Judge's Commentary: The Outstanding Brain-Drug Papers

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The contest problem is of significant importance in the treatment of Parkinson's disease and similar disorders. Medical practitioners rely on experience and common sense in deciding on dosage, frequency, and location of the injections.

The approaches submitted by the 73 teams that chose this problem ranged from too simple to quite elaborate. At the one end of the spectrum, we found papers in which a few parameter-dependent functions were proposed as possible descriptions of the distribution of dopamine and the most suitable was selected on the basis of a statistical analysis. At the other end, we found papers in which the temporal and spatial distribution of absorbed and free dopamine were modeled separately as diffusion processes governed by suitable partial differential equations; the two processes were connected by the assumption that the time derivative of the concentration of absorbed dopamine is proportional to the concentration of the free dopamine.

The judges felt that a successful model should strike a compromise between the complexity of the process and an objective representation of the features essential to its useful analysis.

The winning teams were somewhere in the middle of the spectrum. Both provided a list of reasonable assumptions and explained their importance and relevance to the selected model. In the stage of model development, both teams used a diffusion process governed by a partial differential equation in the concentration. The California Polytechnic team assumed spherical symmetry and used Fick's law, while the Humboldt State team did not assume spherical symmetry but regarded the process as having an instantaneous point source at the start of the process. Both approaches probably oversimplify important features of the process.

In particular, the point-source assumption may be regarded as too coarse an approximation to the reality of an injection. Other teams, in fact, attributed to the dopamine an initial velocity, either radial or in a certain direction. To obtain a reliable estimate of the velocity, often a local hospital was called to get information on the size of the needle, the amount of dopamine normally administered, and the duration of the injection. The

judges were impressed by these efforts; but they decided that for the problem at hand, the point-source assumption is acceptable, at least as a first approximation.

Spherical symmetry, too, may be flawed; and several teams dismissed it as inappropriate. The California Polytechnic team argued that modeling distortions without understanding why they occur is a waste of resources, although they mentioned the inclusion of possible asymmetries as one of the ways of improving their model. The inclusion is straightforward, and the judges felt that it constitutes a better strategy.

Making a reasonable decision about the determinant features of the process is not easy, and the final choice may be a matter of debate. For example, the background dopamine level was neglected by all teams, although some of them mentioned that they were not sure if this assumption was appropriate. Also, some teams mentioned possible transport currents, and others considered them negligible with respect to diffusion. Again, the judges felt that both these features could be neglected in an initial model.

We hope that use of this problem in the MCM will help encourage the medical community to consider a modeling approach in efforts to improve the effectiveness of dopamine therapy for Parkinson's disease.

About the Author

Mario Martelli has been professor of mathematics at California State University, Fullerton, since 1986. He divides his professional time among teaching a variety of courses (including a new course on Discrete Dynamical Systems and Chaos), doing research in applied mathematics, and supervising teams of Harvey Mudd College students working on collaboration projects with local industries. The most recent efforts of his teams include the study of neural networks as image classifiers (for General Dynamics) and the analysis of electron density and energy in the lower Van Allen radiation belt (for McDonnell Douglas).

Prior to coming to California, he was professor of mathematics at Bryn Mawr College in Pennsylvania and at the University of Florence, Italy, where he received his Ph.D. in 1966. He has been visiting professor at the the universities of Warwick, California–Berkeley, California–Davis, Colorado, and Bonn. His primary research interests are in dynamical systems.

Prof. Martelli was an associate judge for the Brain-Drug Problem.