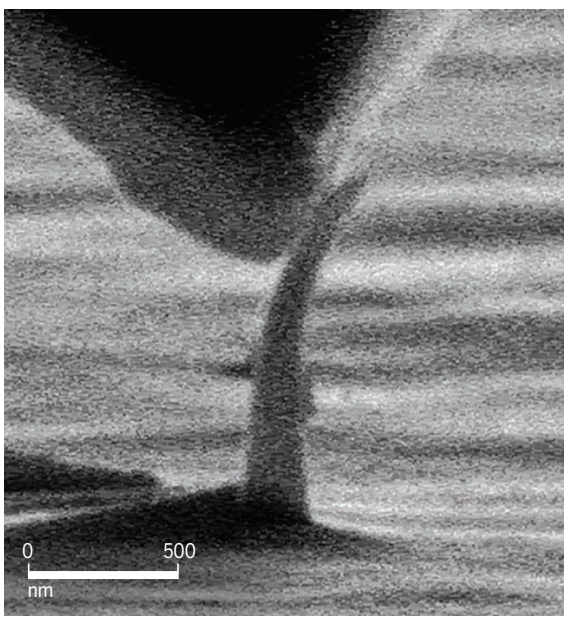
phene (see the figure). Thus, the strength of bulk diamond, which has sp^3 bonds, is equivalent to that reported for carbon nanotubes and graphene with sp^2 bonds.

The authors applied these large elastic strains by bending the nanoneedles (see the image); fracture was not triggered at smaller strains because of the small volume of the nanoscale needles, the paucity of defects, and the smoothness of the surface, which was produced with careful reactive ion etching from a <111>-oriented diamond film produced by means of chemical vapor deposition. Fracture occurred through cleavage along (111) planes, and the strength measured was supported by combined density-functional and molecular-dynamics simulations at 300 K. The latter predicted a maximum critical strain of 13%, corresponding to a tensile strength of 130 GPa.



A nanoindenter tip bends a diamond nanoneedle.

These results open the possibility of modifying fundamental properties of diamond through elastic strain engineering (*9*). The properties of any crystalline material depend on the lattice parameters, which are dictated by the electronic structure. Large elastic deformations (around 10%) modify the electronic structure, leading to changes in electronic, magnetic, catalytic, and other properties that could be tuned as a function of the applied strain tensor. This concept has been used to enhance the drive current in complementary metal-oxide semiconductor technology by improving the electron and hole mobility through lattice straining (*10*). Other applications include the transformation of paramagnetic materials into ferromagnetic ones (*11*) and the manipulation of mechanochemical coupling so as to increase catalytic activity (*12*).

However, the elastic strains applied to modify the properties in all these cases were much lower (below 5%) than those reported for carbon nanotubes, graphene, and diamond needles, which were closer to 10%. Changes in properties should increase with the elastic strain and, as postulated by Gilman (*13*), the electronic structure should be drastically modified near the critical bond-breaking strain, leading to unusual or singular chemical and physical properties. Thus, exploration of the effect of very large elastic strains on the properties of crystalline solids may lead to the discovery of new or unexpected behaviors.

Many applications of elastic strain engineering require the elastic strains to be distributed over a substantial area or volume. This can be achieved by means of epitaxial growth (*10*) or severe plastic deformation (*11*) in the case of bulk materials. However, this task is more challenging in the case of nanoscale objects because it is difficult to maintain the mechanical continuity between these objects. For instance, the maximum strengths reported for carbon nanotube fibers, which are made up of bundles of nanotubes, are ~2.5 GPa, which is well below the values reported for single carbon nanotubes (see the figure) (*14*–*15*). Elastic straining techniques that can be applied to bulk materials, such as the elastic bending of nanoneedles in Banerjee *et al.*, can potentially be extended to large surfaces and different materials. Thus, this strategy can be used to explore the effect of large elastic strains on chemical and physical properties of diamond and other solids. ■

PHOTO: A. BANERJEE *ET AL.*

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NEUROSCIENCE

Whispering neurons fuel cortical highways

Synaptic communication accelerates neuronal migration in the developing brain

By **Alejandro F. Schinder**[1] *and* **Guillermo M. Lanuza**[2]

The mammalian neocortex is one of the most intricate entities found in nature, both in terms of structure and function. It is the brain region responsible for the execution of high-order functions, including sensory perception, motor control, cognition, and speech. Its development is equally complex because it requires that millions to billions (depending on the species) of neurons assemble in distinct layers and connect with exquisite precision to perform complicated information processing operations. During embryonic development, formation of the cerebral cortex involves the migration of excitatory neurons generated in the ventricular zone toward the cortical plate, where they establish their final position in six well-defined horizontal layers consisting of different types of neurons and architecture. Along this migratory phase, developing neurons undergo a morphological transition from multipolar shape to bipolar morphology. Bipolar neurons exhibit faster locomotion, quickly reaching their final destination. On page 313 of this issue, Ohtaka-Maruyama *et al.* (*1*) reveal that this important switch to bipolar neurons is influenced by glutamate release from neurons located at the subplate, just beneath the cortical plate. Subplate neurons trigger this transformation by making transient synaptic contacts with multipolar neurons in transit to the corti-

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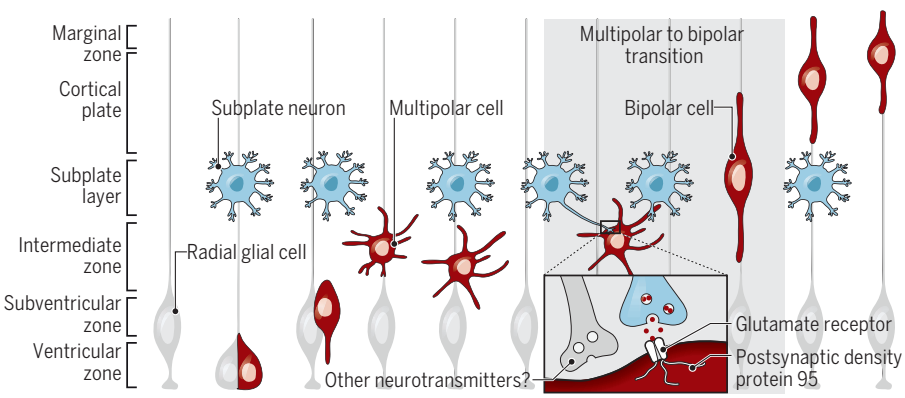
cal laminae. Understanding this process is important because disruption of neocortical migration results in several human neurodevelopmental diseases.

During cortical development, excitatory neurons are derived from radial glial cells located at the ventricular zone (*2*–*4*) (see the figure). The earlier-born neurons form the preplate, which later splits into the more superficial marginal zone and the deeper subplate (SP). The cortical plate then emerges in between these two layers, fueled by the accumulation of neurons migrating from the ventricular zone. Layers are established by the subsequent addition of neurons migrating in an inside-out manner; the most recently generated neurons migrate through older cells toward the marginal zone, giving rise to the neocortex (*3*–*5*). Consequently, the deeper layers are built early and the superficial layers arise toward the end of cortical development.

The migratory journey of cortical neurons

During the multipolar stage at the intermediate zone, neurons receive transient glutamatergic synaptic inputs from subplate neurons, which influence their conversion into fast-locomoting bipolar neurons that ultimately form the cortical layer.



Developing neurons undergo a series of choices regarding their specification (what type of neuron?), migration (what cortical layer?), growth (where to project dendrites and axon?), and selection of their synaptic partners (input and output cells). These choices are made according to a combination of intrinsic programs and extrinsic signaling (*3*–*5*). Cortical lamination involves the formation of transient cell layers that direct the migration and connectivity of new neurons and disappear in the mature brain. The SP is an early transient layer, consisting of heterogeneous neuronal populations exhibiting mature morphological and functional properties (*6*). SP neurons receive functional inputs from thalamic projections and are also connected among themselves and with other cortical neurons through chemical and electrical synapses. Activity of the SP network is relevant for guiding the growth of thalamic axons toward cortical layer IV and for the maturation of excitatory pyramidal cells in that layer (*7*, *8*). Because new neurons navigate across the SP to reach the cortical plate, Ohtaka-Maruyama *et al.* examined whether SP neurons might influence radial migration.

The process of radial migration (*2*, *5*, *9*) is characterized by three phases: Multipolar neurons move slowly, in a winding manner, almost pausing at the intermediate zone before reaching the SP; stalling neurons convert to bipolar morphology; bipolar neurons migrate at faster speed along radial glial fibers through the cortical plate, until reaching their final cortical lamina (see the figure). The authors characterized neuronal migration in brain slices obtained from mouse embryos. The use of fluorescence microscopy techniques revealed that SP neurons project axons toward the intermediate zone. Some of those axons express the vesicular glutamate transporter VGLUT2 and contact multipolar neurons, which suggests that they might form glutamatergic synapses. Further analyses revealed that highly active synapses form in the area where SP axons mingle with multipolar cells. Such activity is likely driven by excitatory thalamocortical projections that directly activate SP networks (*6*, *7*). The authors showed that neuronal migration is halted when electrical activity in SP neurons is reduced or when synaptic release from their axons is blocked. Together, these results suggest that the switch from multipolar cells to bipolar, fast-migrating neurons requires glutamate release from SP neurons, consistent with the role of glutamatergic signaling in neuronal migration during brain development (*10*).

However, it is also conceivable that additional players contribute to radial migration in a manner that relies on synaptic communication. Electron microscopy revealed contacts with heterogeneous structure formed onto multipolar cells. Those synapse-like structures do not resemble canonical glutamatergic synapses (*11*): Most terminals lacked synaptic vesicles, with these seeming to be present in low numbers and in only 20 to 30% of presynaptic terminals; synaptic shape was irregular and bearing atypical ultrastructural morphology. These features might allow multipolar cells to respond to the transient nature of the putative glutamatergic synapses, but this view prompts additional questions regarding the activity-dependent control of radial migration. Is glutamate the main trigger for the switch? Do multipolar cells integrate signals arising from additional neurotransmitters, such as γ-aminobutyric acid (GABA), exerting depolarizing effects that commonly promote neuronal maturation (*12*)? Do multipolar cells receive synaptic signals from other neuronal populations within or outside the developing cortex? It will also be critical to interrogate the mechanisms that link synaptic activity to cytoskeletal reorganization, which ultimately executes the multipolar to bipolar transformation (*13*, *14*).

The experimental approach used by Ohtaka-Maruyama *et al.* bears the potential to explore structure and function of synaptic connections between the SP network and multipolar cells in depth. For instance, optogenetic and electrophysiological recordings would readily allow combining the restricted and specific stimulation of SP neuron terminals with recordings of postsynaptic responses in multipolar cells to unambiguously establish the nature of the chemical and electrical synapses that influence neuronal migration. Ultimately, it will be crucial to develop complete loss-of-function models to unearth the extent to which neurotransmitter release from SP neurons shapes the rules of cell migration and stratification in the mammalian neocortex. ■

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