

The Dynamical Evolution of Seizures: Discriminating Spatiotemporal Patterns in Neurons

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We have performed the first study to demonstrate that the spatiotemporal patterns of epileptic seizures dynamically evolve through a sequence of stages which are differentiated by their synchronous characteristics. This was shown in seizure patterns from epileptic children. Our methodology was based upon a classic technique from the 1930's, which was placed into a modern numerical framework. This technique is broadly applicable to the analysis of any spatiotemporal system, from EEG and fMRI of the brain, to physical systems such as images of fluid turbulence.

The story behind this research is fascinating: it brings together several seemingly unrelated math and science developments that go back over 70 years.

In 1935, a study was made of the differences in measurements (width and length of petals and sepals) of 3 closely related iris flowers by Anderson:

Iris Setosa



Iris Virginica



Iris Versicolor



It is not just that these flowers are hard to identify. The number of genes of these flowers are in multiples of 2, 4 and 6 respectively, and how the genetic load determined the physical characteristics of the flowers (one was a hybrid) was at the time, and now, unknown.

By 1936, Roland Fisher had the chair in statistics at University College London, and published the following paper using Anderson's data set, in the Annals of Eugenics.

**THE USE OF MULTIPLE MEASUREMENTS IN
TAXONOMIC PROBLEMS**

By R. A. FISHER, Sc.D., F.R.S.

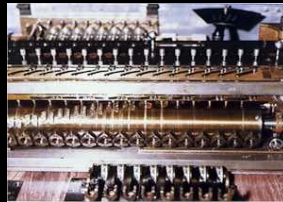
Annals of Eugenics, v. 7, p. 179-188 (1936)

Table I

<i>Iris setosa</i>				<i>Iris versicolor</i>				<i>Iris virginica</i>			
Sepal length	Sepal width	Petal length	Petal width	Sepal length	Sepal width	Petal length	Petal width	Sepal length	Sepal width	Petal length	Petal width
5.1	3.5	1.4	0.2	7.0	3.2	4.7	1.4	6.3	3.3	6.0	2.5
4.9	3.0	1.4	0.2	6.4	3.2	4.5	1.5	5.8	2.7	5.1	1.9
4.7	3.2	1.3	0.2	6.9	3.1	4.9	1.5	7.1	3.0	5.9	2.1

He devised a means of finding the optimal set of coefficients which, when multiplied by these measurements, best discriminate each species. He had at his disposal a 'Millionaire Calculator', pictured below

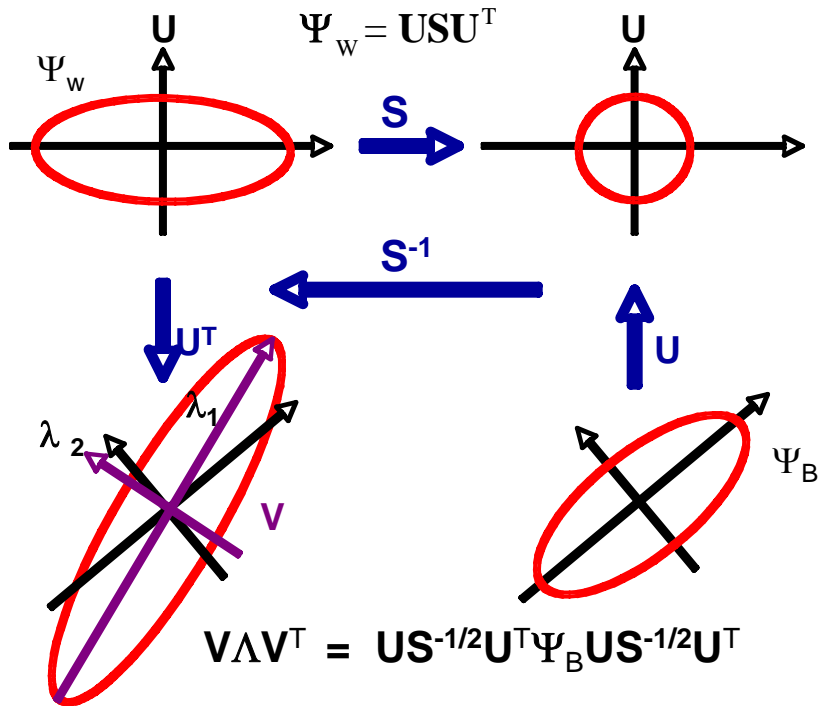
R. A. Fisher, 1890-1962



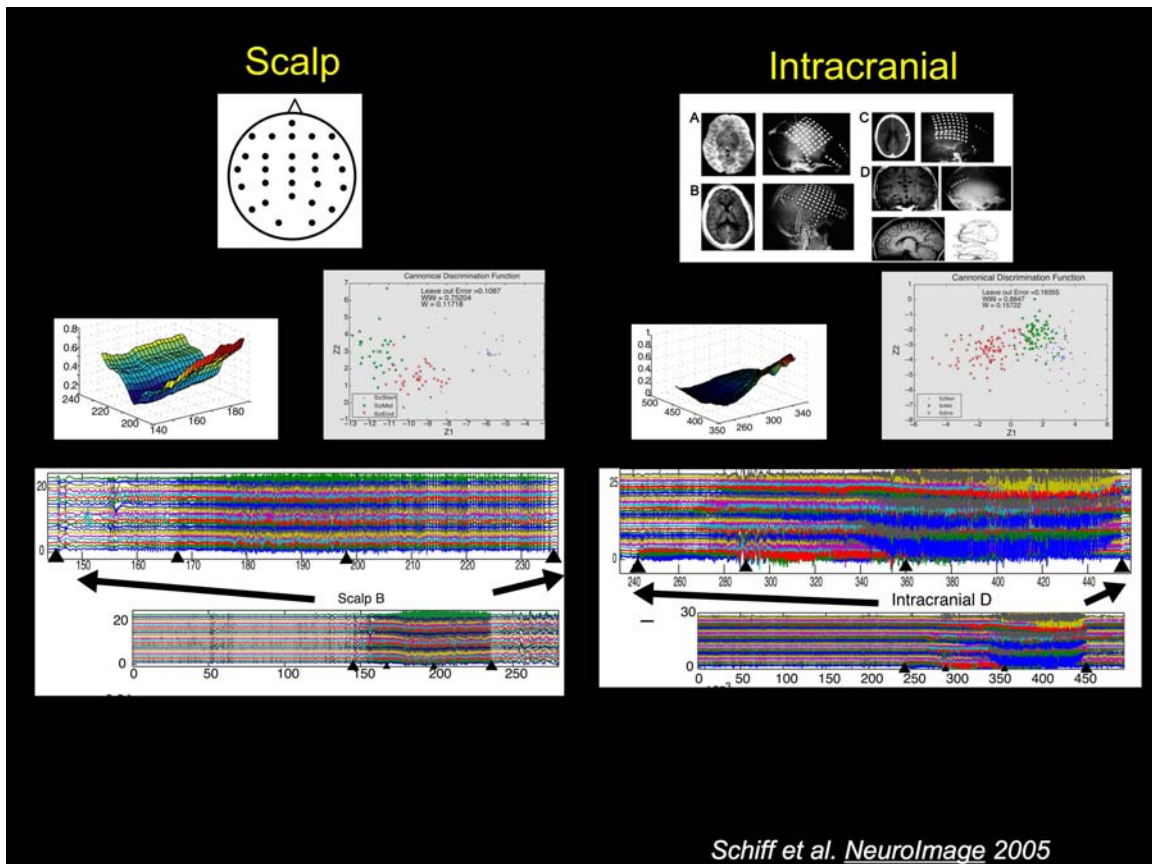
A marvel of machining, this calculator could add, subtract, multiply, and divide, and could carry a certain number of zeros in such calculations. Using this, he stated that 'numerically we find' the optimal solution. So, the best we can understand, is that he literally crunched numbers for several weeks until he had a solution in hand. No interpretation of the geometry of the solution was offered. Most importantly, in an age before digital computers, no approach consistent with modern numerical analysis and digital computation was available.

We wanted to apply this technique to features in the coherent structures from the brain. Specifically, we wanted to ask whether Epileptic Seizures evolved through qualitatively different stages as they organized and then terminated. One would like to know such things for several reasons. First, we want to know whether there is a special state that leads to seizures – a 'preseizure state'. If so, then we can predict when a seizure is likely to occur. Second, we want to know how seizures terminate – from this we can learn how to better stop them.

The first thing that we did was to place Fisher's calculations in a modern matrix formalism, and find a transformation of coordinates that optimized the mathematics required:



We then applied this approach to measures of synchronization between electrodes measuring brain EEG, using both scalp electrodes in the clinic, and intracranial electrodes placed in children who were undergoing evaluation for epilepsy surgery.



We indeed found that we could readily distinguish separate states of synchronization that seizures evolved through as these seizures ran their course. It did not matter whether the measurements were from outside or inside the head, or in fact what kind of epilepsy (there are many different kinds) each child had. These results were recently published in *NeuroImage* (28: 1043 – 1055, 2005). If you are interested in trying out working code for this method, it is archived at the journal website, and also at:

<http://ndl.gmu.edu/~sschiff/public/NeuroImage%20Paper/>

Most recently, we have been using methods from the analysis of fluid turbulence to examine the self-organization of oscillatory activity in the rat brain in the laboratory. We have found a very consistent decrease in complexity as the oscillations organize, and then an increase in complexity as the episodes terminate. When we use the same turbulence methods to examine the coherent structures in these same seizures, the reduction and subsequent increase in dimensionality that the dynamics evolve on follows a very similar pattern.

We are vigorously pursuing trying to understand what underlies the commonalities in the evolution of such dynamical patterns.

I would like to acknowledge my co-authors on this work: Tim Sauer (George Mason Univ), Rohit Kumar (who was a high school student at the time, at the Thomas Jefferson

High School for Science and Technology in VA), and Steven Weinstein, Vice Chairman of Neurology at the Children's National Medical Center in Washington DC. And of course NIH, whose funding supports this research (grants R01MH50006 and K02MH01493).