Barrel Cortex

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*Thomas Woolsey*

Barrel cortex is part of an anatomically visible map of the contralateral body surface in layer IV of the somatosensory cortex of certain mammals.

The introduction of phrenology in the early 1800s stimulated interest in the possibility that different functions of the cerebral cortex were in different cortical 'organs' (Gall and Spurzheim, 1810; Spurzheim, 1826; Temkin, 2002). Hitzig and Frisch first stimulated the exposed cerebral cortex of a dog electrically in 1870, reporting that only selected areas produced movements and that the movements produced differed by the site stimulated (Hitzig and Fritsch, 1870). Consistent regional patterns of histology, some matching functional findings, were described subsequently in the brains of man and many mammals (Campbell, 1905; Brodmann, 1909; Rose, 1929). By the 1930s, a significant body of detailed information was available from direct stimulation of the brain in conscious patients related to movements, evoked sensations or perturbed functions, such as speech (Cushing, 1919; Foerster, 1936; Penfield and Boldrey, 1937) (Figure 1).

*Figure 1:* "[One of three] Diagrams illustrating the more definitively localized of the cortical
centers of the exposed part of the hemisphere in relation to the main fissures and convections; also the 'word centers' (sensory and motor) involved in the special mechanism for speech. (Receiving sensory stations in blue; discharging motor stations in red.)" (Cushing, 1919).

Clinton Woolsey's (my father's) first study was of the dog motor cortex using cortical stimulation, cortical lesions and postoperative behavioral changes (Woolsey, 1933). However, when it was shown that amplified electrical recordings from the exposed brain surface could be used to 'map' responses evoked by sensory stimulation, he immediately began to explore the organization of sensory cortical regions in animals and humans (Marshall et al., 1937; Woolsey et al., 1942; Woolsey et al., 1979). Clinton Woolsey and his colleagues 'mapped' somatic, visual, auditory and motor representations in the brains of many species. In a summary, he proposed that the rat offered a general plan 'prototypical' for the mammalian cortex (Woolsey, 1952) (Figure 2).

![Figure 2: "Evolution of localization in the postcentral tactile area as defined in a series of mammals. The dotted areas show the extent of the areas devoted to the hand and foot. The figures are not all to the same scale, but the proportions of each are approximately correct."

The drawing at the upper left is of a hypothetical 'limbless' mammal. Reproduced from (Woolsey, 1952) Patterns of localization in sensory and motor areas of the cerebral cortex. In: The Biology of Mental Health and Disease, New York: Hoeber, p. 204, Fig. 65 (1952), with permission from Lippincott Williams and Wilkins (http://www.lww.com/index.html).

Apparently, I was witness to an evoked potential study from a bassinet, but I do not recall the incident. Growing up, I spent time in my father's laboratory as an observer and menial worker. Richard Lende, a neurosurgeon, was one of many young trainees who had worked with my father. Lende was interested in the cortical phylogeny and my chance actually to study the brain came when he asked me to spend a summer working in his laboratory at the University of Colorado in the beautiful city of Denver. It was there that I learned the evoked potential technique and surgical approaches to small mammals (Lende, 1970), primitive mammals (Lende, 1964) and mammals with small brains (Lende, 1963).

I suppose someone had asked my father for a map of the mouse cortex and he suggested I record from mice prior to my matriculation at Johns Hopkins. The mouse's brain is significantly smaller than the rat's; nevertheless I recorded regional activation of cortex by sound, light and touch. As in the rat, there was a large representation of the head and face (Figure 3).
At the University of Wisconsin all experimental brains were evaluated by histology (Welker et al., 1964). The Nissl-stained brains I had mapped were available for examination during the subsequent summer. When I started to match cytoarchitecture to physiology the odd pattern of cells in layer IV of the first somatic area leapt out (Figure 4).

Jerzy Rose told me how to relate this architecture to the brain surface. By drawing outlines of the sections on filing cards, cutting along these outlines, extending the patterns of cell densities in layer IV to the surface with radial lines that were then inked on the cut edges of the cards, and stacking the cards (His like), I made a model (Figure 5). The region was the same as that described by many authors, including Rose's uncle Maximillian (Rose, 1929). The model showed a 'cell dense net' and barrels. (I only appreciated the latter in retrospect.) The region obviously included the 'glomerulos' described by Lorente de Nó from Golgi impregnations (Lorente de Nó, 1922). In my paper I proposed that the 'net' was related to the whiskers on the face.
Hendrik Van der Loos had read my paper and I approached him to work in his laboratory. There, I cut the brain in the plane of layer IV so as to look down on the 'net'. Celloidin is a transparent embedding medium and I could see the brain surface for orientation as I cut 50-100 µm sections. The very first section including layer IV showed neurons in a pattern clearly resembling the whiskers on the opposite face (Figure 6).

Figure 6: The first thick (100 µm) section cut in 1968 in the plane of and through layer IV showed grouping of cells in rings organized into 5 rows. The cytoarchitecture matched the pattern of whiskers that activated this cortex.

These were correlated to thicker sections cut perpendicular to the cortical surface. The neurons in layer IV evidently formed cylinders traversing the thickness of layer IV with slightly bowed sides that seemed to resemble a cask more than a ball of yarn as described in earlier cytoarchitectonic and Golgi studies (Figure 7). Accordingly, we termed them barrels; the cortical region containing barrels is the barrel cortex. Photographs and drawings of sections from many hemispheres indicated a remarkable constancy between individuals; in a particular region the barrels were larger, ovoid and, like the mouse's large whiskers, patterned in five rows. The position of these larger barrels was appropriate to the location and organization of the recorded representation of the larger whiskers (Woolsey and Van der Loos, 1970).
Figure 7: 'Model' of the arrangement of cells in layer IV of the mouse cortex hypothesized to constitute part of a cortical column related to a whisker. Reproduced from Figure 7 in Woolsey TA, Van der Loos H (1970) The structural organization of layer IV in the somatosensory region (SI) of mouse cerebral cortex. The description of a cortical field composed of discrete cytoarchitectonic units. *Brain Research* 17:205-242, with permission from Elsevier.

We hypothesized that a single barrel is related to a single whisker (Figure 8).

Figure 8: Direct correspondence of the whiskers on the face and the large barrels in cortex that whisker stimulation activates in the opposite cerebral hemisphere (Woolsey and Van der Loos, 1970). Reproduced from Figure 15 in Woolsey TA, Van der Loos H (1970) The structural organization of layer IV in the somatosensory region (SI) of mouse cerebral cortex. The description of a cortical field composed of discrete cytoarchitectonic units. *Brain Research* 17:205-242, with permission from Elsevier.

Several different strategies were used to prove it. First, we excised selected whisker organs in early postnatal life. The results were striking. Consistent with the functional maps, the pattern of the cortical barrels was altered and was always appropriate to the removed whiskers (Van der
Loos and Woolsey, 1973) (Figure 9).

*Figure 9:* The middle row of barrels was altered in the right cortex (drawing - above, tangential section through layer IV - middle) of a mouse when the middle row of whiskers on the left face (bottom panels) was cauterized shortly after birth (Van der Loos and Woolsey, 1973).

Moreover, the significant potential of this system for studies of cortical and sensory development became compelling. Second, microelectrode recordings, including intracellular recording and staining, showed that cells in a particular barrel are always activated best by deflections of the appropriate whisker (Welker, 1976; Simons, 1978; Simons and Woolsey, 1979). As other functional approaches were developed, the conclusion that neurons in a particular barrel are first and best activated by, and are part of, a cortical column related to the expected whisker has been amply supported (Durham and Woolsey, 1977; Greenberg et al., 1979). The basis for the barrel pattern is: clustered afferents related to a particular whisker (Lorente de Nó, 1922; Killackey, 1973; Senft and Woolsey, 1991; Agmon et al., 1993), clustered synapses from these afferents (White, 1976), concentration of dendritic targets of these synapses (Woolsey et al., 1975a; Woolsey, 1993), and displacement of neuronal somata around these foci of information exchange (Harris and Woolsey, 1983; Feldmeyer et al., 2002).

Subsequent studies from many laboratories have expanded these findings greatly, often quantitatively, as follows.

**Comparative Neurology:** Barrels are in rats, some other rodents, lagomorphs and certain marsupials. Similar sub-nucleation has been described in somatic sensory pathways in other species, including man (Weller, 1972; Woolsey et al., 1975b; Goyal et al., 1992).

**Pathway:** The organization of the entire pathway - brainstem, thalamus and cortex - can be determined in a single individual without special techniques (Killackey, 1973; Van der Loos, 1976; Durham and Woolsey, 1984; Ma and Woolsey, 1984; Varga et al., 2002). Connections: The exact elements, their numbers, spatial relationships, sources, targets and statistical variation have been comprehensively catalogued (White, 1976; Harris and Woolsey, 1983; Jacquin et al., 1984; Williams et al., 1994; Lübke et al., 2000; Petersen and Sakmann, 2000; Varga et al., 2002).

**Molecules:** Housekeeping, structural, transmitter, trophic, signaling, etc., molecules are spatially segregated within the context of the barrel map and are modulated by sustained modifications of activity (D'Amato et al., 1987; Glazewski et al., 1996; Maier et al., 1999; Kesterson et al., 2002).

**Development:** Timing of neurogenesis, pattern formation, synaptogenesis and the influence of various molecules on these can be evaluated at specific loci throughout pre- and postnatal development (Van der Loos and Woolsey, 1973; Senft and Woolsey, 1991; Killackey et al., 1995; White et al., 1997; Fukuchi-Shimogori and Grove, 2001). Plasticity: Disrupting overall somatic activity and use during development and in adults leads to long lasting and/or permanent changes
in structure and function (Woolsey and Wann, 1976; Simons and Land, 1987; Knott et al., 2002).

**Metabolism and Blood Flow:** Direct studies of cerebral blood flow, vessel growth, metabolism and signaling pathways all map precisely to the appropriate barrel (Wong-Riley and Welt, 1980; Dietrich et al., 1981; Gonzalez and Sharp, 1985; Adachi et al., 1994; Woolsey et al., 1996; Brett-Green et al., 2001).

**Behavior:** The roles of motor control, central pattern generators, active exploration, sensory processing discrimination, and integration in whisking are known (Welker, 1964; Bermejo et al., 1996; Hattox et al., 2002; Talwar et al., 2002).

**Genetics:** Influence of different genes on brain form, development, signaling molecules and behavior have been investigated (Dun and Fraser, 1958; Welker et al., 1996; Iwasato et al., 2000; Fukuchi-Shimogori and Grove, 2001).

**Modeling:** Computational aspects of network function, neuronal structure, sensory processing, exploratory activity, pattern development and plasticity have been considered (Pinto et al., 1996; Ahissar, 1998).

**Disease:** Effects of environmental agents, genetic models of disease such as in mental retardation (Galvez et al., 2003), stroke (Wei et al., 1995), brain tumors (Sherburn et al., 1999), trauma (Jacobs et al., 1999) and for therapy and treatment can be interpreted in a standard context.

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**Favorite Sentences**

*Early thoughts on regional variations of the cerebral cortex*

"At this time he [Gall] spoke of the necessity of the brain to the manifestations of mind, of the plurality of the mind's organs, and of the possibility of discovering the development of the brain by the configuration of the head" (Spurzheim, 1826).

*Rodents show a general layout of cortical function*

"The general arrangement ... [is] ... a somewhat distorted image of the rat with its various parts related one to another in much the same way as in the actual animal" (Woolsey, 1952).

*First association of cytoarchitecture and vibrissae*

"The mouse then presents itself as a unique experimental animal, in which one may test the relations here suggested, since the vibrissae can be moved individually to excite more or less discretely the associated sensory endings and the glomeruli [barrels] can be probed with microelectrodes to record unit cellular discharges" (Woolsey, 1967).

*Functional organization of the cortex*

"The data reported in these papers support the view that there is an elementary unit of organization in the somatic cortex made up of a vertical group of cells extending through all the cellular layers. The neurons of such a group are related to the same, or nearly the same, peripheral receptive field upon the body surface" (Mountcastle, 1957).