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In Memoriam

A Tribute to: Keith Worsley — 1951–2009

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Legend has it that Keith's introduction to neuroimaging followed a chance encounter in a verdant corner of McGill University. One of us (Alan Evans) found Keith gathering maple leaves in the fond hope that variations in their shape would provide a useful source of data, against which to test his statistical ideas. This was in the late 80s when PET scanners had just started producing images of cerebral hemodynamics. It was suggested to Keith that there were more than enough data in functional neuroimaging for his machinations: A suggestion that Keith took seriously. This is one of the key events in the inception of modern imaging neuroscience; although probably not the best day for the study of maple leaves.

It is difficult to imagine human brain mapping without Keith's contributions. All mainstream inference in neuroimaging rests upon his ideas and the transcription of those ideas into understandable heuristics and pragmatic computational schemes. Basically, Keith invented a new sort of statistics. Before Keith Worsley, statistical inference in brain mapping was largely limited to discrete or single tests; for example, *T*-tests on activities in regions of interest. However, continuous image data called for a different sort of inference, based on significant topological features like peaks and excursion sets above some threshold. This should not be confused with spatial statistics of the more traditional sort that predated Keith's contributions, which dealt mostly with kriging and related techniques. Keith introduced a fundamentally different way of characterising interesting features in images that could not be described in terms of simple numbers. The trick was to appeal to differential geometry and topology, which provided a description of the probabilistic behaviour of image data under the null hypothesis in terms of special point processes. This description was in terms of topological features such as the number of blobs and holes induced by thresholding an image. The result was a very powerful and general framework for topological inference that was grounded in random field theory (Worsley et al., 1992, 1996, 2004). This approach has been at the heart of all mainstream inference in neuroimaging since the early 90s. It is an integral part of all the commonly used voxel-based analysis software and has placed our community at the forefront of statistical developments in this area. Keith's formulation of the problem and its solutions transcend brain imaging and are likely to reach much further in the fullness of time. Random field theory has been used in the analysis of continuous psychophysical data (Worsley et al., 2007), through to the analysis of foot pressure images in the clinic (Pataky and Goulermas, 2008); from astrophysics though to meteorology (Worsley, 2002) In short, Keith was responsible for a paradigm shift that enabled statistical inference to move from scalar statistics to statistical fields or images.

These advances were particularly important for neuroimaging and, in one sense, define its history. At the time that Keith was introducing random field theory, the first brain mapping experiments were starting to appear in the high profile literature. These reports were greeted with a high degree of scepticism from people in established fields like psychology and electrophysiology; largely because it was impossible to tell which of the visually appealing blobs in activation maps were significant or not. Topological inference finessed the multiple comparison problem and allowed one to assign *P*-values, not to the statistics subtending each blob but to the very occurrence of the blobs themselves (Fig. 1). With this advancement, human brain mapping became one of the most rigorous disciplines in neuroscience, in terms of its careful statistical characterisations and control of false-positive rates. This rigor was an essential component of integrating imaging neuroscience into the broader biological sciences. It is also interesting to reflect that the advent of functional magnetic resonance imaging coincided exactly with the introduction of topological inference and random field theory. The success of fMRI may, in part, reflect the ground-work pioneered by Keith in the analysis domain. One can quantify the impact Keith has had in terms of his explosive citation rates, since the inception of these procedures (Fig. 2).

It is impossible to describe Keith's statistical contributions precisely in such little space, but they are an inspired mix of differential topology (Morse theory), integral geometry (intrinsic volumes and Kinematic formulae) and spatial point processes derived from smooth random fields (Rice–Kac formula). The main idea behind all topological inference is to compute the behaviour of a topological feature of the blobs called the Euler characteristic. The topologically deep results of Morse theory express the Euler characteristic in terms of the number of local maxima (minima and saddle points) contained in the blob. Another branch of geometry, integral geometry, is used to express integrals or averages of Euler characteristics in terms of intrinsic volumes that measure the size and curvature of the search region, in our case, the brain. The final result is a beautiful relationship between the *P*-value of a blob and the volume and surface area of the brain, characterised in terms of the unit-less quantities known as *resels* that Keith pioneered.

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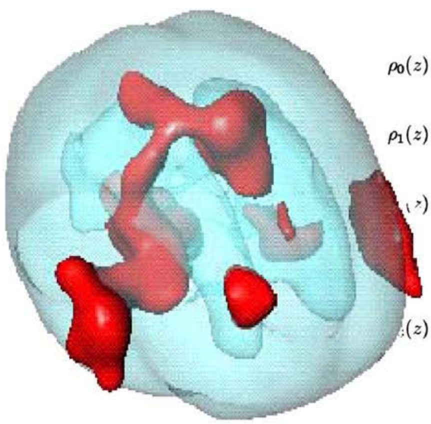
F field with k and ν degrees of freedom, $k+\nu>d$



$$\rho_0(z) = \int_z^\infty \frac{\Gamma\left(\frac{\nu+k}{2}\right)}{\Gamma\left(\frac{\nu}{2}\right)\Gamma\left(\frac{k}{2}\right)} \frac{k}{\nu}\left(\frac{ku}{\nu}\right)^{\frac{1}{2}(k-2)}\left(1+\frac{ku}{\nu}\right)^{-\frac{1}{2}(\nu+k)} du$$

$$\rho_1(z) = \frac{\lambda^{\frac{1}{2}}}{(2\pi)^{\frac{1}{2}}} \frac{\Gamma\left(\frac{\nu+k-1}{2}\right)2^{\frac{1}{2}}}{\Gamma\left(\frac{\nu}{2}\right)\Gamma\left(\frac{k}{2}\right)}\left(\frac{kz}{\nu}\right)^{\frac{1}{2}(k-1)}\left(1+\frac{kz}{\nu}\right)^{-\frac{1}{2}(\nu+k-2)}$$

$$\rho_2(z) = \frac{\lambda}{2\pi} \frac{\Gamma\left(\frac{\nu+k-2}{2}\right)}{\Gamma\left(\frac{\nu}{2}\right)\Gamma\left(\frac{k}{2}\right)}\left(\frac{kz}{\nu}\right)^{\frac{1}{2}(k-2)}\left(1+\frac{kz}{\nu}\right)^{-\frac{1}{2}(\nu+k-2)} \times \left[(\nu-1)\frac{kz}{\nu}-(k-1)\right]$$

$$\rho_3(z) = \frac{\lambda^{\frac{3}{2}}}{(2\pi)^{\frac{3}{2}}} \frac{\Gamma\left(\frac{\nu+k-3}{2}\right)2^{-\frac{1}{2}}}{\Gamma\left(\frac{\nu}{2}\right)\Gamma\left(\frac{k}{2}\right)}\left(\frac{kz}{\nu}\right)^{\frac{1}{2}(k-3)}\left(1+\frac{kz}{\nu}\right)^{-\frac{1}{2}(\nu+k-2)} \times \left[(\nu-1)(\nu-2)\left(\frac{kz}{\nu}\right)^2-(2\nu k-\nu-k-1)\left(\frac{kz}{\nu}\right)+(k-1)(k-2)\right]$$

C	$\mu_0(C)$	$\mu_1(C)$	$\mu_2(C)$	$\mu_3(C)$
Sphere, radius r	1	$4r$	$2\pi r^2$	$(4/3)\pi r^3$
Hemisphere, radius r	1	$(2+\pi/2)r$	$(3/2)\pi r^2$	$(2/3)\pi r^3$
Disk, radius r	1	πr	πr^2	0
Sphere surface, radius r	2	0	$4\pi r^2$	0
Hemisphere surface, radius r	1	πr	$2\pi r^2$	0
Box, $a\times b\times c$	1	$a+b+c$	$ab+bc+ac$	abc
Rectangle, $a\times b$	1	$a+b$	ab	0
Line, length a	1	a	0	0

Fig. 1. Schematic illustrating the notion of an excursion set, induced by a threshold. Measures on this set play the same role in random field theory as *F*-values would in conventional statistics. The equations pertain to the density of blobs per unit volume (upper) and the volume *per se* (lower). The insert was one of Keith's favourite graphics.

Keith's contributions are technically awe inspiring. However, what marks Keith as a great scientist was his ability to disseminate these ideas and help others implement them in a pragmatic and useful way (e.g., Worsley & Friston, 1995). His didactic energies were unparalleled, organising workshops and engaging people from other fields to substantiate and refine the mathematical framework he was creating. A notable recruit in this endeavour was Robert Adler, the world's leading expert on random field theory. It is rumoured that Robert had once seen his work on random field theory as a largely intellectual exercise but returned to it with a passion when he saw how powerfully it could be used for inference on images. Keith's friendship with Robert brought together two of the greatest intellects from disparate fields; with some very productive consequences. Not least among these is the collaboration between one of us (Jonathan Taylor) and Robert Adler that endures to the present day.

Keith's unique application of random field theory to spatially-correlated PET activation data was crystallized in the early 90s at the MNI. A small regular working group comprising Peter Neelin, Sean Marrett, Alan Evans and Keith Worsley would sit and argue for hours about the problem of multiple comparisons in voxel-wise brain

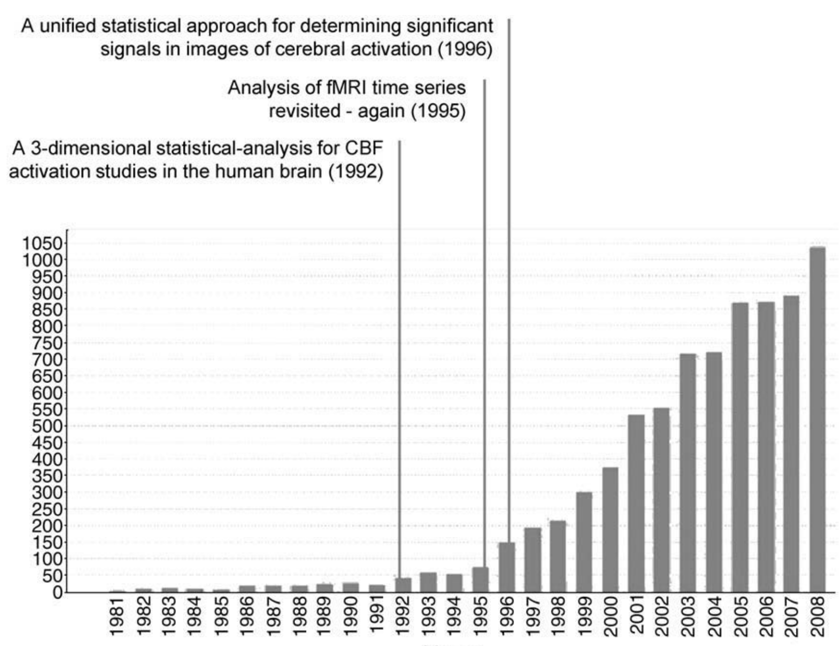


Fig. 2. Citation per year (ISI Web of KnowledgeSM) for Keith Worsley shown in relation to his three most highly cited papers. In 2008 Keith was cited over 1000 times.

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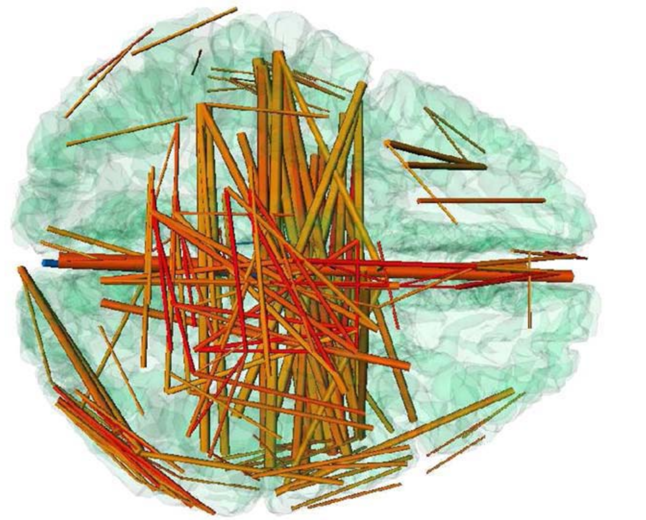

Fig. 3. A connectivity map, identifying significantly-connected regions via cylinders of differing width.

activation data, Keith happily conceding that he did not know one end of the brain from the other while the others received a continuing lesson in random field theory. It was in this crucible that Keith evolved the general solution for excursion set analysis, introducing terms such as "image roughness", "Euler characteristic" and "resel" to a bemused audience. The elegance of the theory was apparent at the time, but not its eventual impact on the field. Keith would turn up at these meetings fresh with some new perspective, be it scale space or correlation or excursions sets on a folded surface manifold, with a barely-suppressed glee at what he'd found. At one such meeting, when Keith was excited about the potential for searching across scale space, i.e. the same data using various smoothing kernels, he was told that the Dutch school had produced a vast body of literature on scale space image processing to detect a signal. His response "Ah, but they can't put a *P*-value on it".

Keith's generosity with those around him was legendary. There wasn't room for a permanent office for Keith at the MNI so, when visiting, he would sit at one of the hallway carrels in the Brain Imaging Centre, tapping away on his PC. His makeshift office was forever surrounded by students asking advice or passing colleagues pressed to see his latest result, usually in the form of some incomprehensible 3D "lava-lamp" plot (Fig. 1) or "kerplunk" plot (Fig. 3) that identified significantly-connected regions. Keith truly enjoyed the successes of the younger scientific community at McGill. Keith was forever pointing out, with no affect or awareness of his own unique ability, that this or that student of his was "a genius". In many cases, this has turned out to be not too far from the mark. Keith has left a tremendous legacy in the new generation of McGill statisticians.

Apart from his local community, Keith had a much broader family. Space does not permit a description of all of his colleagues from India, Cuba, China, Korea, Japan, North America and Europe who have passed through McGill but special mention should be made of Keith's enduring regard for Cuban neuroscience and its leader, Pedro Valdes-Sosa. A never-ending procession of young Cuban neuroimaging scientists have passed through the MNI, interacting with Keith and Alan Evans. One of Keith's most memorable comments was "Alan, the mathematics and statistics we are using in neuroimaging are 30 years old, what they are doing in Havana is 3 months old, straight out of the math journals". Keith was a long-time friend of Cuba and travelled there regularly to discuss science.

It may be difficult for people outside the world of statistics to appreciate the energy and commitment Keith displayed to the imaging community. In moments of sober reflection he would note that publications in the neuroimaging literature counted little to his curriculum vitae. Although most of us prize a publication in NeuroImage, from the point of view of the statistics community, a NeuroImage publication has the academic substance of an in-flight magazine (irrespective of how interesting it is). Despite this, Keith continued to support neuroimaging, carefully translating his deeper mathematical insights to refine the tools that we were using. A nice example of this occurred in about 1998 (Worsley et al., 1999), when Keith realised that to estimate a non-isotropic search volume, one could simply replace the Euclidean coordinates of that volume by normalised residuals in a high-dimensional space and proceed as if the data were isotropic. Keith was extremely excited about this, almost

Fig. 4. "Holiday photos" that arrived from Keith in the summer of 2003, with the text "*Here's something from my trip to India!*". They picture a bust of P.C. Mahalanobis (founder of the Indian Statistical Institute). Keith was taken with the reverse inscription "A SINGLE NEW OBSERVATION MAY CALL FOR A MORE COMPREHENSIVE THEORY". Within months, he reported new random field theory *P*-values for peaks of canonical correlation SPMs. This theory "completes results for all types of univariate and multivariate image data analysis. All other known univariate and multivariate random field theory results are now special cases" (Worsley et al., 2004): This is a comprehensive theory.

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to the point of breathlessness when trying to explain its simplicity and implications. Perhaps only one of us truly understood him. However, this insight led to procedures that are now used, every day to measure the smoothness and implicit volume of statistical search spaces required for inference. Even away from work Keith's preoccupations had a prophetic and distinctly mathematical focus. The holiday photos he sent his friends were not always typical sightseeing photos (Fig. 4).

As Keith's stature grew internationally, he responded by taking his citizenship even more seriously. He continued to elaborate software for others to use and was tireless in supporting younger colleagues in analysing their data and developing specialist applications. In fact, Keith continued to write code up until his illness. His most recent work (*SurfStat*) was still being crafted with care and excitement during quieter moments in the corridors of the OHBM meeting in Melbourne last year. It is worthwhile visiting its website (http://www.math.mcgill.ca/keith/surfstat/) to see the simplicity and beauty of this code; whose functionality will become increasingly relevant as we apply topological approaches to surface based data from EEG and MEG.

However, Keith's citizenship did not stop there; a few years ago he was asked to become Section Editor for Methods and Modelling at NeuroImage. His first response was of typical modesty about his competence to fulfil an editorial role. The irony here was that Keith was the best person in the world to do this job. He excelled and was one of those remarkable Editors who professed to enjoy his role. It is also worth remembering that Keith was serving on the Council for the Organization of Human Brain Mapping when he died (Meetings Liaison). He was an active and enigmatic figure in the Organisations annual meetings, immediately recognisable not least because of his intellectual stature but also his physical stature. One of his more endearing commitments was to the OHBM parties; at which he would religiously sport a rather fetching striped "party jacket" (Fig. 5). Every year, he would take this jacket half way around the world for its annual outing, usually on a Wednesday night in June, at a nightclub populated by a thousand or so young[ish] neuroscientists. It was, in fact, extremely useful for locating Keith at these events, irrespective of whether one wanted some engaging scientific banter or simply a dance (Keith was up for both).

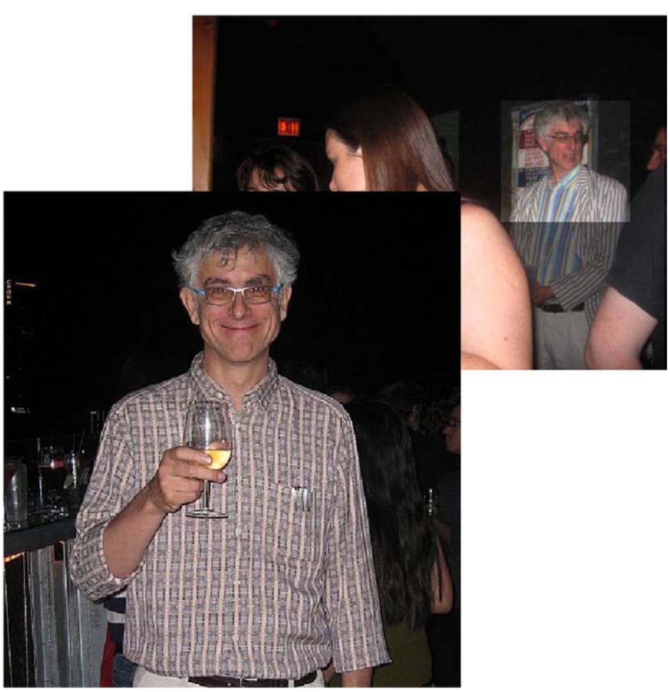

Fig. 5. Keith at the OHBM Annual Meetings (Chicago 2007 and Melbourne 2008), with and without party jacket (but same trousers).

Although Keith was a larger than life personality within the imaging community, his status was also evident in the statistics and mathematics community. It was a great moment for all of us when he won the Gold Medal of the Statistical Society of Canada, 2004. It was a testament to the fact that Keith's bilateral commitment to statistics and neuroimaging had been met with a bilateral acknowledgement of his immense contributions. A further testament to this was his prestigious appointment as Professor of Statistics at the University of Chicago last year; a surprising move for some of us but, in Keith's words he was responding to an offer, "that could not be refused".

Besides being an outstanding researcher, Keith was a great mentor to young researchers, particularly to his students, which include one of us (Jonathan Taylor). Keith encouraged all of his students to engage with real problems in brain imaging, which Keith liked to call statistics' "agricultural field trials of the 21st century". Unflattering as this may sound to bran imaging; agricultural field trials were responsible for a breathtaking amount of statistical development in the early 20th century. Keith also liked to point out that it takes a special type of statistician to undertake the analysis of brain imaging data due to the enormous volume of data entailed by functional brain imaging. As a mentor, Keith was generous with his time, showing by example how important and rewarding it is for statisticians to be involved in cutting edge science. Keith's stories about the scientific discussions going through all hours of the night at the lively HBM parties did not make it difficult to convince his students that brain imaging was a great field to be involved in.

For those people who did not know Keith personally, it is worth pointing out that he died at a relatively young age: He had a new family, a new job and lots of new ideas. His untimely loss may take some time to appreciate properly. He had a wonderful personality and was held in enormous respect and affection by nearly everyone who knew him. One of Keith's most remarkable qualities was a genuine and almost child-like delight in new ideas and a selfless pleasure in other people's achievements. It was entertaining to sit next to him at academic meetings and wait for him to spot an important concept or perspective, usually from a young presenter. He would become visibly excited and grin enthusiastically, as if he wanted to stop the lecture there and then and congratulate the speaker. It was clear that he loved the work in our field and the people in it. At moments like this one could not help thinking "it must be nice to be Keith Worsley"; now, of course, one has to think "it must have been nice being Keith Worsley".

Acknowledgments

We would like to thank Marcia Bennett for helping to prepare this memorial and for the photos of Keith at the annual meetings.

References

Pataky, T.C., Goulermas, J.Y., 2008. Pedobarographic statistical parametric mapping (pSPM): a pixel-level approach to foot pressure image analysis. J. Biomech. 41 (10), 2136–2143 Jul 19.

Worsley, K.J., 2002. Random field, Gaussian. In: El-Shaarawi, A.H., Piegorsch, W.W. (Eds.), Encyclopaedia of Environmetrics, p. 1676.

Worsley, K.J., Friston, K.J., 1995. Analysis of fMRI time-series revisited—again. NeuroImage 2 (3), 173–181 Sep.

Worsley, K.J., Evans, A.C., Marrett, S., Neelin, P., 1992. A three-dimensional statistical analysis for CBF activation studies in human brain. J. Cereb. Blood Flow Metab. 12 (6), 900–918 Nov.

Worsley, K.J., Marrett, S., Neelin, P., Vandal, A.C., Friston, K.J., Evans, A.C., 1996. A unified statistical approach for determining significant signals in images of cerebral activation. Hum. Brain Mapp. 4, 58–73.

Worsley, K.J., Andermann, M., Koulis, T., MacDonald, D., Evans, A.C., 1999. Detecting changes in nonisotropic images. Hum. Brain Mapp. 8 98{101.

Worsley, K.J., Taylor, J.E., Tomaiuolo, F., Lerch, J., 2004. Unified univariate and multivariate random field theory. Neuroimage 23 (Suppl. 1), S189–S195.

Worsley, K.J., Charil, A., Smith, F., Schyns, P., 2007. Detecting connectivity between images: MS lesions, cortical thickness, and the 'bubbles' task in fMRI. NeuroImage, POSTER (pdf) 33, 303 M-AM.

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