



Segregation and Wiring in the Brain

Karl Zilles and Katrin Amunts

Science **335**, 1582 (2012);

DOI: 10.1126/science.1221366

This copy is for your personal, non-commercial use only.

If you wish to distribute this article to others, you can order high-quality copies for your colleagues, clients, or customers by [clicking here](#).

Permission to republish or repurpose articles or portions of articles can be obtained by following the guidelines [here](#).

The following resources related to this article are available online at www.sciencemag.org (this information is current as of April 2, 2012):

Updated information and services, including high-resolution figures, can be found in the online version of this article at:

<http://www.sciencemag.org/content/335/6076/1582.full.html>

A list of selected additional articles on the Science Web sites **related to this article** can be found at:

<http://www.sciencemag.org/content/335/6076/1582.full.html#related>

This article **cites 9 articles**, 3 of which can be accessed free:

<http://www.sciencemag.org/content/335/6076/1582.full.html#ref-list-1>

tion (5). Tracking is one solution, but raises ethical and privacy concerns (6). In equipping the person with a GPS unit—for example, embedded on a smart phone or a wearable wristwatch—models of their behavior can be constructed, deviations from which can lead to alarm generation. Crucially, the decision to activate an alarm can be made on the smart phone or wristwatch, thus removing the need for a centralized tracking approach. Hence, it is possible to balance the privacy of the person with dementia, their autonomy to make their own decisions, their own welfare, and the needs of their carers.

Proof-of-concept studies in these and many other domains, including offices, industry, transport, gaming, and e-commerce, demonstrate the potential of ambient intelligence. Indeed, increased awareness of energy issues suggests that the smart grid and energy efficiency (7) may become pioneering ambient intelligence services. Ultimately, researchers are envisioning “smart cities” (8) in which technologies such as ambient intelligence permeate all aspects of urban life. How can this potential be translated into a coherent vision and practical implementation, marked by scalability, robustness, and intelligence?

A key enabling technology is the Sensor Web (9), which envisages a network of sensors spatially distributed and embedded within the environment. However, a standardized approach is required to achieve interoperability between such physical sensor networks and the Web itself; in this way, seamless connectivity and usability will be achieved through a “Plug and Play” approach (10). The software required to achieve this, as well as being inherently distributed, must encapsulate robustness, scalability, and interoperability among others. Distributed Artificial Intelligence, specifically Intelligent Agents (11), is one mature software paradigm for delivering ambient intelligence.

A major constraint for the development of ambient intelligence systems will be how to power remote devices. Many embedded systems rely on battery or other finite power sources. Their life span may be weeks at most, frequently making ambient intelligence impractical. As the integration of low-power technologies into conventional consumer devices and ambient intelligence increases, energy harvesting from a variety of environmental sources will play a vital role in maintaining the long-term functioning of ambient intelligent environments (12). Sustainability or green computing precepts must also be factored into the design of ambient intelligence infrastructures. This

means that designers must plan for sustainable decommissioning, in much the same way that satellite engineers design satellites to burn on atmosphere reentry rather than being allowed to fall to Earth.

As ambient intelligence becomes mainstream, there is an urgent need for issues of security, privacy, and ethics to be brought to the public’s attention. One interesting legal proposal is that of ambient law (13). This argues that the freedoms that underpin constitutional democracy may be radically altered as ambient intelligence permeates everyday life. Such freedoms may be reinforced in some circumstances; in others, they may be destroyed. Avoiding the latter situation demands greater communication between lawyers and computer scientists, such that appropriate legal norms can be constructed and incorporated into the design and use of ambient intelligence.

References and Notes

1. D. J. Cook, *Science* **335**, 1579 (2012).
2. K. Kabassi, *Telemat. Inform.* **27**, 51 (2010).
3. See RUBICON, <http://fp7rubicon.eu>.
4. M. Reggente *et al.*, *Chem. Eng. Trans* **23**, 273 (2010).
5. J. D. Kasper, A. D. Shore, *J. Appl. Gerontol.* **13**, 371 (1994).
6. R. Landau, G. K. Auslander, S. Werner, N. Shoval, J. Heinek, *Qual. Health Res.* **20**, 409 (2010).
7. N. Gershenfeld, S. Samouhos, B. Nordman, *Science* **327**, 1086 (2010).
8. N. Streitz, in *Smart Cities, Ambient Intelligence and Universal Access*, C. Stephanidis, Ed. (Springer, Berlin/Heidelberg, 2011), pp. 425–432.
9. A. Sheth, C. Henson, S. S. Sahoo, *IEEE Internet Comput.* **12**, 78 (2008).
10. A. Bröring, P. Maué, K. Janowicz, D. Nüst, C. Malowski, *Sensors (Basel, Switzerland)* **11**, 7568 (2011).
11. K. A. De Jong, *Comput. Intell. Mag. IEEE* **3**, 12 (2008).
12. R. J. M. Vullers, R. V. Schaijk, H. J. Visser, J. Penders, C. V. Hoof, *Solid-State Circuits Mag.* **2**, 29 (2010).
13. M. Hildebrandt, in *Regulating Technologies*, R. Brownsword, K. Yeung, Eds. (Hart Publishing, Oxford, 2008), pp. 175–191.

10.1126/science.1217637

NEUROSCIENCE

Segregation and Wiring in the Brain

Karl Zilles^{1,2} and Katrin Amunts^{2,3}

Are there unifying principles behind the structural complexity of the cerebral cortex?

A mosaic of hundreds of interconnected and microscopically identifiable areas in the human cerebral cortex controls cognition, perception, and behavior. Each area covers up to 40 cm² of the cortical surface and consists of up to 750 million nerve cells (1). The architecture—the spatial distribution, density, size, and shape of nerve cells and their processes—varies between different cortical areas. Nerve cells are interconnected within each area and with other brain regions and the spinal cord via fiber tracts, synapses, transmitters, modulators, and receptors. This incredible structural complexity underlies the functional segregation in the cerebral cortex. The ultimate goal—to understand the driving forces and organizational principles of the human brain beyond the cellular and functional details—remains a challenge. Reports by Chen *et al.* (2) and Wedeen *et al.* (3) on pages 1634 and 1628 of

this issue, respectively, accept this challenge by analyzing the genetic topography of the cortex and the spatial course of fiber pathways in the brain. The studies find unifying hierarchical and geometric rules behind the organizational details.

In addition to classical cytoarchitectonics (the spatial organization of cellular composition) of the brain (4), the fields of cell biology, neuroimaging, neuroinformatics, and genetics have provided myriads of valuable data about the structure and function of the cerebral cortex. Only after the advent of modern genetics was it possible to identify the driving forces behind segmentation as an organizational principle of the vertebrate brain. However, a segmentation process in the cortex, similar to that seen in other brain regions and the spinal cord, does not seem likely because an overt segmental or metameric partitioning of the neocortex is not visible during embryogenesis (5). Instead, Chen *et al.* demonstrate a genetically controlled and hierarchically organized structural segregation in the human cortex.

Chen *et al.* investigated human brains by cortical surface reconstruction, advanced

¹University of Düsseldorf, 50001 Düsseldorf, Germany.

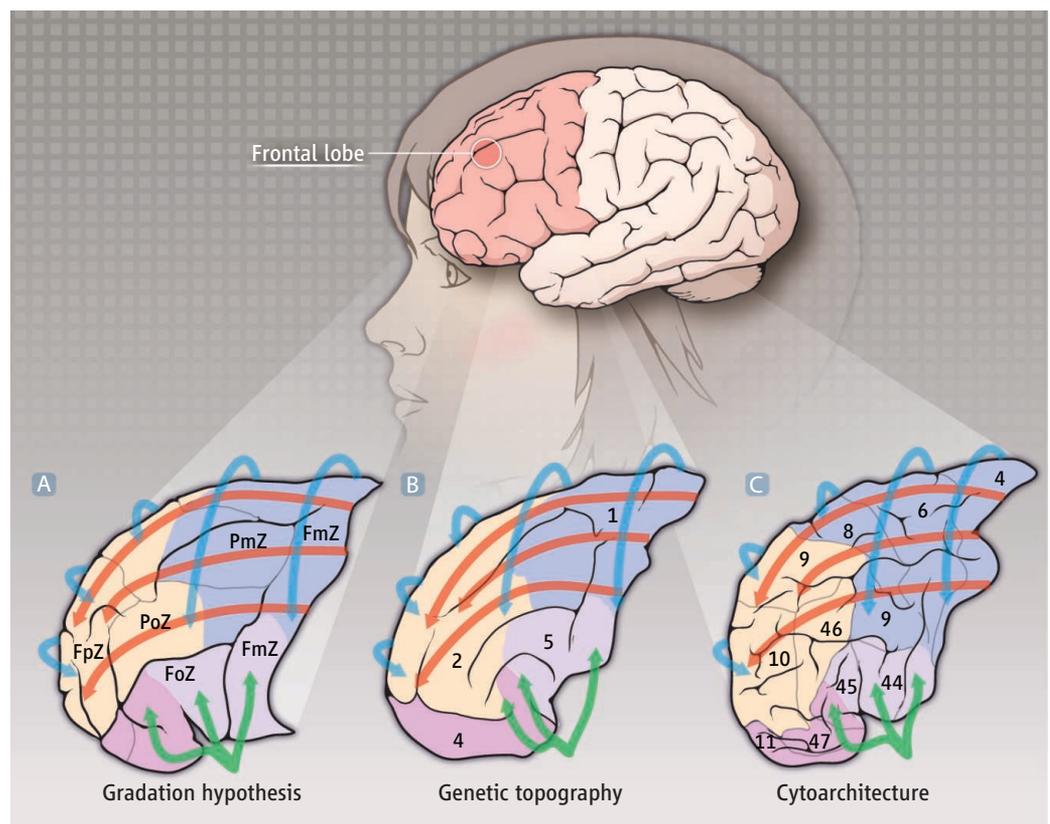
²Institute of Neuroscience and Medicine, Research Centre Jülich, 52425 Jülich, Germany.

³Department of Psychiatry, Psychotherapy and Psychosomatics, RWTH Aachen University, 52056 Aachen, Germany. E-mail: k.zilles@fz-juelich.de

atlas mapping, and genetic analyses. By comparing mono- and dizygotic twins, the authors calculated how shared genetics influence area expansion between cortical regions. A cluster analysis of this genetic topography was performed in the absence of predefined anatomical information. The authors could thus parcel the cortical surface area into 12 genetic regions. A possible correlation between this genetic topography and the cytoarchitecture of the cortex (6) may reveal rules behind the mosaic of cortical area. However, some genetically determined regions are very large, even crossing the borders of cytoarchitectonic areas and expanding into other lobes. For example, the occipital and inferior parietal clusters of Chen *et al.* comprise numerous cytoarchitectonic areas (7, 8).

Although there is mismatch in some details, this should not obscure an important commonality revealed between cytoarchitecture and genetic topography—hierarchical organization. Cytoarchitectonic maps reflect functional and molecular aspects of brain organization. The regional distributions of transmitter receptors (9), cell types (10), and connectivity (8), as well as the genetic topography determined by Chen *et al.*, are hierarchically organized. That is, cortical subdivisions are nested in a common superstructure and interrelated in a tree-like organization. They show different degrees of functional, molecular, or structural similarities. Hierarchical organization of the cortex is thus the unifying rule, which encompasses all scales from the molecular to the systems level.

The concept of hierarchy is reminiscent of an old but unfortunately forgotten finding (11–13): the gradation of architectonic features. This concept explains differences between cortical areas by a stepwise and directed architectonic differentiation of the neocortex. These developmental gradation streams follow non-Euclidean axes. The rostrocaudal axis is bent around the end of the lateral fissure; the other axes are orthogonal to it. In the frontal lobe (see the figure), gradation streams originate in the border regions of the insula, anterior cingulate gyrus, olfac-



Genetic topography, gradation, and cytoarchitecture. Regional organization of the human frontal lobe is shown according to the gradation hypothesis (A), genetic topography (B), and cytoarchitecture (C). Corresponding regions are highlighted with colors. Dark black lines represent sulci; thin gray lines mark boundaries of the zones. Blue, red, and green arrows label the architectonic gradation streams from the cingulate cortex, the central sulcus, and the insular cortex, respectively. Regions in (A): FmZ, frontomotoric zone; FoZ, fronto-opercular zone; FpZ, frontopolar zone; PmZ, paramotoric zone; PoZ, paraopercular zone. Regions in (B): 1, motor-premotor cluster; 2, dorsolateral-prefrontal cluster; 4, orbitofrontal cluster; 5, opercular-subcentral cluster. In (C), numerals indicate Brodmann areas (6) (regions defined according to the structure and organization of cells).

tory area, and central sulcus (13). These regions are phylogenetically old or are located in primary sulci (depressions or fissures in the surface of the brain). Along the gradation streams, the cellular composition and organization change stepwise according to the changing relationship between the sizes of layer V to layer III pyramidal cells in the cortex, along with the development of an inner granular cell layer IV. Thus, the gradation hypothesis describes a hierarchical rule behind the details of architectonic phenotypes. The results of Chen *et al.* suggest that the gradation topography principally corresponds to the genetic topography.

Previous studies of fiber tracts—bundles of nerve fibers—provided a wealth of detail about their spatial orientation in a highly descriptive, but not analytical way. Wedeen *et al.* propose a rectilinear, grid-like geometric organization of fiber pathways in human and nonhuman primate brains. Starting from major paths, the authors identified adjacent paths that cross the initial ones orthogonally.

The crossings form well-defined curved, two-dimensional sheets. The major longitudinal paths provide the long-range anatomical connectivity. The short U-fibers connect adjacent gyri (ridges on the cerebral cortex). As in the case of gradation streams, the three-dimensional grid of fiber tracts follows the three principal axes of growth direction during brain development (longitudinal, mediolateral, and dorsoventral). This organization may be achieved by chemotactic mechanisms of neuronal path finding and incremental rewiring.

Wedeen *et al.* also used the Frobenius theorem from differential geometry to support their argument for the formation of geometric spatial organization of fiber paths. At present it is difficult to decide whether three chemotactic gradients are the basis for the three families of vector fields observed by the authors, and whether other constraints of this theorem are fulfilled. If this “three-families hypothesis” as geometric principle holds true, procedures to map neural fiber

tracts can be constrained, which might make it easier to avoid the limitations of current algorithms and to validate different tracking techniques (across scales, across subjects, across species, etc.).

A common view that arises from the studies of both Chen *et al.* and Wedeen *et al.* is the idea of the brain as a regionally highly differentiated, but hierarchically and geometrically organized, spatial structure. Detailed aspects of this “canonical brain organization” can be modified by environmental conditions including pathology and genetic diversity. Mathematical methods such as hierarchical

clustering and differential geometry can help us to understand the principles behind variable phenotypes and to guide the development of a realistic brain model.

References

1. S. M. Blinkov, I. I. Glezer, *The Human Brain in Figures and Tables: A Quantitative Handbook* (Basic Books, New York, 1986).
2. C.-H. Chen *et al.*, *Science* **335**, 1634 (2012).
3. V. J. Wedeen *et al.*, *Science* **335**, 1628 (2012).
4. K. Zilles, K. Amunts, *Nat. Rev. Neurosci.* **11**, 139 (2010).
5. H. Kuhlenbeck, *The Central Nervous System of Vertebrates: Overall Morphologic Pattern* (Karger, Basel, ed. 3, 1973).
6. K. Brodmann, *Vergleichende Lokalisationslehre der Großhirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues* (Barth, Leipzig, 1909).
7. K. Zilles, K. Amunts, in *The Human Nervous System*, J. K. Mai, G. Paxinos, Eds. (Elsevier, San Diego, 2012), pp. 826–885.
8. D. J. Felleman, D. C. Van Essen, *Cereb. Cortex* **1**, 1 (1991).
9. K. Zilles, K. Amunts, *Curr. Opin. Neurol.* **22**, 331 (2009).
10. K. Amunts, A. Schleicher, K. Zilles, *Neuroimage* **37**, 1061, discussion 1066 (2007).
11. O. Vogt, *J. Psychol. Neurol.* **15**, 221 (1910).
12. H. Brockhaus, *J. Psychol. Neurol.* **49**, 249 (1940).
13. F. Sanides, *J. Hirnforsch.* **6**, 269 (1964).

10.1126/science.1221366

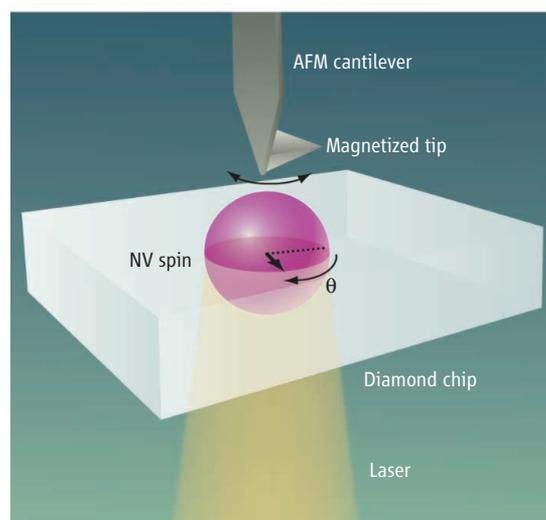
PHYSICS

A Single Spin Feels the Vibrations

Philipp Treutlein

Mechanical resonators find widespread applications as precision force sensors, the most prominent example being the atomic force microscope (AFM). Coupling the vibrations of a mechanical resonator to a fully controlled, microscopic quantum system such as a single spin presents a strategy for detecting and even controlling mechanical vibrations in the quantum regime. The resulting hybrid quantum system would offer new perspectives for precision force sensing and tests of quantum mechanics on a macroscopic scale. On page 1603 of this issue, Kolkowitz *et al.* (1) have taken a first step toward such coupled spin-resonator systems by using a single electronic spin to sense mechanical vibrations of an AFM cantilever with a magnetic tip.

Observing and manipulating quantum behavior of mechanical objects is a goal currently being pursued through several different experimental approaches (2). Although quantum-level control over mechanical vibrations is routinely achieved for atomic-scale objects such as trapped ultracold atoms and ions (3), achieving a similar level of control over microstructured mechanical resonators such as cantilevers, beams, and membranes is far more challenging. Observing quantum behavior with a mechanical resonator that is visible to the naked eye, such as an AFM cantilever, would not only be a beautiful confirmation of quantum theory but may also lead to novel applications in precision force sensing (4).



In order to observe quantum behavior, the resonator must be cooled to sufficiently low temperatures to avoid thermally excited vibrations. Equally important, tools are needed to read out the resonator and to determine and possibly even control its quantum state. One strategy is to couple the mechanical resonator to a microscopic quantum system, ideally a single two-level system (a “qubit”) that can be fully controlled quantum mechanically and can be read out efficiently. In a recent landmark experiment (5), a superconducting phase qubit was coupled to an internal mechanical vibration of a piezoelectric resonator at millikelvin temperatures and used for preparation and detection of nonclassical quantum states. The coherence lifetimes of the qubit and resonator quantum states were in the nanosecond range, and it

The vibrations of a cantilever with a magnetic tip can be detected by changes in the electronic spin state of a defect embedded in a nearby diamond surface.

Spin flips in sync with vibrations. A single spin in a diamond crystal can be used to read out the vibrations of an AFM cantilever. The magnetized cantilever tip induces a coupling between the cantilever vibrations and the spin resulting in a spin rotation by an angle θ . The quantum state of the spin is subsequently detected with a laser.

is desirable to achieve similar control in other systems with longer coherence lifetimes. Moreover, from a standpoint of applications in force sensing, it is important to achieve quantum-level control over the fundamental center-of-mass vibration of a cantilever resonator, as used in an AFM. A number

of different qubit-cantilever systems are currently being investigated for this purpose, involving systems from solid-state physics (6) as well as ultracold atoms and ions (7).

The spin of a single nitrogen vacancy (NV) center in diamond—the qubit system used by Kolkowitz *et al.*—is very promising. Its quantum state can be initialized and read out optically, it can be manipulated by applying microwave radiation, and it shows remarkably long coherence times—up to a few milliseconds even at room temperature (8). The spin can be coupled to the vibrations of a cantilever (9) by attaching a tiny magnet to the cantilever tip and positioning it near the diamond surface (see the figure). The strong magnetic field gradient that is produced translates the vibrations of the cantilever into an oscillating magnetic field, which couples

Department of Physics, University of Basel, Basel, Switzerland. E-mail: philipp.treutlein@unibas.ch