regions in G-protein recognition?

Another crucial question is the location of the ligand binding site. In opsin, the retinal chromophore forms a Schiffs base with a lysine, buried in transmembrane segment VII. However, in the case of the muscarinic receptor, and indeed several other monoamine receptors, there is evidence that carboxylate groups are involved in binding the positively charged ligands. Our group has found that labelling the binding site of a purified rat brain muscarinic receptor with the irreversible antagonist propylbenzilylcholine mustard, followed by proteolytic digestion, yields two peptides whose properties suggest that they are labelled on acidic residues in hydrophobic regions[9]. One of the peptides is glycosylated and so is likely to come from the amino-terminal half of the molecule. It is intriguing to find two buried aspartate residues, one in transmembrane segment II and one in transmembrane segment III, which are conserved in the β_2-adrenergic receptor sequence. Are these key residues in the muscarinic ligand binding site? □

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Mathematics

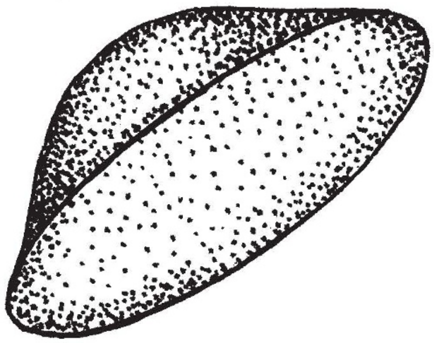
Singular flying pancakes

from Ian Stewart

IF YOU look into a cup of coffee on a summer's day you can often see a bright curve with a sharp tip, where the light is focused after reflecting off the shiny surface of the cup. Such a curve is called a caustic, because heat, as well as light, is concentrated there.

Effects analogous to caustics do not occur solely in optics. The sonic boom of a jet aircraft, and even louder 'superboom' when it turns a corner, are acoustic caustics. So are the signals received by geologists when seeking oil-bearing strata by remote sensing. There are even caustics in quantum mechanics and, perhaps, in the formation of galaxies. J.B. Zeldovitch's model of galaxy formation (*Russian Math. Surv., Uspekhi* **30**, 204; 1975) is based on matter condensing along shock waves. The Zeldovitch theory appears as an example in a celebrated paper of V.I. Arnold (*Commun. Pure Appl. Math.* **29**, 557; 1976) on the singularities of an evolving wavefront. This is the general mathematical setting in which to pose questions about caustics in all of their manifestations. Arnold assumed that the velocity field is governed by a potential, which allowed him to apply general results of V.M. Zakalyukin (*Itogi Nauki* **22**, 53; 1983). Now J.W. Bruce has analysed the non-potential case (*J. London Math. Soc.* **33**(2), 375; 1986) an extension made possible by recent results in singularity theory due to Bruce, A.A. du Plessis and C.T.C. Wall. The main effect of the generalization is to exclude some possible forms for the condensing surfaces that arise in the potential case, and to emphasize instead two new ways in which these surfaces can change their form.

The basic model is as follows. Consider a continuum of non-interacting particles in space, with a smooth initial velocity distribution and a smooth density distribution. As time passes, the particles will move inertially along straight-line paths. These paths can intersect at so-called singularities. By analogy, think of the paths as light rays: the singularities are the caustics, where rays come to a focus. Thus 'collisions' of particles will produce a singular surface in this flow, analogous to a shockwave; and matter will tend to condense around this surface. The mathematical problem, which applies to various physical situations, is to classify the types of singularity that can occur.



The flying pancake is the simplest way that a singularity can evolve in a continuum of non-interacting particles. It may describe the initial condensations of matter in the Universe.

In the potential case the initial velocity field is the gradient of a smooth function, and the singularity is mathematically equivalent to an optical caustic. The simplest singularity that can occur is the 'flying pancake', a lens-shaped surface with a cusped edge and a dent on one side. Initially there are no condensation surfaces; but, then a tiny pancake appears, which grows rapidly (see figure). In a cosmological setting this was interpreted as the formation of a lenticular galaxy, but it is now felt that it more arguably represents the formation of a cluster of galaxies.

How justifiable is the assumption of non-interaction? According to Arnold, in his delightful and unusually readable *Catastrophe Theory* (Springer, Berlin, 1984), it is certainly reasonable up to the point at which pancakes first form. After that it depends on the proportion of neutrons in the Universe, and is justified provided they account for a significant part of the matter present.

The new results of Bruce show that in the more general non-potential case the simplest singularity is still the flying pancake. He obtains a list of nine possible 'typical' ways for the singularity of the wavefront to evolve, seven of which also occur in Arnold's list for the potential case. Three singularities on Arnold's list become atypical in non-potential systems and in practice will break up, in a way described by the remaining two singularities on Bruce's list. Except at this transition, there is no significant difference between the potential and the non-potential cases. The extent to which these ideas really apply to the formation of galaxies is not yet clear, but Zeldovitch's theory does help to make sense of recent observations that matter in the Universe tends to cluster on surfaces, surrounding huge voids. In this picture the pancake (see figure) represents a cluster of galaxies. But the mathematical setting is very natural, and the theory should provide a broad guide to the general types of morphology expected, and a suitable framework for organizing more detailed analyses.

The relation of the mathematical methods to their applications is interesting. Singularity theory is a subject that has grown explosively over the last decade. To cut a long story short, it may be viewed as the mathematical legacy of catastrophe theory, proposed by René Thom in the late 1960s as a model of biological (and other) morphogenesis, and developed by Thom and many other mathematicians (notably J. Mather, B. Malgrange and Arnold and his collaborators). The subject has led a double life, in part as a branch of pure mathematics marching to its own drummer, and in part as a programme guided by various physical and biological problems. An analogy between 'morphogenetic fields' in biology and optical caustics provided some early motivation. Moreover in some sense it has always been clear — or should have been — that singularities are likely to be important in applied science. However, the main techniques used, without which nothing effective can be done, are of purely mathematical origin and were not devised with any specific physical purpose in mind. Anyone who believes that the way to solve a problem is to mount a frontal attack should take a close look at the convoluted but creative history of this particular interaction between mathematics and science. □

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