letters to the editor

artifacts. The absence of gravity and activation-dependent stiffness in my model are discussed at length, without any explanation as to why adding them should change the results. Unlike hand acceleration, which is time-varying, the gravitational force is roughly constant for small variations in limb configuration. Therefore, its effect is absorbed in the baseline (defined as postural activity in the center of the workspace). The constant stiffness approximation is reasonable once a certain activation level is reached[11]. It is true that setting stiffness to zero abolishes the time lag–curvature effect; however, that point is irrelevant—whether or not muscle stiffness is constant, it certainly exists and there is no justification for setting it to zero. To compensate for muscle stiffness, M1 cells have to exhibit well-documented positional gradients—which, in combination with the acceleration term, produce the negative time lag–curvature relationship[1].

Moran and Schwartz have only shown that my model is approximate—which is very different from being "flawed." Still, is it possible that the results are an artifact of the approximation, for reasons that these authors did not identify? To assess the sensitivity to previously unmodeled details, I repeated the analysis using a state-of-the-art muscle model[12] (http://www.nature.com/neuro/web_specials/). Muscle force was expressed as a complex function of muscle length, velocity and stimulation frequency; this function depends on 19 experimentally derived parameters and incorporates numerous results from muscle physiology[12]. For a wide range of parameters, the predicted relationship between PV time lag and path curvature was quantitatively similar to the original result[1] as well as to the experimental data[2,3]. Thus, when Moran and Schwartz wrote that my model "is not consistent with basic physiology, excludes important phenomena, and violates inherent assumptions," their concerns were misplaced.

REPLY TO GEORGOPOULOS AND ASHE—In their letter, Georgopoulos and Ashe address the issue of whether data preprocessing affects M1 cell classification. Their results do not refute my main point[1], which is that previous classification procedures[5,13] can be seriously biased—with or without data preprocessing. Here I focus on the procedure[5] for classifying cells as direction- (D), position- (P), velocity- (V) or acceleration-related (A) according to the largest R^2.

By definition, the bias of a statistical estimator is the expected difference between the correct and estimated values of a given parameter. The identical percentages found by Georgopoulos and Ashe with and without data preprocessing only prove that, for this particular dataset, the bias is equal in both cases. The value of this bias cannot be inferred from their results (or anything else computed on real data), because the correct answer is unknown. In the absence of analytical insight, the only way to identify the bias of an estimator is to apply it to synthetic datasets where the correct answer is known. When applied to synthetic data[1] with no separate directional component, the above classification procedure finds D 43%, V 39%, P 16%, A 2% on smoothed square-root-transformed spike trains, and D 26%, V 56%, P 16%, A 2% on raw binned spike trains (different from continuous mean firing rates which were labelled MFR previously[1]). The effects of the data transformation (8% on average) are to be expected in general, and could exist in other datasets. With or without the transformation, the above percentages are very far from the correct answer: D 0%, V 49%, P 46%, A 5%—that is, the classification procedure itself is biased. Thus the burden of proof lies on Georgopoulos and Ashe. Unless they identify the exact conditions under which their procedure is unbiased, and ascertain by independent means that these conditions hold for the M1 population, their results remain hard to interpret.

To gain more insight into why the R^2 classification procedure fails, I analyzed the family of synthetic responses misclassified as directional (http://www.nature.com/neuro/web_specials/). These responses do not look directional: the temporal fluctuations of the underlying position, velocity and acceleration terms do not cancel out. The artificially created 'directional' region of parameter space is centered at the point where the correct classification boundaries meet. Therfore responses are misclassified as directional just because they do not fit well in the other categories. It would be interesting to re-analyze the data of Georgopoulos and Ashe for that possibility. Do responses labeled as directional vary only with movement direction and contain no systematic temporal fluctuations (which is how a truly directional cell should behave), or do they fluctuate over time in ways that do not happen to fit in any of the alternative categories? The latter type of response is more properly labeled 'unknown' rather than 'directional.'

Finally, this debate obscures a more fundamental problem[1,14] with M1 cell classification, a problem that remains even if unbiased procedures are developed. The different components of the cell response are not fixed, but instead increase monotonically with the magnitude of the corresponding kinematic and kinetic terms. Thus a cell classified in one task as 'velocity-related' could become 'position-related' in another task if the movement is slow enough, 'acceleration-related' if the movement is fast enough, and 'load-related' if a large enough external load is imposed (http://www.nature.com/neuro/web_specials/). Given this sensitivity to task parameters, classifying M1 cells according to the largest component of their response should perhaps be avoided altogether.

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REPLY—The article by Todorov[1] and associated letters illustrate clear opinion differences regarding the function of motor cortex during goal-directed arm movements. This controversy is partially generated by the different experimental protocols used to examine motor cortex function in non-human primates. The first, introduced by Evarts, examines single-joint movements and relates neural activity to muscle-based or joint-based variables[15]. The second, introduced by Georgopoulos, examines whole-arm movements and relates neural activity to hand-based variables[16]. Practitioners of the former find correlates of muscle-based or joint-based variables; practitioners of the latter find correlates of hand-based variables.

T. S. Kuhn captures the present situation: "proponents of competing paradigms practice their trades in different worlds ... the two groups of scientists see different things when they look from the same point in the same direction."[17] With regard to motor cortex function, neural correlates of hand direction are seen as evidence by one group that hand direction is an important and potentially dominant signal, whereas the other group views this observation as an obvious by-product of neural activity that controls muscles to move the limb.

These differences of opinion are important for understanding not only the function of motor cortex, but also the function of other cortical and subcortical regions of the CNS, such as the spinal cord. At the extremes, the spinal cord could be viewed as the central location where all decisions on the details of motor selection are generated from a simple descending command specifying the global goal of the task. Alter-

natively, it could be viewed as evolutionary baggage that simply conducts fully orchestrated signals generated in higher motor regions onto motoneurons. As usual, the truth likely lies in the middle.

Todorov states that many neural correlates of hand-based variables can be explained if motor cortical activity simply encoded muscle activation patterns. Related arguments have been proposed for neural correlates of mental rotation in motor cortex[18]. Neither of these articles disprove that neural activity reflects hand-related or cognitive functions; they simply demonstrate that there are alternative interpretations for these experimental observations. Although one can argue whether Todorov's model can predict the details of each hand-based correlate, this muscle-based model reveals how little we know about the function of motor cortex during whole-limb motor tasks.

Although the model by Todorov challenges the use of hand-based frameworks for interpreting motor cortical activity, it is important to recognize the technical difficulty of these experiments. It was a logical and sensible decision to relate neural activity to movements of the hand when Georgopoulos and colleagues introduced this paradigm over 20 years ago[16]. This hand-based model has provided an influential contribution to both motor and cognitive neuroscience. However, substantial progress in our understanding of the function of primary motor cortex now requires a change in the experimental framework[19]. Such a change must allow for exploration of the rich and diverse activation patterns of motor cortical neurons related not only to global features of the task, but also to features of movement related to the peripheral motor apparatus.

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'What', 'where' and 'how' in auditory cortex

TO THE EDITOR—In their commentary on Romanski *et al.*'s findings of (at least) two streams of auditory projections to the prefrontal cortex[1], Kaas and Hackett have suggested that this anatomical segregation reflects, as in visual cortex, a functional segregation of the object-related and space-related aspects of auditory processing ('What' and 'Where,' respectively)[2,3]. This model derives from the increasingly accepted notion that the cortical systems for different sensory modalities may share principles of functional organization[3,4]. However, the 'What/Where' model of auditory functional specialization remains conjectural. In particular, there is little evidence that circumscribed areas of the auditory cortex are specialized to process spatial information[5] or that topographic spatial maps exist in auditory cortex, although such maps do exist in the colliculi[6]. Results suggest that auditory spatial location is represented in the auditory cortex as a distributed code based on spike timing[7].

Here we propose an alternative model of functional segregation in the auditory cortex. Our model agrees that the ventral pathway is probably involved in perceiving auditory objects by extracting 'acoustic signatures,' the invariant set of auditory features that allow identification of sound sources ('What'). However, our model suggests that the dorsal pathway is primarily involved in perceiving the evolution in time of the signal emitted by one or several auditory objects, a process based on accurate analysis of spectral motion (SM, 'Where-in-frequency' or 'How'). SM corresponds to changes in position of the peaks of acoustic energy in frequency space, and is especially present in animal vocalizations (reflecting motion of the vocal apparatus), in particular in speech, where the time-course of the formant frequencies contain most of the phonemic information. Perception of SM is thus an important aspect of auditory cognition, in particular of speech perception, which supports the existence of a dedicated neuronal pathway. Neuroimaging and lesion studies in humans suggest that speech perception is highly dependent on the posterior part of the auditory cortex[8,9] ; this corresponds with the location of the putative 'How' pathway in caudal parts of auditory cortex.

Auditory SM is analogous to visual spatial motion[3]. Both are related to distribution changes of energy across the sensory epithelium: as visual motion corresponds to movements of light on the retina, SM corresponds to movements of acoustic energy across the basilar membrane, along the frequency dimension. Because topographical relationships along the sensory epithelium are conserved up to and beyond primary sensory cortices, our model implies that functions of the dorsal pathways in the auditory and visual cortex are based on similar neuronal computations. Pursuing this analogy, a major processing stage of the caudal auditory pathway could consist of a cortical area sensitive to SM, analogous to visual area V5/MT. Neuroimaging suggests that such an area can be found bilaterally in the posterior part of the superior temporal gyrus, in the presumed caudal pathway[10].

Thus, our model suggests that anatomical segregation in dorsal and ventral auditory pathways reflects two different modes of auditory processing, analogous to those of the visual pathways. Applied to speech perception, our model suggests that the dorsal pathway extracts the verbal message contained in a spoken sentence, while the