2. Robinson, G.E. (1992). Regulation of division of labor in insect societies. Ann. Rev. Entomol. *37*, 637–665.
3. Page, R.E., and Erber, J. (2002). Levels of behavioral organization and the evolution of division of labor. Naturwissenschaften *89*, 91–106.
4. Hughes, W.O.H., Sumner, S., van Borm, S., and Boomsma, J.J. (2003). Worker caste polymorphism has a genetic basis in *Acromyrmex* leaf-cutting ants. Proc. Natl. Acad. Sci. USA *100*, 9393–9397.
5. Fewell, J.H., and Page, R.E. (2000). Colony level selection effects on individual and colony foraging task performance in honey bees, *Apis mellifera L*. Behav. Ecol. Sociobiol. *48*, 173–181.
6. Jones, J.C., Myerscough, M.R., Graham, S., and Oldroyd, B.P. (2004). Honey bee nest thermoregulation: diversity promotes stability. Science *305*, 402–404.
7. Ben-Shahar, Y., Robichon, A., Sokolowski, M.B., and Robinson, G.E. (2002). Influence of gene action across different time scales on behavior. Science *296*, 741–744.
8. Robinson, G.E., Grozinger, C.M., and Whitfield, C.W. (2005). Sociogenomics: social life in molecular terms. Nat. Rev. Genet. *6*, 257–270.
9. Ingram, K.K., Oefner, P., and Gordon, D.M. (2005). Task-specific expression of the foraging gene in harvester ants. Mol. Ecol. *14*, 813–818.
10. Ravary, F., Lecoutey, E., Kaminski, G., Châline, N., and Jaisson, P. (2007). Individual experience alone can generate lasting division of labor in ants. Curr. Biol. *17*, 1308–1312.
11. Dupuy, F., Sandoz, J.-C., Giurfa, M., and Josens, R. (2006). Individual olfactory learning in *Camponotus* ants. Anim. Behav. *72*, 1081–1091.
12. Dreier, S., van Zweden, J.S., and D'Ettorre, P. (2007). Long term memory of individual identity in ant queens. Biol. Lett., doi:10.1098/rsbl.2007.0224.
13. Menzel, R., and Giurfa, M. (2001). Cognitive architecture of a mini-brain: the honeybee. Trends Cogn. Sci. *5*, 62–71.
14. Menzel, R., and Giurfa, M. (2006). Dimensions of cognition in an insect, the honeybee. Behav. Cogn. Neurosci. Rev. *5*, 24–40.
15. Menzel, R. (1999). Memory dynamics in the honeybee. J. Comp. Physiol. A *185*, 323–340.
16. Deneubourg, J.L., Goss, S., Pasteels, J.M., Fresneau, D., and Lachaud, J.P. (1987). Selforganization mechanisms in ant societies. II. Learning in foraging and division of labor. In From Individual to Collective Behavior in Social Insects, J.M. Pasteels and J.L. Deneubourg, eds. (Basel: Birkhauser), pp. 177–196.
17. Theraulaz, G., Bonabeau, E., and Deneubourg, J.-L. (1998). Response threshold reinforcements and division of labour in insect societies. Proc. R. Soc. Lond. B *265*, 327–332.

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Brain Science: From the Very Small to the Very Large

We still lack a clear understanding of how brain imaging signals relate to neuronal activity. Recent work shows that the simultaneous activity of neuronal ensembles strongly correlates with local field potentials and imaging measurements.

Gabriel Kreiman

As in other areas of science, in brain research our understanding of the underlying processes is significantly constrained by what we can measure. A host of different techniques is available to the aficionados in neuroscience, ranging all the way from X-ray crystallography of specific ion channels all the way to measurements of behavioral performance of the whole organism. At the level of single neurons or populations of single neurons, the gold standard for systems neuroscience, most of our knowledge comes from studies in animal models. Measurements of brain activity in the human brain usually come from low-resolution tools including functional imaging. The non-invasive nature of these imaging tools has allowed a generation of cognitive scientists to venture into the brain.

How to interpret the signals derived from functional imaging measurements has been a major challenge, given that they are only indirectly related to neuronal activity. Brain activity requires energy and, consequently, blood flow changes following activity modulation in a given brain region. The paramagnetic nature of oxygen bound to hemoglobin allows the use of magnetic resonance imaging to measure the slow changes in blood flow. How do these blood flow changes relate to the underlying neuronal activity? Major progress towards understanding the relationship between blood flow and neuronal activity has come from simultaneous measurements of neuronal spiking activity, local field potentials (LFPs, which measure the responses of a large ensemble of neurons), and blood oxygen level dependent (BOLD) signals in functional magnetic resonance imaging (fMRI) experiments [1,2].

These landmark studies showed that LFPs correlate better with BOLD measurements than do spikes (see also [3,4]). This has led to the (oversimplified) notion that BOLD measurements represent an aggregate measure of local processing plus input signals, whereas spiking signals constitute the actual output of a given brain area. These observations have also reignited the general interest in understanding LFPs and their relationship with spiking activity (for example [5–8]).

In general, the conclusions from many functional imaging studies have been concordant with knowledge derived from single neuron measurements (for example [9,10]). Moreover, a recent study [11] has shown that fMRI can successfully select a brain area in monkeys for subsequent electrophysiological scrutiny. However, the results obtained in different experimental paradigms have not always been consistent — ranging from claims of high correlation between spikes and BOLD to reports of markedly reduced correlations and different conclusions (for example [12]).

It is possible, in a unique experimental setting, to monitor the activity of single neurons as well as LFPs in the human brain [13]. This type of recording can be done in human epileptic patients who are monitored using depth electrodes to map the areas responsible for seizure onset.

Patients typically remain in the hospital for a period of about one week. During this week, the patients can perform cognitive tasks while researchers examine brain activation at high resolution. As they recently reported in *Current Biology*, Nir *et al.* [14] took advantage of this opportunity to directly examine human physiological activity by comparing intracranial recordings in epileptic patients with the fMRI activity in human auditory cortex of non-epileptic subjects.

Recent work has shown that there is a strong match in human auditory cortex between spiking activity in a local population of neurons, LFPs and BOLD measurements [15]. While the patients studied by Nir *et al.* [14] watched a movie, the audio-visual stimulation elicited strong and reproducible changes in auditory cortex activation at the spike, LFP and fMRI levels (similar observations have been made for intracranial electroencephalogram data in the visual cortex [16]). Additionally, there was a strong correlation between the spike rates and the power in the high-frequency gamma band of the LFP signal. Whether these changes and coupling represent sensory responses to the stimuli, attentional changes, memory processes or other possibilities remains unclear.

Because Nir *et al.* [14] simultaneously recorded activity from multiple electrodes, they could ask whether the observed coupling between spiking activity and gamma LFP was related to the correlations in neuronal firing. There was a high level of variability in the coupling between individual neurons and the LFP. Notably, this variability could be explained by correlations between neighboring spiking neurons. Periods that showed strong coupling between the spiking activity and the LFP also showed stronger correlations between the neuron and its neighbors over timescales of several hundred milliseconds (not to be confused with precise synchronization at the millisecond level).

Moving upward in spatial scale, Nir *et al.* [14] pondered whether there is a relationship between neural signals and fMRI measurements. They filtered the electrical signals with a fixed hemodynamic function that aims to capture the differences in temporal scales between these signals. The power in the gamma band of the LFP showed a strong correlation with the BOLD measurements, as previously reported [2,15]. Expanding on previous work, the correlation between the spiking activities of single neurons and BOLD was highly variable during the presentation of the movie. Several experimental observations and theoretical models have suggested that the synchronous firing among neurons could play a crucial role in conveying information within and across brain areas (for example [8,17–19]). Nir *et al.* [14] therefore hypothesized that the changes in how well single neuron responses accounted for BOLD measurements may be due to the level of simultaneous firing in an ensemble of neurons. To test this hypothesis, they computed the firing correlations among single neurons in windows of hundreds of milliseconds. Interestingly, those periods where BOLD signals better reflected the single neuron activity also showed high levels of correlation among neurons in the population. This finding can be illustrated through a chorus metaphor: consider the recorded neuron as a singer in a chorus during a concert. Whenever the recorded neuron has a ‘solo’ part, its activity becomes decoupled from both the BOLD and the gamma power LFP. Whenever the neuron ‘sings along’ with the rest of the chorus, there is a high correlation between the neuron’s spiking activity and the more global BOLD and gamma power LFP.

It is tempting to speculate that both BOLD signals and the gamma band of the LFPs represent a temporally and spatially low-pass filtered version of the ensemble spiking activity in a population. The degree of coupling between spikes, LFPs and BOLD may be dependent on the specific architecture of the brain circuitry since medial temporal lobe areas show lower correlation among neighboring neurons [20]. The relationship between spikes, LFPs and BOLD signals observed in [14] may therefore rely on the strong topography present in neocortical structures. Using the chorus metaphor: whether a chorus in a cortical region is oriented towards collective ‘singing’ or to solo performances will have a strong impact in the extent of the coupling between single neuron, LFPs and BOLD measurements.

Relating theories and measurements across widely different scales constitutes a fascinating question in multiple disciplines ranging from physics to biology. It is therefore not surprising that understanding the relationship between the spiking activity of small neuronal ensembles and large brain circuits constitutes a key challenge for systems neuroscience. Making progress to solve this challenge will require the careful interplay of theoretical models with experimental tools that survey different scales and different species. The fascinating possibility of monitoring human brain activity at high resolution provides a unique opportunity to shed light on this question.

References

1. Logothetis, N., Pauls, J., Augath, M., Trinath, T., and Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. Nature *412*, 150–157.
2. Logothetis, N.K. (2002). The neural basis of the blood-oxygen-level-dependent functional magnetic resonance imaging signal. Philos. Trans. R. Soc. Lond. B *357*, 1003–1037.
3. Kayser, C., Kim, M., Ugurbil, K., Kim, D.S., and Konig, P. (2004). A comparison of hemodynamic and neural responses in cat visual cortex using complex stimuli. Cereb. Cortex *14*, 881–891.
4. Mathiesen, C., Caesar, K., and Lauritzen, M. (2000). Temporal coupling between neuronal activity and blood flow in rat cerebellar cortex as indicated by field potential analysis. J. Physiol. *523*, 235–246.
5. Kreiman, G., Hung, C., Quian Quiroga, R., Kraskov, A., Poggio, T., and DiCarlo, J. (2006). Object selectivity of local field potentials and spikes in the inferior temporal cortex of macaque monkeys. Neuron *49*, 433–445.
6. Bedard, C., Kroger, H., and Destexhe, A. (2004). Modeling extracellular field potentials and the frequency-filtering properties of extracellular space. Biophys. J. *86*, 1829–1842.
7. Pesaran, B., Pezaris, J., Sahani, M., Mitra, P., and Andersen, R. (2002). Temporal structure in neuronal activity during working memory in macaque parietal cortex. Nat. Neurosci. *5*, 805–811.

8. Bichot, N.P., Rossi, A.F., and Desimone, R. (2005). Parallel and serial neural mechanisms for visual search in macaque area V4. Science *308*, 529–534.
9. Rees, G., Friston, K., and Koch, C. (2000). A direct quantitative relationship between the functional properties of human and macaque V5. Nat. Neurosci. *3*, 716–723.
10. Grill-Spector, K., and Malach, R. (2004). The human visual cortex. Annu. Rev. Neurosci. *27*, 649–677.
11. Tsao, D.Y., Freiwald, W.A., Tootell, R.B., and Livingstone, M.S. (2006). A cortical region consisting entirely of face-selective cells. Science *311*, 670–674.
12. Blake, R., and Logothetis, N. (2002). Visual competition. Nat. Rev. Neurosci. *3*, 13–21.
13. Engel, A.K., Moll, C.K., Fried, I., and Ojemann, G.A. (2005). Invasive recordings from the human brain: clinical insights and beyond. Nat. Rev. Neurosci. *6*, 35–47.
14. Nir, Y., Fisch, L., Mukamel, R., Gelbard-Sagiv, H., Arieli, A., Fried, I., and Malach, R. (2007). Coupling between neuronal firing rate, gamma LFP, and BOLD fMRI is related to inter-neuronal correlations. Curr. Biol. *17*, 1275–1285.
15. Mukamel, R., Gelbard, H., Arieli, A., Hasson, U., Fried, I., and Malach, R. (2005). Coupling between neuronal firing, field potentials, and FMRI in human auditory cortex. Science *309*, 951–954.
16. Privman, E., Nir, Y., Kramer, U., Kipervasser, S., Andelman, F., Neufeld, M., Mukamel, R., Yeshurun, Y., Fried, I., and Malach, R. (2007). Enhanced category tuning revealed by iEEG in high order human visual areas. J. Neurosci. *6*, 6234–6242.
17. Niebur, E., and Koch, C. (1994). A model for the neuronal implementation of selective visual attention based on temporal correlation among neurons. J. Comput. Neurosci. *1*, 141–158.
18. Salinas, E., and Sejnowski, T.J. (2001). Correlated neuronal activity and the flow of neural information. Nat. Rev. Neurosci. *2*, 539–550.
19. Engel, A., and Singer, W. (2001). Temporal binding and the neural correlates of sensory awareness. Trends Cogn. Sci. *5*, 16–25.
20. Ekstrom, A., Viskontas, I., Kahana, M., Jacobs, J., Upchurch, K., Bookheimer, S., and Fried, I. (2007). Contrasting roles of neural firing rate and local field potentials in human memory. Hippocampus, in press.

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Centrioles: Duplicating Precariously

To assemble a mitotic spindle and accurately segregate chromosomes to progeny, a cell needs to precisely regulate its centrosome number, a feat largely accomplished through the tight control of centriole duplication. Recent work showing that the overexpression of centriolar proteins can lead to the formation of multiple centrioles in the absence of pre-existing centrioles challenges the idea that it is a self-replicating organelle.

Laurence Pelletier

The centrosome is the primary microtubule-organizing center of the cell. At its core lies a pair of barrel-shaped structures of ninefold symmetry termed centrioles, which play a key role in the organization of centrosomes and in templating the assembly of flagella and cilia. In interphase cells, the centrosome participates in a range of functions, including signaling, cytoskeletal organization and cell motility. During mitosis, two centrosomes are needed to correctly organize the mitotic spindle and to accurately segregate chromosomes. Failure to properly regulate the number of centrosomes can lead to the formation of monopolar or multipolar spindles, conditions often associated with aneuploidy, a hallmark of cancer cells (Figure 1) [1]. It is therefore imperative that the single interphase centrosome duplicates once and only once per cell cycle, a process largely regulated through the tight control of centriole duplication.

The characteristic orthogonal arrangement of centrioles within the centrosome has led to the proposal that, much akin to DNA replication, the mother centriole acts as a template for the assembly of a daughter centriole during duplication (Figure 2). For this reason, nucleic acids have long been thought to be embedded within centrioles to instruct the assembly of another centriole. This idea was recently rejuvenated from work in the surf clam that led to the identification of specific RNA molecules enriched at centrosomes [2]. Interestingly, centrioles can also form *de novo* during normal development or when centrioles are destroyed via laser ablation challenging the idea that pre-existing centrioles are needed for the assembly of new centrioles [3]. Regardless, the mechanisms that orchestrate centriole duplication and assembly as well as the mechanisms that regulate the number of centrioles per cell have remained elusive.

Work from many laboratories recently culminated in a molecular and structural understanding of daughter centriole assembly in *Caenorhabditis elegans*. It was shown using a combination of RNA interference, epistatic protein recruitment assays and electron tomography that the SPD-2 protein acts upstream in this pathway by recruiting the ZYG-1 kinase to the site of daughter centriole assembly. This process then leads to the recruitment of SAS-5 and SAS-6, two coiled-coil proteins necessary for central tube formation. Another coiled-coil protein, SAS-4, is later required upon elongation of this central tube for the assembly of the symmetric array of singlet microtubules [4,5].

How conserved is this assembly pathway in other organisms and how does it relate to the control of centriole duplication? Sequence homologues of *C. elegans* SPD-2 have been identified in flies (CG15524) and mammals (hSPD-2/Cep192) and it has been proposed that the Polo kinase family member SAK/PLK-4, which is necessary for centriole duplication in mammals and flies, is related to ZYG-1 [6–8]. It was elegantly shown that the *Drosophila* homologue of SAS-4 localized to centrioles and was required for centriole duplication, with the mammalian homologue