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On the fractal nature of nervous cell system

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In a detailed study entitled "Morphological development of thick – tufted layer V pyramidal cells in the rat somatosensory cortex," an international team of scientists (Romand et al., 2011) reported a series of results pertaining to an analytical investigation of the morphological development of thick-tufted layer V pyramidal cells (also called the principal cells) in the rat somatosensory cortex. At the end of the Introduction Section, the Authors stated "all compartments of a TTL5 cell undergo different developmental changes, supporting the notion that multiple functional compartments receive different inputs and may integrate distinct signal transduction systems." Following on a careful reading of this stimulating report a main question rose which concerned the epistemic view adopted by the Authors and in turn the analytical procedure chosen for investigating neural cells from an highly organized system, privileging in fact the recourse to "conventional" morphometry. These morphometric approaches are usually termed conventional because being based on single *scale* measuring which may suite well for evaluating biological objects assumed to be or arbitrary approximated to regular Euclidean structures, but inappropriate to quantitatively describe the morphology of thick-tufted layer V pyramidal cells, characterized by complex functional properties and irregular morphological features. Therefore an objective estimation could be reached only by applying the principles and rules of the Fractal geometry proposed by the mathematician Mandelbrot (1982) in the early 1980s. The Authors specified that most neural parameters, including lengths and diameters of individual segments, surface area, branch angles, and other cellular elements were "subjectively classified" and thereafter analyzed either from reconstructed figures or obtained from unrealistic representations. Another incongruous sentence was found in the Somatic Development Section: "Somata were subjectively classified into three formats according to shape: triangular, round, and oval. Although three shapes were found at all ages, somata of TTL5 neurons appeared to be mostly triangular or round at P7 and predominantly triangular thereafter." It is by far evident from Figures 1 and 3 of Romand et al. (2011) that somata, dendrites and axons are neither round or triangular bodies, nor linear segments, but appeared as irregularly shaped anatomical entities susceptible to be adequately investigated by the "non-conventional" fractal morphometry. Suffices it to mention that, during the last two decades, several studies have been performed on brain tissue and nervous system cells by adopting fractal concepts and methods, which has enabled to quantitatively elucidate most developmental, morphological, and spatial pattern avoiding arbitrary approximation or smoothing of cellular shapes and structures. (Smith and Bejar, 1994; Smith et al., 1996; Bernard et al., 2001; Grizzi and Chiriva-Internati, 2005; Milosevic and Ristanovic, 2006; Ristanovic et al., 2006; Di Ieva et al., 2007; Jelinek et al., 2008; Di Ieva, 2011). Therefore, it may not be surprising that the Authors, despite a huge investigative effort, were obliged to recognize a frank blank, honestly admitted, when they were trying to interpret the data in the light of Methodological considerations (Page 20), with the words: "Variations in results across different studies can be due to many methodological factors such as differences in the staining procedure, the section thickness, the measuring, and analyzing method, the cell selection criterion, the sample size, and the cortical area. These differences make it difficult to directly compare results between different studies." Proper considerations indeed, but not unpublished, because they evoked considerations much similar reported as far as thirty years ago by a Swiss Group (Paumgartner et al., 1981) in a pioneer study which clearly demonstrated the influence of resolution scale, i.e., objective magnification, on the estimates of geometric irregular features of liver cell membranes, or in other words the role of resolution scale at which the measurements were performed. The large observed discrepancy was consistently annulled while the variations reported by different investigators could be explained by taking into account the "resolution effect" according to the concepts of the Fractal geometry, such as the irregularity, the statistical self-similarity, the scale invariance of form, the occurrence of repetitive morphologic determinants and the fractal, i.e., non-integer dimension, rather than the trivial methodological factors called upon to explain estimate variations across different studies. Biologic structures with irregular shape and complex morphology should not be approximated to ideal geometric objects, since far from the real pictures, while a single scale of measurements should not be adopted *a priori* if an objective morphological description of complex objects has to be achieved (Losa and Nonnenmacher, 1996). It should be pointed out that fractal and conventional morphometric approaches, built up on distinct epistemological principles, may set the understanding of the biologic reality at different level. The former describes the morphological complexity within an experimental interval of observation scales that obviously encompasses the Euclidean dimension, while the latter proceeds at a primary level, i.e., by reducing cellular shapes and tissue structures to monotone elements which could be described by means of deterministic rules. Nevertheless, fractal and conventional morphometry may represent complementary analytical/

quantitative tools to elucidate the diversity of morphological patterns and functional parameters which characterize neural cells and brain structures.

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