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Cortical circuits and modules in movement generation: experiments and theories

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Here we review recent studies of the cortical circuits subserving the control of posture and movement. This topic is addressed from neurophysiological and evolutionary perspectives describing recent advancements achieved through experimental studies in humans and non-human primates. We also describe current debates and controversies concerning motor mapping within the motor cortex and the different computational approaches aimed at resolving the mystery around motor representations and computations. In recent years there is growing interest in the possibly modular organization of motor representations and dynamical processes and the potential of such studies to provide new clues into motor information processing. Hence this review focuses on motor modularity, highlighting the new research directions inspired by empirical findings and theoretical models developed within the last several years.

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Introduction

In recent years considerable progress has been made in gaining new information concerning the structure and processing within motor cortical circuits [1]. Recently developed optogenetic and brain imaging methods and advanced techniques for electrophysiological recording of neural activities from a large number of cells have offered a new promise for gaining greater understanding of motor information processing and organization. Nevertheless, we are still far from achieving a more comprehensive understanding of neural computations carried out by cortical and subcortical networks and the mechanisms subserving motor planning and control. A fundamental reason for our difficulties in deciphering neural cortical and subcortical activities might be partially due to the complex nature of the non-linear relations existing between neural commands and movement kinematic and kinetic variables. Hand and joint kinematics at any point in time result from the actions of multiple muscles exerting their forces on several joints. The muscles themselves behave more like visco-elastic elements than pure force generators and their stiffness and viscosity vary with the number and types of muscle fibers recruited. Also, net joint torques causing multi-link movements emerge from the net effect of not only muscle forces but also centripetal and Coriolis torques. Other sources of complexity are the considerable redundancy at the neural, muscular and kinematic levels and the highly distributed nature of the motor system. Here we review findings from several recent studies that have combined neurophysiological, behavioral and computational approaches to examine movement control. The particular focus of the current review is on motor modularity [2] and the new insights gained into cortical control of movement. Describing the promises made by this line of research we also conclude by discussing the challenges lying ahead.

Investigations of cortical and subcortical neural circuits

Recently developed optogenetic methods for controlling neural functions are now widely utilized. Despite the promise offered by these methods and the progress made in understanding motor development and gene expression, we are still far from deciphering the brain mechanisms underlying movement generation. Even the simplest actions involving the movements of a single or of a few joints require a large number of muscles and, hence, muscle fibers. How the CNS copes with this large number of degrees of freedom is one of the fundamental questions in motor system neuroscience. The remarkably effective solutions found by biological systems must have imposed and shaped the architecture and the functional organization of the CNS. That the solution could be based on modularity has occurred to many investigators. Most recently Saltiel *et al.* [3] and Levine *et al.* [4••] showed that spinal interneurons are organized in functional modules, each module activating a particular set of muscles in distinctive proportions (a muscle synergy). This modular spinal structure is the centerpiece of a discrete combinatorial system utilizing a finite number of discrete elements to express movements. The same synergies contribute to different movements and different behaviors, possibly constructed by linearly combining the same synergies with different timing and scaling factors [5••]. The combinatorial system is controlled by cortical neurons via corticospinal fibers [4••]. Motor behavior is thus like language-discrete elements and a set of rules for combining them enable the system to generate a large number of meaningful entities distinct from and more complex than their underlying elements.

Neurophysiological, computational and behavioral studies are now identifying the basic building blocks used to generate different movements at the spinal and cortical levels. One possible general strategy in the CNS to simplify motor control is using two types of cells in the old cortex, one acting directly on lower motor interneuron pools, while the other exerts its influence on descending commands transmitted through cells terminating on spinal inter-neuronal pools [6••]. Recently it was suggested that the different functional uses of a muscle are generated by separate populations of cortico-motorneuronal cells [7].

Theories/computational issues

There is a large gap between behavioral observations of movement and data on activities of individual neurons and of neuron populations. Shenoy *et al.* [8] argue that representational approaches attempting to identify the kinematic and dynamic variables represented by recorded neuron activity cannot provide sufficient insights into the internal motor processes. Even though neuron firing rates and population vectors may show significant correlations with a single or several kinematic or dynamic variables, more appropriate would be a dynamic approach (see also [9]) examining the evolvement of time-dependent neural population activities during motion preparation and execution. Exploring the hypothesis that motor cortex activity reflects neural dynamics appropriate for generating temporally patterned outgoing commands, Kaufman [10] examined motor cortical activity during motor preparation when a movement is withheld before a go signal. In another study [11] a recurrent neural network was trained to reproduce the observed EMG patterns. The solution of the trained network was a low-dimensional oscillator resembling the observed neural data at both the single cell and population levels.

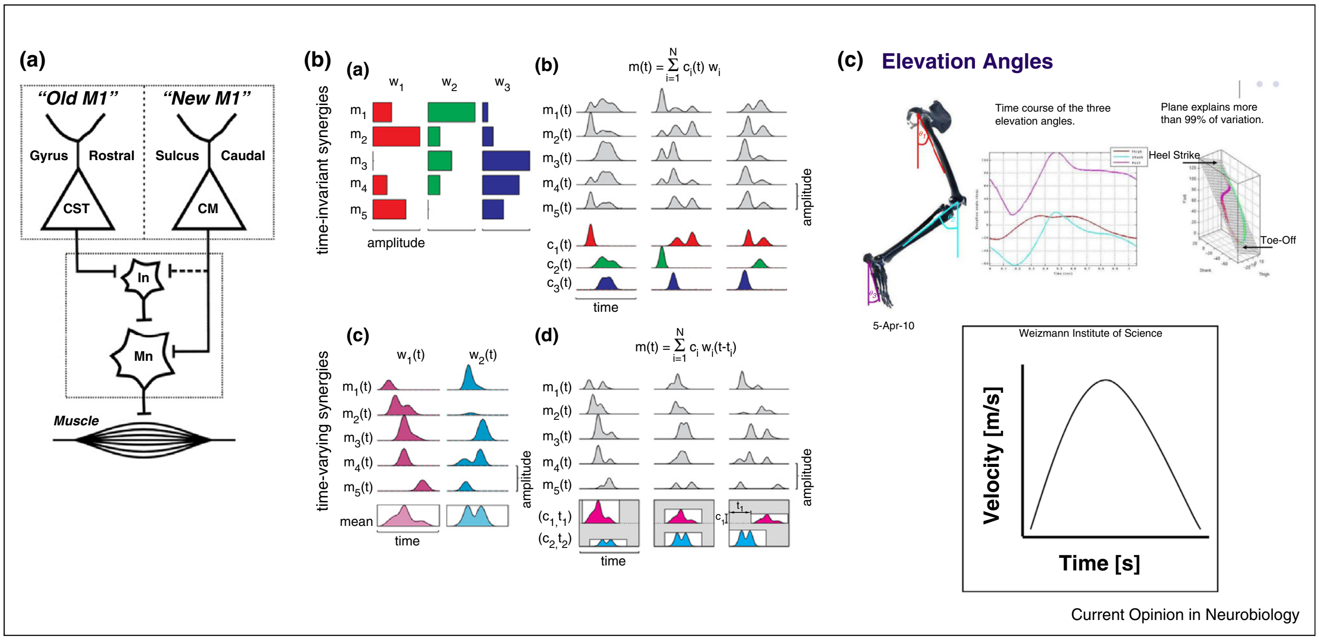
Given the time-dependent nonlinear mapping and transformations involved in movement generation at all levels of the neuro-muscular hierarchy, linear additive models attempting to find sufficiently strong correlations between neural activities and various motor variables are too simplistic. Still, finding strong linear correlations between the magnitude and direction of M1 population vectors speaks strongly in favor of neural populations indeed modulating their activities in correlation with instantaneous hand velocity vector [12,13••] although direction is more strongly encoded than speed [14]. To overcome the complexities associated with interpreting neurophysiological observations, various dimension reduction approaches have been developed [15], including efforts to infer motor primitives and syntactic rules from brain mapping and neural recording [16,17] (see Figure 1).

One mainly descriptive approach for inferring motor primitives at the muscular, kinematic and neural levels [18] is based on unsupervised source decomposition methods (PCA, ICA, NMF, so on). This approach aims to reconstruct the original data using a relatively small number of elementary units and deriving their descriptions by minimizing the error between the predicted system outputs and the original data. System outputs examined have mainly been joint rotations or EMG signals. A weighted sum of muscle synergies has been used to reconstruct EMG signals, each synergy being represented by the magnitudes of activations of the muscles belonging to that synergy. Alternatively, the weights acting on each synergy were taken to be time-independent, and the base functions representing the different synergies were assumed to depend on time [19,20]).

Omlor *et al.* [21] have recently developed a third method for decomposing EMG or joint position data. This computational method, recently implemented in the FADA toolbox [22], is based on representing the data by an anechoic mixture — a model usually used to decompose acoustic signals into underlying independent sources. The data were assumed to be represented by a weighted sum of time-shifted sources with the same set of sources used across different degrees of freedom (muscles or joints). Model parameters (source weights and time delays between sources initiation) were selected to minimize the errors between the predicted and measured time-dependent signals. This method was implemented in both locomotion [23,24] and arm movement studies [22]. Other computational schemes using HMM or Bayesian models to segment time-dependent movement data have also been developed ([25,26]), as well as approaches to inferring the underlying kinematic and dynamic primitives using optimization of single or combined costs, for example, motion smoothness by minimizing jerk [27,28], variance [29], effort/variance [30], smoothness/accuracy, or smoothness/time [31] tradeoffs. In this approach the motion units themselves are assumed to be selected according to some optimization process [32] or to obey some geometrical symmetry [33••] or spatial or temporal invariance [34].

Another requirement for a meaningful segmentation or decomposition scheme may be the simplicity of the derived primitives [11] and their generalization either for generating different movements within the same class of movements or across different behaviors [18,35]. Thus,

Figure 1



Cortical activations of muscles, muscle synergies and kinematic primitives. **(a)** New and old M1. New M1 is located caudally in the CS and has CM cells that make direct connections with motoneurons. By contrast, old M1 is located rostrally on the precentral gyrus and lacks CM cells. However, old M1 has CST neurons that influence motoneurons indirectly through their connections with spinal interneurons. CM, cortico-motoneuronal; CST, corticospinal; In, interneurons; Mn, motoneurons (taken from [6••]). **(b)** Time-invariant and time-varying synergies. *(a)* Three different activation balances among five muscles are expressed by three vectors ($\mathbf{w}_i$), whose components are represented by horizontal bars of different lengths. *(b)* A time-varying muscle pattern [$\mathbf{m}(t)$] is generated by combining the synergies with time-varying scaling coefficients [$c_i(t)$]. Different patterns can be obtained by changing the scaling coefficient waveforms. *(c)* Each one of the two time-varying synergies illustrated is composed by a collection of muscle activation waveforms. The profile inside the rectangle below each synergy represents the mean activation waveform for that synergy. *(d)* A time-varying muscle pattern [$\mathbf{m}(t)$] is generated by multiplying all waveforms of each synergy by a single scaling coefficient, shifting them in time by a single delay (t_i), and summing them together. Different patterns are obtained by changing two scaling coefficients and two delays (taken from [20]). **(c)** Kinematic primitives. Top: rotations of elevation angles of the human leg during human locomotion giving rise to intersegmental coordination plane (see [23,46–48]). **(d)** Kinematic primitives at the hand level-bell shaped velocity profiles in the case of reaching. For further discussion and examples see [32,33].

in spite of the argument against the representational approach to neural data, we are inclined to prefer decomposition schemes yielding primitives having stronger semantically, physically or biologically meaningful attributes. Other tests for assessing the plausibility of assumed decomposition schemes could be based on developmental or evolutionary considerations [36,37] or on lesion studies where the disruption or deletion of primitives may allow predicting the overt impairments in motor performance [38,39].

The interest in modularity and compositionality for constructing well adapted motor behavior has influenced robotics research. A very prominent computational model used to represent kinematic or kinetic building blocks involves the use of dynamic primitives [40]. This is based on a mathematical description originally developed in the VITE model [41] incorporating ideas and descriptions derived from the equilibrium point/equilibrium trajectory control schemes [42–44]. Such dynamic primitives were also used to model human and animal arm and locomotion movements [45–48] and grasping [49,50]. A rich movement repertoire may be built from the composition of both discrete and rhythmic primitives. Hogan and Sternad [24] have added impedance as a third type of primitive, simultaneously controlled during the generation of both discrete or continuous primitives.

There is ongoing debate whether the production of rhythmic versus discrete movements involves distinct control mechanisms and brain areas. Ivry and Breska [51] suggested that the different functions hypothesized for the cerebellum and basal ganglia in motor timing, — the cerebellum mainly involved with interval timing and the basal ganglia with emergent timing — may actually reflect their different functions in controlling discrete versus rhythmic movements.

Discussion and conclusions

This review focuses on circuits controlling generation and organization of multi-joint movement. We review recent publications on cortical encoding, mainly by M1, and recent research focusing on modular control, using muscle synergies and kinematic primitives. Synergetic control of different body parts (e.g., hand and mouth synergy [52] or pelvic floor and gluteal muscles [53]) has also been explored using combined fMRI and brain stimulation methods. EEG, fMRI and connectivity analysis [34,54,55] have revealed the neural correlates of kinematic primitives and their invariant properties as well as possible neural substrates [56] for etiologically relevant [52,57] complex inter body part synergies. Synergistic control of several body parts have also served as a basis for the notion of cortical organization according to action maps [58••]. Biological modularity has also inspired a focus on modularity in robotics and suggests novel neural rehabilitation techniques [40,49,59]. Further behavioral, neurophysiological and computational research should focus on how modules at one level of the motor hierarchy map into modules at lower levels. A further challenge is to investigate how brain oscillations can be related to compositionality-based schemes, such as Aumann and Prut [60] hypothesis that beta rhythm oscillations strengthen cortico-muscular connectivity within synergies. In this way, beta oscillations help maintain accurate and discrete representations of muscle synergies in M1. New multidisciplinary approaches should be developed to further explore the modularity hypothesis.

Conflict of interest

Nothing declared.

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References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

•• of outstanding interest

1. Brecht M, Hatsopoulos NG, Kaneko T, Shepherd GM: **Motor cortex microcircuits**. *Motor Cortex Microcircuits (Front Brain Microcircuits Series)* 2015:4.

2. d'Avella A, Giese M, Ivanenko YP, Schack T, Flash T: **Editorial: modularity in motor control: from muscle synergies to cognitive action representation**. *Front Comput Neurosci* 2015:9.

3. Saltiel P, d'Avella A, Wyler-Duda K, Bizzi E: **Synergy temporal sequences and topography in the spinal cord: evidence for a traveling wave in frog locomotion**. *Brain Struct Funct* 2015:1-22.

4. •• Levine AJ, Hinckley CA, Hilde KL, Driscoll SP, Poon TH, Montgomery JM, Pfaff SL: **Identification of a cellular node for motor control pathways**. *Nat Neurosci* 2014, **17**:586-593.

Single spinal interneurons make synaptic connections with a set of motor neurons controlling different muscles. The data indicate that interneurons are organized in functional modules and each module activate a particular set of muscles.

5. •• Bizzi E, Ajemian R: **A hard scientific quest: understanding voluntary movements**. *Daedalus* 2015, **144**:83-95.

The vertebrate motor system produces movements by combining a small number of muscle synergies. Evidence that different motor behaviors are constructed by combining the same synergies with different timing and amplitudes.

6. •• Rathelot JA, Strick PL: **Subdivisions of primary motor cortex based on cortico-motoneuronal cells**. *Proc Natl Acad Sci U S A* 2009, **106**:918-923.

The primary motor cortex was found to contain two subdivisions: a rostral region that contains cells whose descending commands are mediated via inter-bneuronal pools within the spinal cord and a rostral region that mediate their commands through direct contact with lower motorneurons.

7. Griffin DM, Hoffman DS, Strick PL: **Corticomotoneuronal cells are "functionally tuned"**. *Science* 2015, **350**:667-670.

8. Shenoy KV, Sahani M, Churchland MM: **Cortical control of arm movements: a dynamical systems perspective**. *Annu Rev Neurosci* 2013, **36**:337-359.

9. Rokni U, Sompolinsky H: **How the brain generates movement**. *Neural Comput* 2012, **24**:289-331.

10. Kaufman MT, Churchland MM, Ryu SI, Shenoy KV: **Cortical activity in the null space: permitting preparation without movement**. *Nat Neurosci* 2014, **17**:440-448.

11. Sussillo D, Churchland MM, Kaufman MT, Shenoy KV: **A neural network that finds a naturalistic solution for the production of muscle activity**. *Nat Neurosci* 2015, **18**:1025-1033.

12. Mahan MY, Georgopoulos AP: **Motor directional tuning across brain areas: directional resonance and the role of inhibition for directional accuracy**. *Front Neural Circuits* 2013, **7**:92.

13. •• Schwartz AB: **Movement: how the brain communicates with the world**. *Cell* 2016, **164**:1122-1135.

This paper reviews the topics of feedforward and feedback control of movement and the literature concerning neural coding of limb trajectories. This perspective emphasizes intentional and prediction aspects of movement generation.

14. Golub MD, Yu BM, Schwartz AB, Chase SM: **Motor cortical control of movement speed with implications for brain–machine interface control**. *J Neurophysiol* 2014, **112**:411-429.

15. Cunningham JP, Yu BM: **Dimensionality reduction for large-scale neural recordings**. *Nat Neurosci* 2014, **17**:1500-1509.

16. Overduin SA, d'Avella A, Carmena JM, Bizzi E: **Muscle synergies evoked by microstimulation are preferentially encoded during behavior**. *Front Comput Neurosci* 2014, **8**:20.

17. Overduin SA, d'Avella A, Roh J, Carmena JM, Bizzi E: **Representation of Muscle synergies in the primate brain**. *J Neurosci* 2015, **35**:12615-12624.

18. Giszter SF: **Motor primitives — new data and future questions**. *Curr Opin Neurobiol* 2015, **33**:156-165.

19. d'Avella A, Portone A, Fernandez L, Lacquaniti F: **Control of fast-reaching movements by muscle synergy combinations**. *J Neurosci* 2006, **26**:7791-7810.

20. d'Avella A, Lacquaniti F: **Control of reaching movements by muscle synergy combinations**. *Front Comput Neurosci* 2013, **7**:42.

21. Omlor L, Giese MA: **Anechoic blind source separation using wigner marginals**. *J Mach Learn Res* 2011, **12**:1111-1148.

22. Chiovetto E, d'Avella A, Giese MA: **Unifying framework for the identification of motor primitives**. arXiv preprint arXiv:1603.06879 2016.

23. Barliya A, Omlor L, Giese MA, Berthoz A, Flash T: **Expression of emotion in the kinematics of locomotion**. *Exp Brain Res* 2013, **225**:159-176.

24. Hogan N, Sternad D: **Dynamic primitives in the control of locomotion**. *Front Comput Neurosci* 2013, **7**:71.

25. Abeles M, Diesmann M, Flash T, Geisel T, Herrmann M, Teicher M: **Compositionality in neural control: an interdisciplinary study of scribbling movements in primates**. *Front Comput Neurosci* 2013:7.

26. Endres D, Meirovitch Y, Flash T, Giese MA: **Segmenting sign language into motor primitives with Bayesian binning**. *Front Comput Neurosci* 2013:7.

27. Flash T, Hogan N: **The coordination of arm movements: an experimentally confirmed mathematical model**. *J Neurosci* 1985, **5**:1688-1703.

28. Huh D, Sejnowski TJ: **Spectrum of power laws for curved hand movements**. *Proc Natl Acad Sci U S A* 2015, **112**:E3950-E3958.

29. Harris CM, Wolpert DM: **Signal-dependent noise determines motor planning**. *Nature* 1998, **394**:780-784.

30. Todorov E, Jordan MI: **Optimal feedback control as a theory of motor coordination**. *Nat Neurosci* 2002, **5**:1226-1235.

31. Berret B, Jean F: **Why don't we move slower? The value of time in the neural control of action**. *J Neurosci* 2016, **36**:1056-1070.

32. Polyakov F, Drori R, Ben-Shaul Y, Abeles M, Flash T: **A compact representation of drawing movements with sequences of parabolic primitives**. *PLoS Comput Biol* 2009, **5**:e1000427.

33. •• Bennequin D, Fuchs R, Berthoz A, Flash T: **Movement timing and invariance arise from several geometries**. *PLoS Comput Biol* 2009, **5**:e1000426.

This paper describes a general framework for movement representation emphasizing the role of non-Euclidean geometries, the mapping from geometry to time and using this framework as a basis for motor compositionality models.

34. Kadmon Harpaz N, Flash T, Dinstein I: **Scale-invariant movement encoding in the human motor system**. *Neuron* 2014, **81**:452-462.

35. Bizzi E, Cheung VC: **The neural origin of muscle synergies**. *Front Comput Neurosci* 2013, **7**:51.

36. Lacquaniti F, Ivanenko YP, d'Avella A, Zelik KE, Zago M: **Evolutionary and developmental modules**. *Front Comput Neurosci* 2013, **7**:61.

37. Dominici N, Ivanenko YP, Cappellini G, d'Avella A, Mondi V, Cicchese M, Fabiano A, Silei T, Di Paolo A, Giannini C *et al.*: **Locomotor primitives in newborn babies and their development**. *Science* 2011, **334**:997-999.

38. Ting LH, Chiel HJ, Trumbower RD, Allen JL, McKay JL, Hackney ME, Kesar TM: **Neuromechanical principles underlying movement modularity and their implications for rehabilitation**. *Neuron* 2015, **86**:38-54.

39. Cheung VC, Turolla A, Agostini M, Silvoni S, Bennis C, Kasi P, Paganoni S, Bonato P, Bizzi E: **Muscle synergy patterns as physiological markers of motor cortical damage**. *Proc Natl Acad Sci U S A* 2012, **109**:14652-14656.

40. Ijspeert AJ, Nakanishi J, Hoffmann H, Pastor P, Schaal S: **Dynamical movement primitives: learning attractor models for motor behaviors**. *Neural Comput* 2013, **25**:328-373.

41. Bullock D, Bongers RM, Lankhorst M, Beek PJ: **A vector-integration-to-endpoint model for performance of viapoint movements**. *Neural Netw* 1999, **12**:1-29.

42. Feldman AG: **Space and time in the context of equilibrium-point theory**. *Wiley Interdiscip Rev Cogn Sci* 2011, **2**:287-304.

43. Feldman AG, Levin MF: **The equilibrium-point hypothesis — past, present and future**. *Adv Exp Med Biol* 2009, **629**:699-726.

44. Hogan N, Bizzi E, Mussa-Ivaldi FA, Flash T: **Controlling multijoint motor behavior**. *Exerc Sport Sci Rev* 1987, **15**:153-190.

45. Roether CL, Omlor L, Christensen A, Giese MA: **Critical features for the perception of emotion from gait**. *J Vis* 2009, **9**:11-32.

46. Barliya A, Omlor L, Giese MA, Flash T: **An analytical formulation of the law of intersegmental coordination during human locomotion**. *Exp Brain Res* 2009, **193**:371-385.

47. Zelik KE, La Scaleia V, Ivanenko YP, Lacquaniti F: **Can modular strategies simplify neural control of multidirectional human locomotion?** *J Neurophysiol* 2014, **111**:1686-1702.

48. Cappellini G, Ivanenko YP, Poppele RE, Lacquaniti F: **Motor patterns in human walking and running**. *J Neurophysiol* 2006, **95**:3426-3437.

49. Santello M, Bianchi M, Gabiccini M, Ricciardi E, Salvietti G, Prattichizzo D, Ernst M, Moscatelli A, Jorntell H, Kappers AM *et al.*: **Hand synergies: Integration of robotics and neuroscience for understanding the control of biological and artificial hands**. *Phys Life Rev* 2016.

50. Latash ML: **The hand: shall we ever understand how it works?** *Motor Control* 2015, **19**:108-126.

51. Breska A, Ivry RB: **Taxonomies of timing: where does the cerebellum fit in?** *Curr Opin Behav Sci* 2016, **8**:282-288.

52. Desmurget M, Richard N, Harquel S, Baraduc P, Szathmari A, Mottolese C, Sirigu A: **Neural representations of ethologically relevant hand/mouth synergies in the human precentral gyrus**. *Proc Natl Acad Sci U S A* 2014, **111**:5718-5722.

53. Asavasopon S, Rana M, Kirages DJ, Yani MS, Fisher BE, Hwang DH, Lohman EB, Berk LS, Kutch JJ: **Cortical activation associated with muscle synergies of the human male pelvic floor**. *J Neurosci* 2014, **34**:13811-13818.

54. Meirovitch Y, Harris H, Dayan E, Arieli A, Flash T: **Alpha and beta band event-related desynchronization reflects kinematic regularities**. *J Neurosci* 2015, **35**:1627-1637.

55. Dayan E, Sella I, Mukovskiy A, Douek Y, Giese MA, Malach R, Flash T: **The default mode network differentiates biological from non-biological motion**. *Cereb Cortex* 2016, **26**:234-245.

56. Zeharia N, Hertz U, Flash T, Amedi A: **Negative blood oxygenation level dependent homunculus and somatotopic information in primary motor cortex and supplementary motor area**. *Proc Natl Acad Sci U S A* 2012, **109**:18565-18570.

57. Kaas JH, Gharbawie OA, Stepniewska I: **Cortical networks for ethologically relevant behaviors in primates**. *Am J Primatol* 2013, **75**:407-414.

58. •• Graziano MS: **Ethological action maps: a paradigm shift for the motor cortex**. *Trends Cogn Sci* 2016, **20**:12-132.

The paper reviews evidence from animal studies showing that the motor cortex contains action maps — that is, functional zones each of which emphasizes ethologically relevant behaviors.

59. Paraschos A, Daniel C, Peters JR, Neumann G: **Probabilistic movement primitives**. *Advan Neural Inform Process Syst* 2013:2616-2624.

60. Aumann TD, Prut Y: **Do sensorimotor β-oscillations maintain muscle synergy representations in primary motor cortex?** *Trends Neurosci* 2015, **38**:77-85.