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Integration of feedforward and feedback control in the neuromechanics of vertebrate locomotion: a review of experimental, simulation and robotic studies

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Abstract

Animal locomotion is the result of complex and multi-layered interactions between the nervous system, the musculo-skeletal system and the environment. Decoding the underlying mechanisms requires an integrative approach. Comparative experimental biology has allowed researchers to study the underlying components and some of their interactions across diverse animals. These studies have shown that locomotor neural circuits are distributed in the spinal cord, the midbrain and higher brain regions in vertebrates. The spinal cord plays a key role in locomotor control because it contains central pattern generators (CPGs) – systems of coupled neuronal oscillators that provide coordinated rhythmic control of muscle activation that can be viewed as feedforward controllers – and multiple reflex loops that provide feedback mechanisms. These circuits are activated and modulated by descending pathways from the brain. The relative contributions of CPGs, feedback loops and descending modulation, and how these vary between species and locomotor conditions remain poorly understood. Robots and neuromechanical simulations can complement experimental approaches by testing specific hypotheses and performing what-if scenarios. This Review will give an overview of key knowledge gained from comparative vertebrate experiments, and insights obtained from neuromechanical simulations and robotic approaches. We suggest that the roles of CPGs, feedback loops and descending modulation vary among animals depending on body size, intrinsic mechanical stability, time required to reach locomotor maturity and speed effects. We also hypothesize that distal joints rely more on feedback control compared to proximal joints. Finally, we highlight important opportunities to address fundamental biological questions through continued collaboration between experimentalists and engineers.

Summary statement: Comparative animal studies and neuromechanical modeling have revealed diversity in the integration of feedback and feedforward control, related to body size, mechanical stability, time to locomotor maturity and movement speed.

Short title: Integration of feedforward and feedback control in locomotion

Introduction

Animal locomotion arises from complex and rich interactions between the nervous system, the musculoskeletal system and the environment (Dickinson et al., 2000; Nishikawa et al., 2007). Animal sensorimotor control involves multi-layered and distributed systems, with central networks, reflexes and mechanics all contributing to sensorimotor responses on varied timescales (Büschges, 2005; Buschmann et al. 2015; Bidaye et al. 2018; Grillner, 1985; Grillner & El Manira, 2019; Loeb et al., 1999; Nirody, 2023; Pearson, 1995; Pearson & Gramlich, 2010; Rossignol et al., 2006). Because of this inherent complexity, it has been a longstanding challenge in biology to rigorously understand the structure, function and integration of animal sensorimotor systems. Integrative approaches are needed to address this challenge. Exchange between biology, physics and engineering disciplines can be particularly useful for generating and rigorously testing hypotheses about how mechanics and control interact to produce agile locomotion. In this Review, we discuss how the exchange between comparative experimental biology, physics and engineering can provide fundamental insights into the neuromechanics (see Glossary) of vertebrate locomotion.

Historically, comparative approaches have been essential for providing mechanistic understanding of the control of movement, and Journal of Experimental Biology (JEB) has been an important venue for comparative studies across diverse taxa. In the 1930s–1940s, Gray and co-authors published numerous papers on animal movement in JEB, characterizing the locomotor movements, reflex responses and locomotor pattern generation in the eel, dogfish, toad, leech and earthworm (Gray, 1933, 1936; Gray et al., 1938; Gray & Lissmann, 1938, 1940; Gray & Sand, 1936). Subsequent studies continued to expand on this diversity and contribute to mechanistic understanding of sensorimotor control (e.g. Hughes, 1952; Hughes, 1957; Wilson 1965; Wilson 1967). Many of the early studies were foundational for understanding both the basic biomechanics and neural control circuitry for movement. At that time, it was often necessary to study movement mechanics and neural control together, because so little was known about both.

In recent decades, the fields of comparative biomechanics and sensorimotor physiology have been relatively isolated, as each field focused on more detailed mechanistic understanding of specific systems. Simultaneously, studies of sensorimotor control have increasingly focused on a few genetic animal models, such as the mouse, zebrafish, fruit fly, and *Caenorhabditis elegans*, which enable the use of the most richly developed genetic and molecular tools (Bidaye et al. 2018; Fetcho & McLean, 2010; Fouad et al 2018; Kiehn, 2011; Lewis & Eisen, 2003; Zhong et al., 2012; Mantziaris et al. 2020). Nonetheless, this narrow focus has its drawbacks, and important questions remain about the diversity and specialization of sensorimotor control across species. We suggest that it is important to continue to expand studies beyond the classic genetic animal models, because comparative approaches provide opportunities to address fundamental questions about the evolution and diversity of neuromechanical integration. Critical gaps in understanding remain in how the different elements of the sensorimotor system are integrated with each other, and how this integration varies with body size and among animals adapted for different locomotor environments.

The interdisciplinary field of comparative neuromechanics has emerged over the last 15 years or so (Nishikawa et al., 2007; Ting & McKay, 2007), focusing on the study of mechanics and control of movement in a comparative framework. In this Review, we highlight principles and hypotheses that have emerged from this field, with a specific focus on sensorimotor and neuromechanical integration in vertebrates. We discuss current conceptualization of the role of central pattern generators (CPGs; see Glossary) and their integration with reflexes and limb mechanics, and the interactions between feedforward and feedback control mechanisms (see Glossary). In the sections below, we first summarize current understanding in

84　biology based on both historical and recent experimental evidence, then discuss contributions from bio-
85　inspired robotics and simulations, and then highlight current open questions and future directions that are
86　enabled through direct integration of engineering and experimental biology. Our Review focuses mainly on
87　vertebrate locomotion; however, we note that many principles of locomotor control have parallels between
88　vertebrates and invertebrates, and readers are directed to recent reviews of invertebrate systems (Nirody
89　2023; Mantziaris et al. 2020; Bidaye et al. 2018).

Biology: historical experimental evidence, current understanding and new hypotheses

Integration of CPGs and sensory feedback in the spinal cord

94　The spinal cord plays a key role in integrating predictive and reactive elements of vertebrate locomotor
95　control (Grillner & El Manira, 2019; Rossignol et al., 2006). Animal control involves inherently long
96　sensorimotor delays (see Glossary; More et al., 2010; More & Donelan, 2018). Because of these delays,
97　animals cannot rely entirely on reactive, feedback-driven control, but must instead use a combination of
98　predictive and reactive control mechanisms for stable movement (Fig. 1). The spinal cord contains neural
99　circuits involved in integrating CPGs (see Box 1), reflex responses, and descending and ascending
100　pathways to the brain (Grillner & El Manira, 2019; Pearson, 1995; Rossignol et al., 2006). CPGs in the spinal
101　cord provide a type of predictive, feedforward controller for locomotion that helps to overcome delays.
102　CPGs are activated by a descending 'drive' signal and produce predetermined motor outputs for
103　locomotion. These outputs provide complex muscle activation for the anticipated mechanical demands,
104　resulting in, for instance, traveling waves for undulatory locomotion and alternation of stance and swing
105　phases for legged locomotion. CPGs therefore resemble feedforward controllers in control theory (see
106　Glossary), because they produce complex and detailed motor commands given a simpler high-level
107　descending signal for the desired behavior, such as movement at a specific speed. However, CPGs do not
108　act in isolation. The CPG receives continuous modulation through descending drive commands and reflex
109　feedback (Grillner et al., 2008; Rossignol et al., 2006). Consequently, the CPG can be thought of as a type
110　of feedforward controller nested within a feedback control system (Holmes et al., 2006).

112　Current evidence suggests that animal locomotion makes use of a nested, multi-layered control
113　architecture that organizes sensing and action (Grillner & El Manira, 2019; McLean & Dougherty, 2015;
114　Pearson, 1995; Rossignol et al., 2006). A nested architecture enables separation of task selection (starting,
115　stopping, gait and speed), task coordination (e.g. generation of coordinated rhythmic leg movements) and
116　stabilization in response to disturbances. As a first approximation of the hierarchical organization, CPGs
117　generate rhythmic commands that act as feedforward signals for task coordination, whereas descending
118　commands activate and modulate CPGs for task selection, and reflexes provide stabilizing responses to
119　perturbations (Fig. 1). We will later see that neuromechanical models suggest more complexity, with
120　sensory feedback also contributing to task coordination (Owaki et al., 2013; Thandiackal et al., 2021).
121　Sensorimotor delays give rise to temporal scaling of control responses based on the spatial distribution of
122　system elements (Fig. 1). Inner loops deal locally with perturbations, relying on fast peripheral mechanisms,
123　including intrinsic mechanics (Brown & Loeb, 2000; Daley et al., 2007; Dickinson et al., 2000; Full &
124　Koditschek, 1999; Jindrich & Full, 2002) and short-latency reflexes (Af Klint et al., 2010; Daley et al., 2009;
125　Hiebert & Pearson, 1999; Moritz & Farley, 2004). Intermediate loops modify task-level variables, such as
126　joint and leg stiffness, and outer loops integrate sensorimotor information in the brain to select and switch
127　among different tasks and update internal models (see Glossary; Pearson & Gramlich, 2010). However,

128 many uncertainties remain in how different control layers are integrated and modulated based on
129 experience, learning and different locomotor contexts.

130

131 There was a longstanding historical debate about the relative importance of feedforward and feedback in
132 control of animal locomotion. Sherrington's work on reduced animal preparations revealed that reflex
133 actions could generate the component motions necessary for rhythmic walking (Sherrington, 1910). Thus,
134 Sherrington argued that locomotion could be viewed as the result of a chain of reflexes (Sherrington, 1900,
135 1906, 1910). Subsequent work by Graham Brown demonstrated that motor patterns for locomotion could
136 be generated in deafferented preparations and did not require sensory input. Graham Brown argued that
137 'spinal centers' (later named central pattern generators) acted as the primary unit of motor activity, not the
138 reflex (Graham Brown, 1911, 1914). He suggested that the reflexes regulate rather than generate motor
139 activity (Graham Brown, 1911). To this day, the relative roles of central and reflex-generated contributions
140 to locomotion remain somewhat controversial; however, it has become clear that both mechanisms co-
141 exist and provide redundancy and flexibility in the system.

142

143 Subsequent work has confirmed the existence and shared features of spinal CPGs across vertebrates (see
144 Box 1). Vertebrates also share a common mechanism for descending drive to CPGs to control gait speed
145 and initiation. Stimulation of the mesencephalic locomotor region, invokes gait initiation and gait
146 transitions across species, inducing swimming in fish and walking in terrestrial animals (Cabelguen et al.,
147 2003; Grillner & Wallen, 1985; Shik et al., 1966; Steeves et al., 1987). As the strength of the stimulation
148 increases, swimming speed increases in the fish, and a quadruped increases speed and transitions
149 between gaits from a walk to trot to gallop (Shik et al., 1966; Wallén, 1982).

150

151 In vertebrates, sensory feedback plays an essential role in entraining CPG rhythms to the mechanics of the
152 body and the interaction with the environment. In the lamprey, periodic bending of the spinal cord results
153 in entrainment (see Glossary) of the patterns of fictive locomotion (see Glossary), through sensory
154 feedback from mechanosensitive edge cells in the spinal cord (Grillner et al., 1981; Grillner & Wallén, 1984).
155 Similarly, proprioceptive feedback entrains gait rhythm and the timing of stance−swing transitions in
156 quadrupedal gait (Pearson, 2008; Whelan, 1996). In decerebrate and spinal preparations (see Glossary),
157 increasing belt speed leads to gait transitions from walk to trot and gallop, suggesting a role for sensory
158 feedback entrainment in gait transitions (Barbeau & Rossignol, 1987; Forssberg et al., 1980; Kriellaars et
159 al., 1994; Pearson, 2008; Whelan, 1996; Yanagihara et al., 1993). With increasing knowledge of the
160 interneuronal networks and cellular mechanisms underlying sensorimotor control, it has become clear that
161 sensory feedback is integrated at multiple levels: as distinct reflexes, as modulators of central pattern
162 generation and integrating with longer-latency feedback loops to regulate navigation and task selection
163 (Grillner & El Manira, 2019; Rossignol et al., 2006; Fig. 1).

164

165 ## Diversity in the integration of feedforward, feedback and model-based neural control
166 Recent evidence and modeling studies (see below) suggest that the relative contributions of feedforward
167 and feedback can vary depending on size of the animal, speed, terrain and risks of falling. Below, we discuss
168 emerging hypotheses about specialization and diversification of control components among vertebrates.
169 Loosely speaking, we suggest two types of feedforward control, one in the spinal cord, based on CPGs, and
170 one in higher brain centers, based on internal models, which we will here call (cephalized) model-based
171 neural control (see Glossary). We call them both feedforward because they represent an anticipatory
172 component as opposed to the reactive nature of feedback.

173

174 **Body size and scaling of neuromechanical delays**

175 Body size is one important source of diversity in control mechanisms for locomotion (Fig. 2). Sensorimotor
176 loop delay increases with body size (M), in proportion to $M^{0.21}$ (More et al., 2010, 2013; More & Donelan,
177 2018). Large animals experience longer sensorimotor delays relative to movement durations compared
178 with the same ratio in small animals. For example, at speeds near the trot–gallop transition, a shrew has a
179 total delay of 10ms, 25% of its stance duration, but an elephant has a total delay of about 180 ms, 60% of
180 its stance duration (More & Donelan, 2018). Delay relative to stance duration is important because this
181 represents the time available to apply force for a corrective response to a disturbance. If an animal cannot
182 respond to a disturbance within the stance phase, the response requires coordination of multi-step and
183 multi-legged strategies, which involve longer-latency feedback loops. Delays therefore challenge the ability
184 of large animals to respond effectively to perturbations, even though they have slower dynamics and step
185 cycles compared to smaller animals (Mohamed Thangal & Donelan, 2020; More & Donelan, 2018).
186
187 To compensate for the relatively longer delays, it is expected that larger animals rely more on model-based
188 control, using sensory feedback and internal models in the brain to generate state estimates for stable
189 movement. Internal models can allow animals to compensate for delayed and noisy sensory feedback to
190 predict future states, enabling generation of appropriate motor outputs for stable movement (Todorov,
191 2004; Todorov & Jordan, 2002; Wolpert & Ghahramani, 2000). The synaptic delays associated with internal
192 model computations are a higher fraction of the total sensorimotor delay in very small animals (Thangal &
193 Donelan, 2020; More & Donelan, 2018). Consequently, the benefits of model-based control may not
194 outweigh the costs of increased computation times in small animals (Thangal & Donelan, 2020; More &
195 Donelan, 2018). Thus, overall, it is expected that larger animals are likely to have more cephalized model-
196 based control, with higher brain involvement compared to small animals (Fig. 2), whereas small animals
197 can achieve agile and robustly stable movement through more spinalized control mechanisms coupled to
198 intrinsic mechanical preflexes (see Glossary).
199

200 Spinalization versus cephalization of feedforward control may relate to mechanical stability and the time
201 to locomotor maturity
202 Although all vertebrates share similar component systems for locomotor control, a source of diversity
203 among vertebrates is the degree of involvement of the brain and the complexity of descending drive
204 modulation (Fig. 3). This distinction may be related to different developmental demands between precocial
205 and altricial species (see Glossary). Precocial species tend to have relatively small brains as adults;
206 whereas altricial species tend to have larger adult brain size (Bennett & Harvey, 1985; Garwicz et al., 2009).
207 We hypothesize that these developmental differences may also be related to the relative degree of
208 'spinalization' versus 'cephalization' of locomotor control. That is, precocial species have more spinalized
209 locomotor control, relying mainly on spinal CPG networks as a feedforward controller, coupled to intrinsic
210 mechanics of the body, with short-latency reflexes. In contrast, altricial species have more cephalized
211 control, relying more on model-based control in the brain, with longer-latency reflexes updating internal
212 models. Through experience and optimization, animals can optimize the use of efference copy (see
213 Glossary) and sensory feedback to estimate current states and predict future states to determine desired
214 motor outputs (Todorov, 2004; Todorov & Jordan, 2002; Wolpert & Ghahramani, 2000). Multiple brain
215 regions may be involved in the generation, maintenance and updating of internal models, including the
216 cerebellum and the posterior parietal cortex (Ito, 2008; McVea et al., 2009; Pearson & Gramlich, 2010).
217 Multi-layered model-based control can overcome delays by predicting mechanical conditions over a wide
218 range of contexts and adjusting feedforward commands through descending pathways (Nakahira et al.,
219 2021).
220
221 The contrast between precocial and altricial species can be appreciated when comparing large ground
222 birds (such as ostriches and rheas) to humans. Although birds and humans have independently evolved

bipedalism, they have converged upon walking and running gaits with similar mechanical and energetic demands (Gatesy & Biewener, 1991; Roberts et al., 1998; Rubenson et al., 2004; Watson et al., 2011). Yet, they exhibit important differences in development and sensorimotor control features. Ground birds are precocial, able to walk and run very shortly after hatching (Muir et al., 1996; Muir & Chu, 2002; Y. U. Ryu & Bradley, 2009; Smith et al., 2010), whereas humans are exceptionally altricial, requiring many months of practice to walk without falling. We suggest that these developmental differences also reflect differences in spinalization versus cephalization of locomotor control. Birds have relatively more spinalized locomotor control compared to more cephalized control in mammals, including humans. Neurophysiological studies have demonstrated that spinal circuits are sufficient to generate complete locomotor patterns for self-supported walking in birds (Ho & O'Donovan, 1993; Sholomenko et al., 1991; Sholomenko & Steeves, 1987; Ten Cate, 1960). Birds do possess a common descending pathway with other vertebrates, from the mesencephalic locomotor region to the spinal CPGs, but lack a direct telencephalic–spinal projection analogous to the mammalian corticospinal tract (Sholomenko & O'Donovan, 1995; Sholomenko & Steeves, 1987; Steeves et al., 1987; Webster & Steeves, 1988). A recent study genetically silenced interneurons in the dorsal spinal tract in chicks, which increased kinematic variability in walking (Haimson et al., 2021), suggesting that sensory feedback and descending modulation contribute to stability of walking in birds. Nonetheless, locomotor control appears to be relatively more spinalized in birds compared to the more cephalized sensorimotor control observed in mammals.

The relatively spinalized versus cephalized locomotor control in ground birds versus mammals, respectively, might represent different solutions to the problem of neural delays. Cephalization allows more sophisticated internal models and model-based control; this allows delays to be overcome by predicting mechanical conditions over a wide range of learned contexts and adjusting descending commands accordingly. In contrast, spinalization relies on simpler CPG-based feedforward control, with the feedback-entrained rhythm providing estimates of current state and generation of motor output. We hypothesize that animals with more spinalized control also tend to have more intrinsically stable biomechanics (Fig. 3). Among bipeds, birds have a relatively flexed limb posture compared to humans, a forward horizontal position of the body and high elasticity in the distal leg muscles, features that increase mechanical stability (Badri-Spröwitz et al., 2022; Daley, 2018; Daley et al., 2009; Daley & Biewener, 2011; Daley & Birn-Jeffery, 2018). Humans, in contrast, have a straight leg posture with the body vertically balanced over the hips, which is highly unstable without active control.

Among quadrupeds there is also diversity in intrinsic mechanical stability that may relate to degree of cephalization versus spinalization of control. Large ungulates have parasagittal limb posture with relatively straight legs, a high body center of mass and a relatively narrow base of support. These features benefit locomotor economy by minimizing the active muscle force required to support body weight against gravity (Biewener, 1989). However, upright postures are relatively unstable compared to the sprawled posture and wide base of support typical of many amphibians and lizards (Alexander, 2002; Ijspeert, 2020). Note that here we mainly refer to static stability (see Glossary) rather than dynamic stability. At least at slow speeds, static stability in quadrupeds is proportional to the size of the support polygon, and inversely proportional to the ratio of body height to stance width (Alexander, 2002). We hypothesize that there is a control gradient in which mechanical stability enables spine-localized feedforward control, whereas mechanical instability is associated with brain-dominated feedforward control (Fig. 2). We also hypothesize that unstable animals require better proprioception for monitoring their posture and loads on limbs, and hence have a larger role for spinal sensing than mechanically stable animals. A similar hypothesis has been proposed in Ryczko et al. (2020).

Proximo-distal differentiation in control

Across diverse tetrapod animals, limbs have a proximo-distal distribution in muscle−tendon morphology, which may also result in differentiation in control mechanisms (Daley et al., 2007). The largest, most powerful muscles are proximal, concentrating mass near the body. Distal muscles have lower mass and high mass-specific force due to their short, pennate muscle fiber arrangement, and high in-series compliance (see Glossary). The pennate architecture of distal muscles leads to a load-sensitive architectural gear ratio (Azizi et al., 2008; Eng et al., 2018; Roberts et al., 2019), which is likely to make them sensitive to external perturbations. In contrast, the high inertia and lower compliance of the proximal muscles is likely to make them less sensitive to external perturbations. Based on these mechanical differences between proximal and distal muscles, we hypothesize that proximal muscles use higher-gain feedforward control, with length and position feedback entraining CPG rhythm, whereas distal muscles rely more on intrinsic mechanics (i.e. preflexes) and short-latency load and stretch reflexes (Fig. 4). Indeed, evidence from cats suggests that proximal muscles at the hip contribute to regulation of stance−swing transitions, whereas the distal ankle extensors use force feedback to regulate stance load bearing (Donelan & Pearson, 2004; Gorassini et al., 1994; Hiebert et al., 1994; Pearson et al., 1998). Modeling studies also support this hypothesis (Dzeladini et al., 2014; see below).

Using neuromechanical simulations and biorobots to investigate animal motor control

One theme that has emerged from neuromechanical studies is the importance of effective tuning of control to the biomechanical properties of the system and to physical interactions with the environment. However, the multi-layered, distributed and redundant nature of animal sensorimotor systems makes it challenging to rigorously understand the relationships and connections among the component systems through experiments alone. Neuromechanical simulations (i.e. numerical simulations of both neural circuits and bodies interacting with a virtual environment) can be useful tools to tackle these challenges and test hypotheses about animal motor control. Additionally, simulated neural circuits can also be tested in the real world with biomimetic robots used as physical models of animal bodies.

Since the modeler is in control of all components, models are ideally suited to study motor control in animals with an integrative perspective, following Richard Feynman's famous quote: "What I cannot create, I do not understand". Neuromechanical simulations and biorobots present multiple interesting properties: (i) they allow the modeler to explicitly determine, implement and modify different components (e.g. feedback loops, CPGs, muscle models); (ii) they provide access to many internal states, including quantities which are impossible to measure in moving animals; (iii) they offer the option to systematically change some properties (e.g. sizes and masses); (iv) they allow for repeatable experiments; (v) they allow 'what-if' scenarios and testing of motor behaviors not observed in nature; and (vi) they allow for multiple types of perturbations and lesion studies. Modeling experiments benefit from an iterative approach, with iterations between animal studies, hypothesis design, model design, (numerical) experiments and predictions (Webb, 2001). They are particularly useful for experiments that cannot be performed on real animals for practical, financial and/or ethical reasons.

The use of neuromechanical simulations and robots to investigate animal behavior has a fairly long history and finds its roots in early work in cybernetics (Ashby, 1957; Wiener, 2019) and in robotics, for instance, with Grey Walter's tortoise robots (Walter, 1950, 1951). Other reviews have addressed the use of simulations and robots to investigate animal behavior (Dickinson et al., 2000; Floreano et al., 2014; Holmes et al., 2006; Ijspeert, 2014; Pearson et al., 2006; Webb, 2001, 2020; Ramdya and Ijspeert 2023). Here, we

314   focus in particular on locomotion and on how simulations and robots can help in the investigation of the
315   interactions between CPGs, sensory feedback loops and descending modulation, and more specifically on
316   interactions between feedforward and feedback control.

Models of lamprey swimming highlight the importance of the CPG in mechanically stable locomotion

319   The lamprey represents a good example of how numerical modeling has contributed to decoding how
320   neural circuits interact with the body to generate swimming. A first contribution of numerical modeling has
321   been to decipher the neuronal and network properties of rhythm generation in the local segmental circuits.
322   The lamprey spinal cord is composed of approximately 100 segments and each segment contains neural
323   oscillators (see Glossary) that are part of the locomotor CPG. Biophysical models of these segmental
324   circuits have shown that several mechanisms play a role in rhythm generation, including contralateral
325   inhibition, frequency adaptation and stretch-sensitive cells (Ekeberg et al., 1991; Hellgren et al., 1992;
326   Traven et al., 1993; Wallén et al., 1992). The relative importance of these mechanisms likely depends on
327   the cycle frequency, which varies extensively in the lamprey (Traven et al., 1993; Wallén et al., 1992).

328   Numerical and mathematical models have also investigated the complete CPG circuits, and how traveling
329   waves of neural activity are generated along the 100 segments of the spinal cord to produce forward
330   swimming (Buchanan, 1992; Ekeberg, 1993; Ekeberg et al., 1995; Ijspeert, 1996; Williams, 1992a, 1992b;
331   Cohen et al., 1982; Kopell et al., 1991; Kopell & Ermentrout, 1988; Williams et al., 1990). It is known that
332   neurons in the local segmental oscillators project up and down the spinal cord, therefore creating couplings
333   between oscillators. The models have shown that the most likely mechanisms to explain the phase lags
334   between oscillators are asymmetries of inter-oscillator couplings, and that other potential explanations
335   such as gradients of intrinsic frequencies and conduction delays are less likely.

336   Finally, models of the lamprey spinal cord have also been connected to simulated bodies in the water, i.e.
337   to form complete neuromechanical simulations (Fig. 5A), in order to relate CPG activity to actual swimming
338   behavior (Ekeberg, 1993; Ekeberg et al., 1995; Ekeberg & Grillner, 1999; Ijspeert, 1996; Thandiackal et al.,
339   2021; Williams & McMillen, 2015). These neuromechanical simulations have demonstrated that the
340   traveling waves of neural activity indeed generate forward swimming, and that modulating the descending
341   drive signals applied to the CPG models can change the speed of swimming as well as induce turning, when
342   symmetric and asymmetric left–right descending pathways are activated (Ekeberg, 1993). These
343   simulations and robotic experiments (Ijspeert & Crespi, 2007) have shown that lamprey-like swimming can
344   be obtained using CPG models without sensory feedback, supporting our hypothesis that CPGs play an
345   important role in mechanically stable locomotion (Fig. 3). In this case the surrounding water provides a
346   kind of mechanical stability (i.e. by preventing large accelerations).

347   Note that sensory feedback still plays a useful role in lamprey swimming. Sensory feedback is necessary
348   for handling perturbations in the water, and neuromechanical simulations have shown the role of stretch
349   receptors (that provide feedback about curvature to the CPG) in coping with changes of flow velocity in the
350   water (Ekeberg et al. 1995; Ijspeert et al., 1999). Thus, there are specific environments that can only be
351   crossed when sensory feedback is included, and cannot be crossed with the CPG in open-loop.

352   Remarkably, a lamprey-like robot (Fig. 5B; Thandiackal et al., 2021) has furthermore shown that local
353   sensory feedback alone (in this case from pressure-sensitive cells in the lamprey skin) could synchronize
354   the oscillators that comprise the CPG when direct coupling is removed. See Hamlet et al. (2023) for a
355   similar finding in a neuromechanical simulation with stretch feedback. In other words, sensory feedback

356 presents an alternative and redundant mechanism for traveling wave generation, separate from direct CPG
357 coupling. This offers a high robustness against lesions, similar to that seen in eels, which can continue
358 swimming despite full transection of the spinal cord (Wallén, 1982). It also suggests that inter-oscillator
359 couplings might be less strong than previously thought (see discussion below).

Models show that CPGs can induce transitions between swimming and walking in amphibians

362 The transition between swimming and walking has been studied in the salamander using neuromechanical
363 simulations and robots (Fig. 5C), (Bicanski et al., 2013; Ijspeert, 2001; Ijspeert et al., 2007; Karakasiliotis et
364 al., 2013, 2016; Knüsel et al., 2020). Because of its amphibious locomotion, the salamander represents an
365 interesting animal to study the transition from water to ground locomotion and to create a bridge between
366 aquatic and terrestrial vertebrate studies (Ryczko et al., 2020).

367 Modeling studies in salamanders have demonstrated that the transition from swimming to ground
368 locomotion can, in principle, be obtained by extending an undulatory swimming circuit with neural
369 oscillators for the limbs, rather than by creating a completely new locomotor circuit for ground locomotion
370 (Ijspeert, 2001; Ijspeert et al., 2007). Modeling reveals that the modulation of two descending drives applied
371 to the left and right sides of the simulated circuits can vary speed, heading and even the type of gait in the
372 simulated and robotic bodies. Thus, the patterns generated by CPGs are not rigidly fixed but can be
373 modulated extensively for adaptive locomotion. Modeling also shows that for simple environments,
374 locomotion can be generated purely in open-loop, i.e. using CPG models without sensory feedback (Ijspeert
375 et al., 2007). This is due to the high mechanical stability of the sprawling posture of salamanders, with a
376 large support polygon and a low center of mass. This therefore supports our hypothesis that mechanically
377 stable locomotion can largely be CPG-driven (Fig. 3). But sensory feedback loops also play an important
378 role. Local proprioceptive (stretch) feedback can reduce the variability of intersegmental phase lags toward
379 values appropriate for locomotion and can simplify the generation of different motor behaviors (Knüsel et
380 al., 2020). Furthermore, sensory feedback could, in principle, also replace direct coupling of CPG oscillators
381 (Suzuki et al., 2021), similarly to what has been found for lamprey-like swimming (Thandiackal et al., 2021)

Models of mammalian legged locomotion inform our understanding of sensory feedback and task coordination

384 The importance of sensory feedback in mammalian legged locomotion has been investigated by Ekeberg
385 and Pearson who developed a neuromechanical simulation of cat (Fig. 5E) with a focus on hindlimbs
386 (Ekeberg & Pearson, 2005). They studied two types of feedback involved in determining the duration of the
387 stance in a leg: one proportional to limb loading and the other proportional to hip extension. Their model
388 did not include a CPG. The study showed that these two types of sensory feedback can generate interlimb
389 coordination corresponding to an alternating gait and can handle irregular terrain. The findings also
390 suggested that limb loading is more important than hip extension in providing sensory feedback. A related
391 study investigated the role of hip extension feedback and CPGs in rat locomotor adaptation to split-belt
392 conditions, in which the right and left legs are on belts with different speeds (Fujiki et al., 2018). Under these
393 conditions, hip extension could be used as a phase-resetting signal to keep the CPG entrained with the
394 mechanical movements of the legs, such as to adapt to the split-belt conditions. These findings are
395 consistent with the hypothesized proximo-distal differentiation in control mechanisms summarized in Fig.
396 4.

397 Controllers inspired by animal CPGs and reflex loops have become popular for the control of legged robots
398 and have also provided new scientific insights (Aoi et al., 2017; Bellegarda & Ijspeert, 2022; Fukuoka et al.,
399 2003; Manoonpong et al., 2007). For instance, load feedback similar to that of Ekeberg and Pearson was
400 used to generate different gaits on a quadruped robot (Fig. 5D) (Owaki et al., 2013; Owaki & Ishiguro, 2017).
401 Each limb was driven by a local oscillator without direct coupling to other oscillators, representing CPGs
402 without direct couplings. Local loading feedback was sufficient to generate stable gaits, showing the
403 importance of the body and physical interactions as mechanisms for synchronizing CPGs. Interestingly,
404 transitions between walking, trotting and galloping gaits could be produced by simply increasing the
405 frequency of the oscillators, as previously shown in decerebrated cats (Shik et al., 1966). This shows the
406 potential role of sensory feedback as a task coordination mechanism (in addition to a role in perturbation
407 responses). Similar principles have been shown in insect models, for instance, for the stick insect (Cruse,
408 1990; Cruse et al., 1995; Daun-Gruhn, 2011; Schilling et al., 2013).

409 More detailed models of mammalian CPGs have been developed by Rybak and colleagues (Danner et al.,
410 2016, 2017; Markin et al., 2016; Rybak et al., 2015). These models reveal how CPG circuits with two layers,
411 one for rhythm generation and the other for pattern formation, can produce several features of quadruped
412 locomotion in open loop (without a body); even gait transitions can be produced by the activation of specific
413 descending pathways (Danner et al., 2017). Thus, it appears that multiple mechanisms could explain gait
414 transition (consistent with our view that animal neuromechanical systems show high redundancy); some
415 transitions are mainly induced through descending modulation, whereas others are mainly driven by
416 sensory feedback. The development of new full-body models of mammalian musculoskeletal systems (see,
417 for instance, Tata Ramalingasetty et al., 2021), will allow the community to investigate gait generation and
418 modulation in more detail. Overall, evidence suggests that CPGs and sensory feedback are equally
419 important in gait generation in quadruped mammals. It is likely that gaits in complex environments require
420 more complex modulation of descending pathways than in simple environments, and therefore involve
421 more cephalized, rather than spinalized, control. Similarly, slow gaits might require more descending
422 modulation than fast gaits, to allow the animal to maintain posture and balance (Fig. 3).

Numerical models suggest that biped locomotion relies more on sensory feedback than on CPGs

425 Some of the first neuromechanical simulations of biped locomotion were developed by Taga and
426 colleagues (Taga, 1995, 1998; Taga et al., 1991). These simulations of human walking demonstrated how
427 robust locomotion could emerge from the interaction of CPGs and reflexes. Multiple studies have since
428 explored the interplay of CPGs and reflexes in biped locomotion with simulations and robots (Aoi et al.,
429 2019; Fujiki et al., 2015; Geyer & Herr, 2010; H. X. Ryu & Kuo, 2021; Van der Noot et al., 2018, 2019). A
430 particularly influential neuromechanical model developed by Geyer and Herr (2010) demonstrated that a
431 limited number of reflexes can generate stable locomotion without the need for CPG circuits (Fig. 5G). The
432 simulated gaits closely match human gait recordings in terms of joint kinematics, ground reaction forces
433 and muscle activities. Although the model did not include a CPG, it did depend on a finite-state machine
434 that selectively activates and deactivates reflexes, so that they are only active at particular phases of the
435 locomotor cycle. One could argue such a gating mechanism represents a similar function as a CPG and
436 could in fact be implemented in a CPG circuit.

437 The Geyer and Herr model has inspired several follow-up models to investigate gait modulation (Dzeladini
438 et al., 2014; Ramadan et al., 2022; Russo et al., 2021; Song & Geyer, 2015), 3D walking and running (Wang
439 et al., 2012), and locomotor pathologies (Bruel et al., 2022; Ong et al., 2019; Song & Geyer, 2018). Control
440 of speed is difficult to achieve with a purely sensory-driven circuit, as it requires the modulation of multiple

441 reflex gains with non-linear functions. Dzeladini et al. (2014) demonstrated that adding CPG circuits to the
442 sensory-driven model of Geyer and Herr could simplify the control of speed (Fig. 5H). They achieved speed
443 regulation over a large range using simple drive signals that modulated the frequencies and amplitudes of
444 the CPG oscillations. Interestingly, they obtained the best speed control by adding oscillators only to the
445 muscles controlling the hip joints. These simulations support the hypothesis proposed by Daley et al.
446 (2007) – based on perturbations to running gaits of birds – that proximal joints are controlled with higher-
447 gain feedforward (CPG) signals and distal joints are controlled by higher-gain feedback signals (Fig. 4).

448 Overall, it is clear from these simulation studies that sensory-feedback loops are essential for human
449 locomotion, supporting our hypothesis that mechanically unstable locomotion is more sensory driven than
450 CPG driven (Fig. 3). CPGs are likely to contribute mainly to speed and gait modulation. Interestingly, the
451 simulations of Geyer & Herr (2010) and most follow-up simulations are not capable of producing slow and
452 very slow walking, because the simulated models simply fall. This suggests more sophisticated balance
453 control mechanisms are missing in the models, and hence these models do not yet properly implement the
454 more important role of descending modulation that we hypothesize for unstable locomotion (Fig. 3).

455 The neuromechanics of bipedal locomotion of birds has been less commonly modeled than human
456 locomotion. One neuromechanical simulation study demonstrated that the sensory-driven control
457 architectures of Geyer & Herr (2010) and Wang et al. (2012) could be adapted to control an ostrich-like
458 body (Geijtenbeek et al., 2013). A number of bird-like robots have also been developed (Apgar et al., 2018;
459 Badri-Spröwitz et al., 2022; Pratt et al., 2001). Among these, BirdBot is particularly interesting, because it
460 implements a bird-inspired tendon system that uses mechanical coupling to control leg stiffness in the
461 stance and swing phases (Fig. 5F). The mechanically coupled design provides self-stable and energy-
462 efficient walking and running with simple CPG-based control and no sensory feedback, highlighting
463 intrinsically stable features of the avian distal limb. This represents therefore another source of
464 redundancy, in which the intrinsic musculoskeletal mechanics contributes to intralimb coordination and
465 balance, aspects that are often considered to be pure control problems.

Open questions

467 Here, we have reviewed historical and current perspectives on the organization of locomotor circuits based
468 on experimental and modeling evidence. Although there are shared features of the component elements
469 across vertebrates, there is also diversity in the relative contributions of these components. We have
470 proposed several hypotheses about how the respective roles of CPGs, reflexes and descending modulation
471 vary across vertebrates: depending on body size, the mechanical instability of gaits, the speed of
472 locomotion and the developmental time to locomotor maturity. We have also hypothesized that these roles
473 can vary within the body, between proximal to distal joints, and depending on the speed and gait. However,
474 to rigorously confirm or reject these hypotheses, we need further integration of animal experiments and
475 neuromechanical simulations.

476 Numerical models can be particularly useful to test some of these hypotheses. For instance,
477 neuromechanical simulations of a pendulum (which can be viewed as a very simple model of a leg) have
478 shown that periodic behaviors can be obtained by either purely feedback or purely feedforward (CPG-
479 based) mechanisms; however, circuits that combine both feedback and feedforward contributions are
480 more robust against unexpected disturbances and sensorimotor noise (Kuo, 2002). Similar results are
481 obtained with a simulation of biped locomotion (Ryu & Kuo, 2021). An interesting proposition from Kuo and
482 colleagues is that CPGs can be viewed as 'state estimators' that predict the state of limbs (and therefore

483 sensory signals). Based on this, a CPG could be viewed as a "filter for processing sensory information
484 rather than as a generator of commands" (Kuo, 2002). In our view, this perspective underestimates the role
485 of CPGs in coordinating and modulating locomotion (e.g. for regulating speed, gait and heading), but it has
486 the merit of analyzing the tradeoff between feedforward and feedback control using rigorous optimal
487 estimation principles. Importantly, the potential roles of the CPG as a pattern generator and a state
488 estimator are not necessarily mutually exclusive – CPGs may act as a type of internal model that filters
489 sensory inputs, estimates current state and generates rhythmic outputs based on current state estimates.

490 Another important open question is related to the degree of centralization of locomotion control and to the
491 strength of inter-oscillator couplings within and across animals (Aoi et al., 2017; Holmes et al., 2006; Neveln
492 et al., 2019; Revzen et al., 2009). Historically, fictive locomotion experiments gave the impression that
493 locomotor patterns were mainly generated by CPGs, and that inter-oscillator couplings serve as the
494 mechanism for inter-joint coordination. However, as presented above, modeling has shown that sensory
495 feedback is another mechanism for synchronization that can replace inter-oscillator couplings (Cruse et
496 al., 1995; Owaki et al., 2013; Thandiackal et al., 2021, Suzuki et al 2021). Biological evidence also shows
497 that local sensory feedback is directly integrated into segmentally distributed CPGs (Grillner et al., 1981;
498 Grillner & Wallén, 1984; Pearson, 2008; Rossignol et al., 2006; Whelan, 1996). Inter-oscillator couplings
499 might therefore be weaker than previously thought. This relatively decentralized control organization would
500 allow for flexible motor patterns to be adapted to environmental constraints, through sensing and
501 modulation of descending pathways.

502 Neveln et al. (2019) have proposed an interesting framework based on mutual information to quantify
503 centralization in animal locomotion, which could help systematically investigate the degree of
504 centralization across species and conditions. They suggest that locomotor coordination "could either be
505 achieved through strong, global coupling with dense connections between components" – representing
506 high centralization – or "through weak, local coupling with sparse connections", representing low
507 centralization. Furthermore, centralization can also be affected by the strength of mechanical coupling and
508 the organization of sensory feedback, whether it is processed centrally or locally (Holmes et al., 2006). They
509 tested their approach in simulation, with robots, and in cockroach experiments. This model-free, empirical
510 method of quantifying centralization will be useful for analyzing future neuromechanical models and
511 animal experiments. It is likely that the level of centralization depends on the morphology and stability of
512 locomotion, as well as on environmental conditions (speed of locomotion and complexity of the
513 environment). Consistent with this, the strength of coupling between legs appears to be speed-dependent
514 in invertebrates (*Drosophila*), with no coupling at low speeds of walking and high coupling at high speeds
515 (Berendes et al 2016). Further research is needed to clarify the mechanisms that enable variation in
516 coupling strength with speed, and to understand the diversity of oscillator coupling strengths across
517 species with varying locomotor demands.

518 Concerning descending modulation, we do not yet know exactly how many independent descending
519 pathways exist, how many local spinal locomotor circuits they project to (global versus local joint-specific
520 projections), and their effect (activating oscillators, changing a joint offset or modulating reflexes, for
521 instance). From several studies (Arber & Costa, 2022; Ferreira-Pinto et al., 2018; Rossignol et al., 2006), we
522 know that descending projections present a mix of these properties. Modeling studies have started
523 exploring how different aspects of legged locomotion (e.g. frequency, step size, ground clearance and
524 others) can be modulated by descending pathways (Song & Geyer 2015, Bellegarda & Ijspeert 2022,
525 Ramadan et al. 2022). But more studies are needed to investigate the diversity of descending pathways
526 across species and how they relate to motor behaviors and mechanical features of the body. Decoding
527 descending pathways will be particularly important in allowing us to understand what types of voluntary

movements an animal can perform (for instance, for gait transitions and for limb placement in visually guided locomotion). Animals can smoothly switch between steady-state locomotion and highly modulated locomotion as needed when crossing a complex terrain. It is likely that this is done by switching from activating a small number of descending pathways to more complex time-varying activations of multiple descending pathways. This is related to the concept of relatively spinalized versus cephalized control, discussed above. Also, some animals appear to be better than others at performing fine-tuned movements, and this may reflect a higher number of descending pathways and a larger role of descending modulation in mammals than in amphibians, for example (Fig. 3). Integration of experimental and modeling work is needed to test these ideas.

Conclusions and outlook

We envision a bright future for the next 100 years of research in this area, with exciting opportunities to integrate experiments and modeling to address open questions about the neuromechanical control of locomotion. Thanks to new imaging techniques and genetic identification methods, future full atlases and connectomes of spinal circuits and descending and ascending pathways will be tremendously useful to improve our understanding of the underlying circuits involved in vertebrate locomotion. For instance, by quantifying the proportion of sensory neurons within the spinal cord and the number of independent descending pathways (Arber & Costa, 2022; Ferreira-Pinto et al., 2018), it will be possible to more quantitatively estimate the respective roles of sensory feedback, CPG and descending modulation across different vertebrate animals. We hope that these techniques will not be limited to classic genetic model animals (e.g. zebrafish and mice), but also used extensively across diverse species to allow comparison between different morphologies and locomotor modes. In particular, compared to the rich literature on terrestrial locomotion, there has been relatively little research on diversity of sensorimotor control mechanisms among flying vertebrates, which is an important area for further study.

Additionally, advances in opto- and chemogenetic techniques represent a tremendous opportunity to selectively activate or deactivate specific cell types, performing experiments that were previously possible only in simulation. There are exciting opportunities for new 'virtual twin' experiments that combine experimental technologies and computing power for simulations; for example, by creating neuromechanical simulations that replicate animal behavior in real-time, it could become feasible to conduct state-dependent animal experiments, in which a perturbation is applied when a modeled internal state from the simulation (e.g. tension in a tendon or phase of an oscillator) reaches a specific threshold. It might also become possible to create hybrid experiments in which a spinal cord preparation is connected in closed loop with a musculoskeletal simulation moving in a virtual physics-based environment. In such an experiment, recorded activity from ventral roots would be used to activate simulated muscles, and virtual sensory signals from the simulated moving body would be used to stimulate sensory neurons. Such preparations would allow one to record and investigate spinal cord circuits with all the technologies available for controlled bench experiments while still approximating *in vivo* conditions of unconstrained locomotion. These kinds of integrative studies will be essential for testing hypotheses about of the fundamental principles of locomotion in vertebrates, understanding how control varies among species, and for guiding functional restoration and therapeutic approaches such as electric epidural stimulation (van den Brand et al., 2012; Wagner et al., 2018).

Figure legends:

Figure 1. Schematic of the neuromechanical system of vertebrates, including the brain, descending drive, spinal networks and intrinsic musculoskeletal mechanics. Temporal scaling of control arises from the spatial distribution of the system components and delays inherent to animal sensorimotor systems. Central pattern generators (CPGs) in the spinal column receive relatively simple descending signals and generate complex rhythmic motor outputs. The CPG rhythm is entrained by sensory feedback in intact animals but generates fictive locomotor patterns in the absence of feedback. Sensory feedback acts in multiple layers, through 1) short-latency monosynaptic reflexes, 2) entraining CPGs, 3) longer latency multi-synaptic sensory feedback, and 4) ascending pathways that contribute to internal models, task planning and modulation of descending commands. Efferent copy from the spinal networks also contributes input into internal models, enabling prediction of sensory signals that are compared to sensory feedback. The plus symbol indicates summation of multiple signal paths to the motor neurons (MN).

Figure 2 Hypothesized differences in the integration of mechanics and control between small and large animals. A) Estimated differences in delays between a shrew and an elephant (More and Donelan 2018; Thangal & Donelan, 2020). Small animals have faster reflex responses relative to movement durations, but synaptic delays are a larger fraction of reflex delays (More and Donelan 2018). Large animals have relatively longer inertial delays (Thangal & Donelan, 2020). **B)** These differences may lead small animals to rely more on reflex feedback, with higher-gain short-latency reflexes (indicated by thicker arrows in B) and intrinsic mechanical preflexes for corrective responses. **C)** In contrast, inertial delays exceed reflex delays in the largest animals, suggesting that reflexes and intrinsic mechanics may not be sufficient to allow stable corrective responses. Consequently, it is expected that large animals must rely more on higher-gain sensory input to internal models for predictive control (indicated by thicker arrows in C). Predictive control is enabled by computations in the brain involving many synapses. The ratio of reflex delay to synaptic delay is much greater in large animals compared to small animals, suggesting a lower penalty for increased computational complexity.

Figure 3: Hypothesized control gradients in the diversity of animal locomotion. A) We hypothesize that the relative roles of spinal sensing and reflexes, CPGs and descending modulation vary among species and between gaits depending on several factors: size, static mechanical stability/instability (estimated based on the ratio between the height of the center of mass and the size of the support polygon), cycle period, which decreases with speed, and time to locomotor maturity, which varies substantially between precocial and altricial species. Animals on the left of these axes rely more on CPGs whereas animals on the right rely more on spinal sensing and reflex, and on descending modulation. We hypothesize that the functional gradients shown exist across taxa; nonetheless, phylogenetic differences are not represented here, and the contributions of descending control likely vary substantially among taxa. The gradients should be interpreted conceptually rather than as an absolute scaling. B) Static mechanical instability is related to the ratio of the height of the center of mass compared to the size of the support polygon.

Figure 4. Hypothesized proximo-distal differentiation in the balance of feedforward and feedback control of limb muscles. Due to differences in muscle−tendon architecture and inertia of the proximal versus distal limb, it is expected that proximal muscles exhibit higher-gain feedforward control, with length and position feedback entraining the rhythm of the CPG oscillators, influencing stance and swing frequencies. In contrast, distal muscles, with higher compliance and lower inertia, are expected to have higher-gain short-latency reflexes, and higher contributions from intrinsic mechanics ('preflexes'). The width of the arrows showing the reflexes (purple) and CPG (green) are proportional to the hypothesized gains. For clarity, the peripheral circuits are drawn only for the flexors, but similar connections exist for the extensors. The plus symbol indicates summation of multiple signal paths to the motor neurons (MN).

Figure 5. Robots and neuromechanical simulations. Multiple robots and neuromechanical simulations have been used to investigate the roles of CPGs, sensory feedback and mechanical properties in the generation of animal locomotion. (A) Ekeberg (1993), image used with permission from Springer Nature.

Glossary

Altricial: Animals that take extended time after birth to reach locomotor maturity.

Central pattern generator (CPG): Neural circuits that can generate the basic rhythmic motor patterns for movement and breathing without any sensory inputs. These circuits produce periodic signals that are often mathematically modeled as oscillators (see below). A defining feature of a CPG is that it can generate a periodic motor output without a periodic input.

Compliance: Elastic deformation of a mechanical system. Compliance can be viewed as the opposite of stiffness.

Control theory: Field of applied mathematics that deals with the control of dynamical and engineered systems.

Decerebrate preparations: An experimental manipulation in which cerebral brain function is eliminated by transection or removal of the cerebrum. The extent to which longer-latency feedback pathways remain intact or eliminated depends on the specific location of the transection.

Dynamic stability: Stability of a gait that requires movement to prevent falling (as opposed to static stability, see below). Typically, a dynamically stable gait exhibits convergence to a limit cycle behavior, namely periodic behavior that is robust against (small) perturbations.

Efferent copy: A copy of the motor signals that are used as inputs to internal models to predict dynamics and sensory feedback.

Entrainment: Synchronization of oscillatory dynamical systems such that they converge to the same frequency and therefore to constant phase differences. Two dynamical systems can mutually entrain each other (and converge to a frequency that is typically an average of their intrinsic frequencies), or one dynamical system can entrain another (and impose its intrinsic frequency on the other).

Feedback control: A control pathway in which sensory signals are returned back to generate an error signal that regulates the input commands towards desired output dynamics.

Feedforward control: A control pathway that generates a predefined command signal based on the anticipated load and dynamics of the system. In this article, we discuss two types of feedforward control mechanisms: spinal CPGs and supraspinal internal models.

Fictive locomotion: The generation of the basic rhythmic muscle activation patterns required for locomotion in isolated spinal cords, such as the alternating activation of flexors and extensors in the

leg of walking animals or the transmission of an undulatory wave down the body in swimming animals.

Internal models: Internal neural representations that can predict the interactions between the nervous system, the musculoskeletal system and the environment. Forward internal models can predict causal relationships between actions and their consequences. Inverse internal models can predict which actions are needed to reach particular consequences.

Model-based control: Control architecture that uses internal models for performing anticipatory (as opposed to reactive) movements. An example of model-based control in robotics is model-predictive control, which uses a model of the robot and an optimization criterion to define motor commands over a finite-time horizon.

Neuromechanics: The scientific field focused on the interactions between biomechanics of the musculoskeletal system and sensorimotor control and their integration for robust and agile movement.

Oscillators: Dynamical systems or neural networks that exhibit stable limit cycle behavior, i.e. they produce periodic signals.

Precocial: Animals that locomote effectively shortly after birth.

Preflexes: The intrinsic dynamic properties of the musculoskeletal system in its activated state that automatically stabilize movements through visco-elastic properties. These form a kind of zero-delay feedback stabilizing movement.

Sensorimotor delay: The time lag between the onset of a mechanical perturbation and its reception by a sensory organ to the development of peak muscle force in response to the perturbation. It includes sensing delay, nerve conduction delay, synaptic delay, neuromuscular junction delay, electromechanical delay and muscle force development delay.

Spinal preparations: An experimental manipulation in which the brain and brainstem function are completely removed by transection of the spinal cord, typically in the thoracic region.

Static stability: Stability of a posture or a gait in which the center of mass is always maintained above the (possibly time-varying) support polygons formed by the contacts between the limbs (or any body parts) and the ground. An animal that is statically stable will not fall when it freezes its posture.

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Box 1: Central Pattern Generators (CPGs)
CPGs play important roles in the generation of coordinated motor patterns for both vertebrate and invertebrate locomotion. CPGs are neural circuits that can generate the basic rhythmic motor patterns for movement and breathing without any sensory inputs. Locomotor CPG circuits are located in the spinal cord of vertebrates (Grillner and El Manira, 2019), and in the ventral nerve cord of invertebrates (Mantziaris et al., 2020). The existence of CPGs has been demonstrated across diverse vertebrate species through the observation of fictive locomotion in spinal preparations, with all inputs from the brain and periphery transected (Gray, 1936; Gray and Lissmann, 1940; Grillner and Wallén, 1982; Ho and O'Donovan, 1993; Sholomenko et al., 1991; Sholomenko and Steeves, 1987; Ten Cate, 1964, 1965). The CPG circuits in the isolated spinal cord generate fictive swimming in aquatic species (e.g. lamprey, zebrafish), fictive walking in terrestrial species (birds, mammals), and both fictive swimming and fictive walking in amphibious species (e.g. salamanders) (Chevallier et al., 2008; Fetcho and McLean, 2010; Grillner and El Manira, 2019; Grillner and Wallen, 1985; Ryczko et al., 2010; Whelan, 1996). Genetic studies have identified specific subpopulations of interneurons involved in rhythm generation that are conserved across vertebrates (Grillner and El Manira, 2019; Kiehn, 2016; Rybak et al., 2015). Locomotor CPGs are distributed segmentally along the spinal cord as interconnected rhythmic units (Grillner et al., 1995; Kiehn, 2016; McLean and Dougherty, 2015; Rybak et al., 2015), typically one per pair of antagonist muscles or even one per muscle (Cheng et al., 1998). Specific ventrolateral regions of the spinal cord generate flexor/extensor alternation, and specific ventromedial interneurons generate left/right coordination (Kiehn, 2016; McLean and Dougherty, 2015). Note that although there is no direct evidence of CPG circuits in humans, there is ample indirect evidence that humans possess CPG circuits similar to those of other vertebrate species (Minassian et al., 2017).

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Neuromechanical system
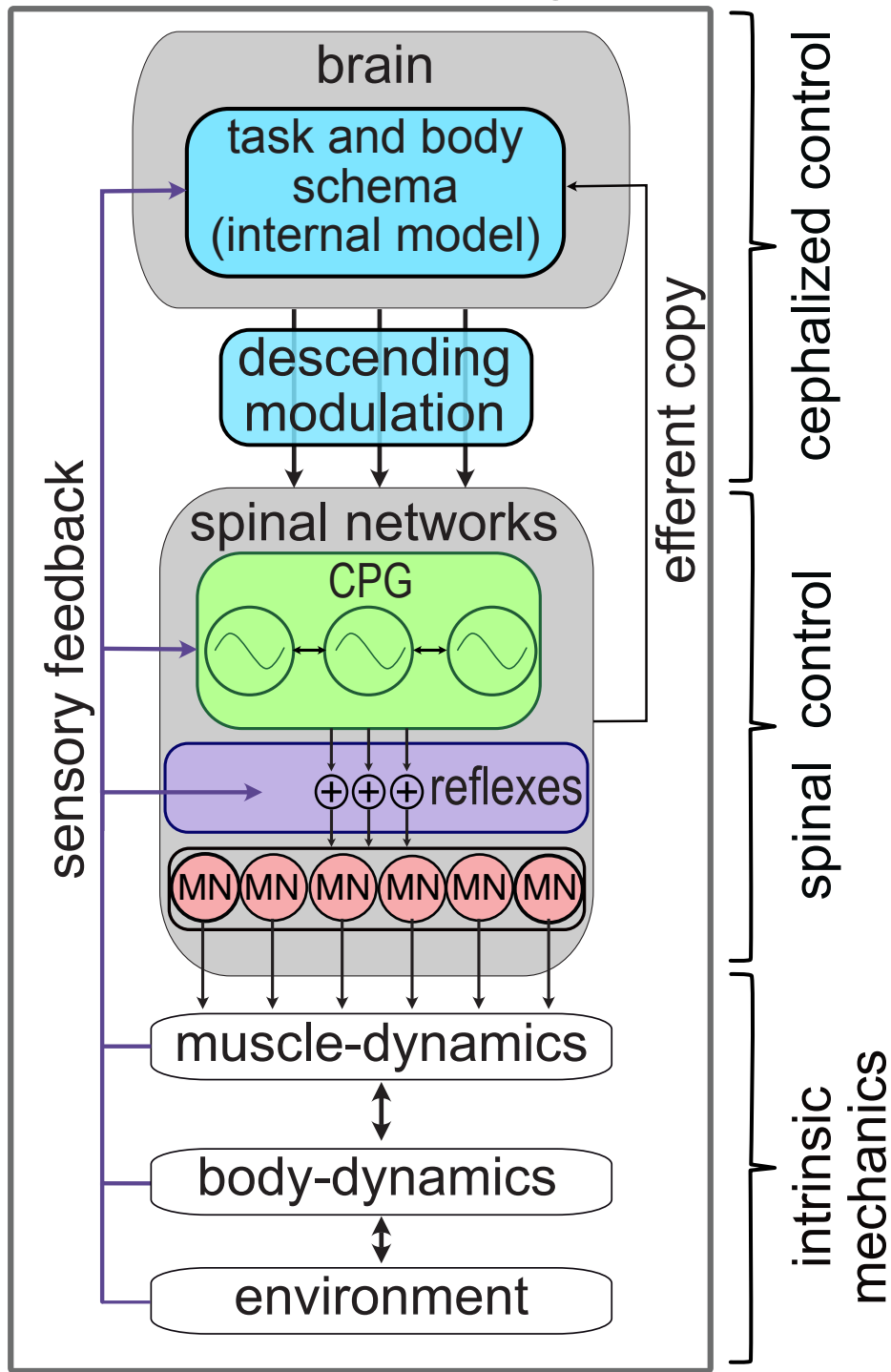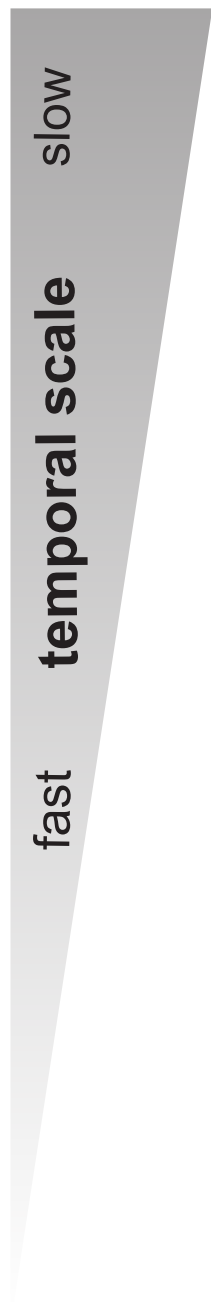
A Delay estimates
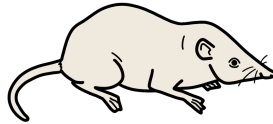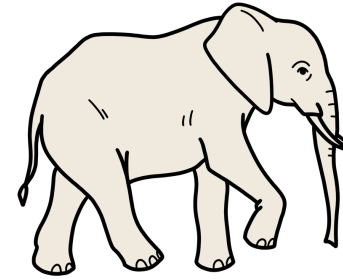
	shrew	elephant
synaptic	0.7 ms	0.7 ms
monosynaptic reflex	10 ms	180 ms
inertial delays	3−5 ms	200−400 ms
reflex:inertial	2−3.3	0.9−0.5
reflex:synaptic	14	260
reflex:stance duration	0.25	0.6

B Small animals

brain
task and body schema (internal model)
descending modulation
spinal networks
CPG
reflexes
MN MN MN MN MN MN
muscle-dynamics
body-dynamics
environment
sensory feedback
efferent copy

Simpler internal models

Simpler descending modulation

Faster reflexes

Lower inertia, **faster** corrective responses

C Large animals

brain
task and body schema (internal model)
descending modulation
spinal networks
CPG
reflexes
MN MN MN MN MN MN
muscle-dynamics
body-dynamics
environment
sensory feedback
efferent copy

More complex internal models

More complex descending modulation

Slower reflexes

Higher inertia, **slower** corrective responses

A

Respective Role in motor control

100%

Descending modulation — Cephalized control

Central pattern generators

Spinal sensing and reflexes — Spinal control

Size
Shrew
Elephant
Small animals
Large animals

Mechanical (static) instability
Lamprey
Salamander
Cat
Ostrich
Human
Low instability
High instability

Locomotor period
Cockroach
Galloping horse
Walking horse
Stick insect
Fast locomotion
Slow locomotion

Time to locomotor maturity
Chicken
Deer
Dog
Pelican
Human
Precocial species
Altricial species

B

Height of center of mass

Size of support polygon

Mechanical (static) instability

Proximal

Mainly CPG-driven
Length and position feedback
High inertia
Low compliance
Low 'preflexes'

Distal

Mainly sensory-driven
Force and velocity feedback
Low inertia
High compliance
High 'preflexes'

Descending modulation

Reflexes

CPG

Proximal
Flexors

Proximal
Extensors

Distal
Flexors

Distal
Extensors

MN

A Neuromechanical simulation of lamprey: CPG circuits can control speed and heading

Descending modulation
CPG

B Robotic anguiliform swimmer Agnathax: Sensory feedback can replace intersegmental couplings for generating swimming

Descending modulation
CPG
Pressure Feedback

C Salamandra robotica: CPG circuits can modulate speed, heading and type of gait

Descending modulation
CPG

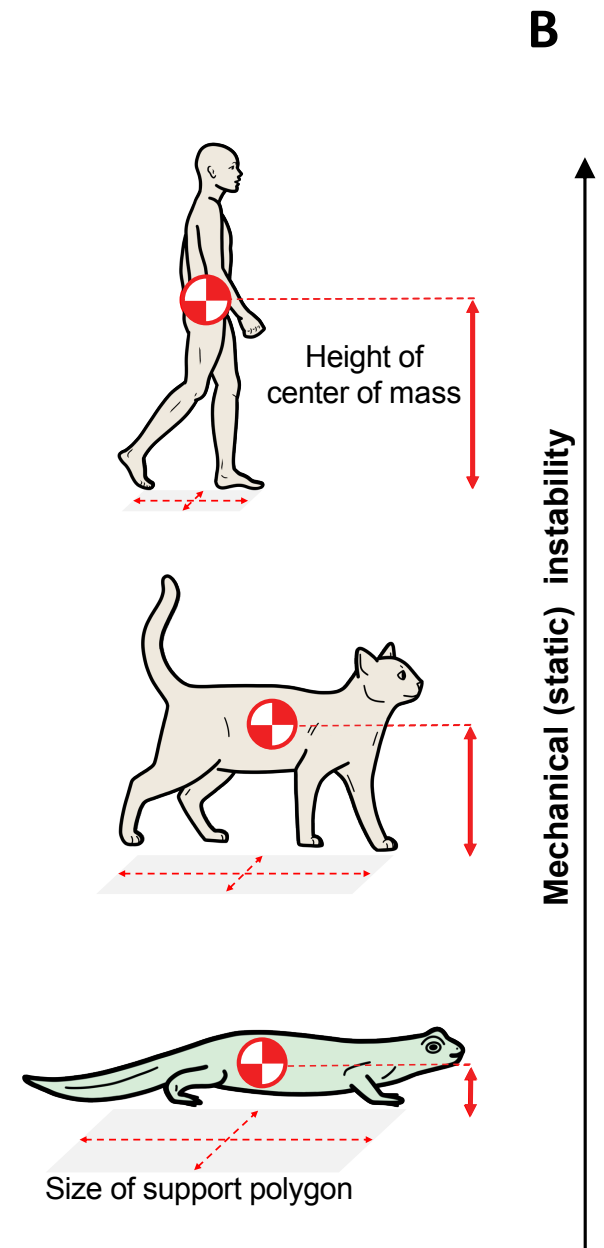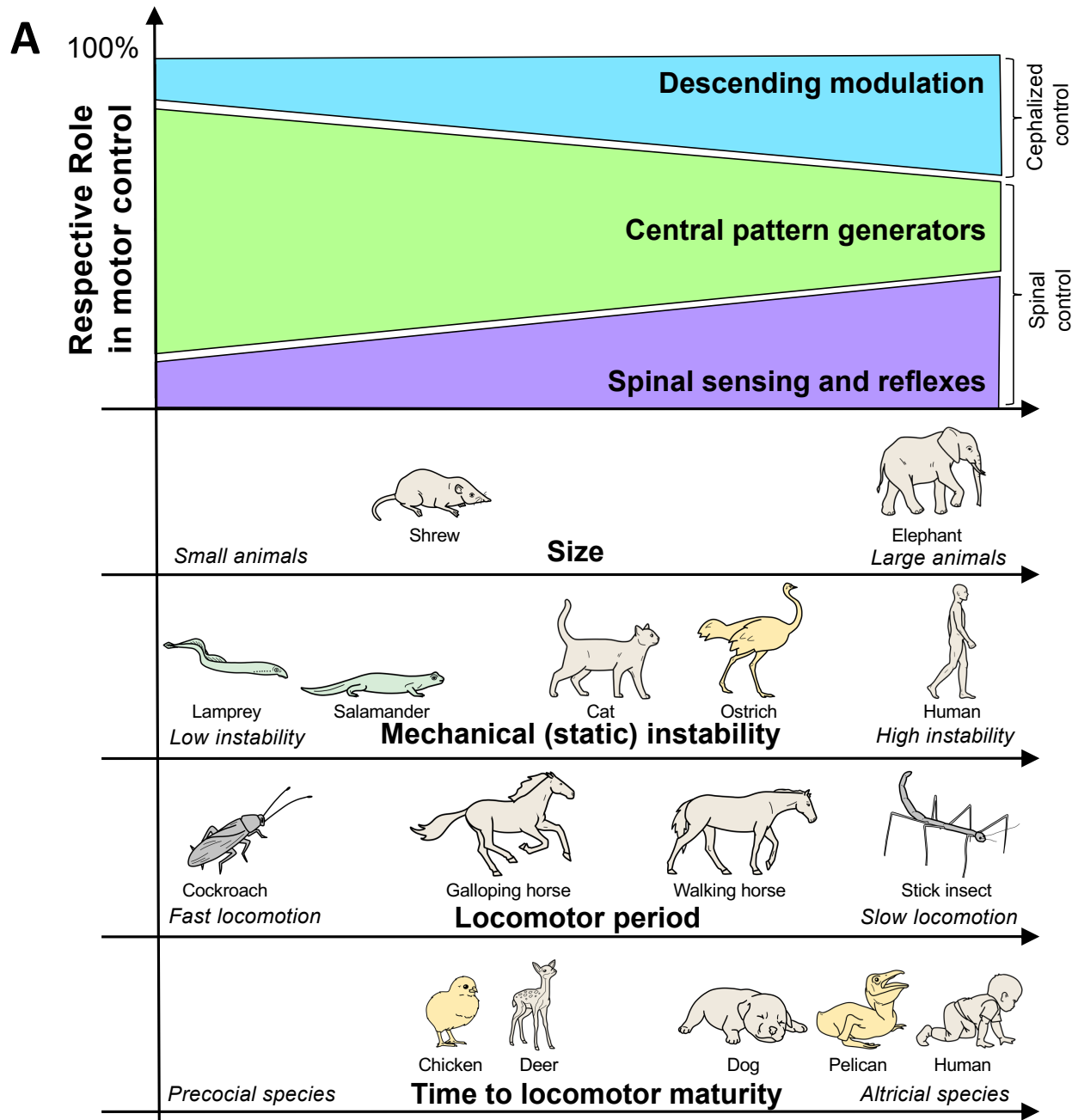**D** Quadruped robot: different synchronized gaits can be generated based on load feedback, direct coupling between oscillators is not necessary

Descending modulation
CPG
Limb load Feedback

E Neuromechanical simulation of cat: two feedback loops based on ankle-loading and hip extension can generate stable alternating gaits

Hip extension Feedback
Limb load Feedback

F Biped bird-like robot BirdBot: mechanical couplings lead to self-stabilizing and energy efficient walking and running

Descending modulation
CPG

G Neuromechanical simulation of human: stable locomotion can be generated based on sensory feedback loops without CPGs

Multiple Feedbacks
GLU   HFL
HAM   VAS
SOL   TA
GAS

H Neuromechanical simulation of human: CPG can simplify the control of speed (compared to sensory feedback control)

Descending modulation
CPG

Lamprey

Salamander

Cat

Ostrich

Human

Low instability → **Mechanical (static) instability** → *High instability*