuits and perhaps even some of the cell interactions that were defined constitute an important base for future theoretical considerations.

Much of the thinking that went into the development and utilization of the circuits model that we proposed was conditioned by a rudimentary knowledge of basic electronic circuitry and computer programming techniques. The living organism is clearly not a computer and, although it owes much to the transmission of electrical signals, is clearly not definable simply in terms of flip-flops and other electrical gadgets. Nevertheless, we have found that much can be gained by searching for ways in which the behaviour of biological mechanisms can be understood through analogies with processes utilized in computer hardware and software systems.

Unfortunately, contemporary biologists tend to be poorly trained for this approach. By and large, our language and thought processes are less analytical and more phenomenologically oriented than those used in mathematics and engineering. This perhaps is the source of our creativity, but it also limits our ability to think and speak about our work. Therefore, I wonder whether the next conference in this series might be well spent considering the contribution that application of some of the concepts used in digital electronics and artificial intelligence would make in clarifying current thinking in immunology. Perhaps we could develop a synthesis that would expand our vocabulary without overly regimenting our minds.

References

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