PROCEEDINGS B

rspb.royalsocietypublishing.org

Research

**Cite this article:** More HL, Donelan JM. 2018 Scaling of sensorimotor delays in terrestrial mammals. *Proc. R. Soc. B* **285**: 20180613. http://dx.doi.org/10.1098/rspb.2018.0613

Received: 19 March 2018
Accepted: 31 July 2018

**Subject Category:**
Neuroscience and cognition

**Subject Areas:**
biomechanics, neuroscience, physiology

**Keywords:**
motor control, biomechanics, neuromechanics, locomotion, nerve, muscle

**Author for correspondence:**
J. Maxwell Donelan
e-mail: mdonelan@sfu.ca

Electronic supplementary material is available online at https://dx.doi.org/10.6084/m9.figshare.c.4189679.

THE ROYAL SOCIETY PUBLISHING

# Scaling of sensorimotor delays in terrestrial mammals

Heather L. More and J. Maxwell Donelan

Department of Biomedical Physiology and Kinesiology, Simon Fraser University, 8888 University Drive, Burnaby, British Columbia, Canada V5A 1S6

HLM, 0000-0002-7514-2199; JMD, 0000-0003-3880-893X

Whether an animal is trying to escape from a predator, avoid a fall or perform a more mundane task, the effectiveness of its sensory feedback is constrained by sensorimotor delays. Here, we combine electrophysiological experiments, systematic reviews of the literature and biophysical models to determine how delays associated with the fastest locomotor reflex scale with size in terrestrial mammals. Nerve conduction delay is one contributor, and increases strongly with animal size. Sensing, synaptic and neuromuscular junction delays also contribute, and we approximate each as a constant value independent of animal size. Muscle's electromechanical and force generation delays increase more moderately with animal size than nerve conduction delay, but their total contribution exceeds that of the four neural delays. The sum of these six component delays, termed total delay, increases with animal size in proportion to $M^{0.21}$—large mammals experience total delays 17 times longer than small mammals. The slower movement times of large animals mostly offset their long delays resulting in a more modest, but perhaps still significant, doubling of their total delay relative to movement duration when compared with their smaller counterparts. Irrespective of size, sensorimotor delay is likely a challenge for all mammals, particularly during fast running.

## 1. Introduction

An animal's life can hinge on how quickly it can sense and respond to stimuli. Responding slowly to a large disturbance, such as when tripped by an unseen rock or ambushed by a predator, risks injury or death. Effective feedback control can allow an animal to sense when it is pushed, chased or otherwise disturbed, and then generate the appropriate motor command to recover, escape or otherwise reject the disturbance. However, long sensorimotor delays limit the effectiveness of using feedback during fast movements—when an animal's state is changing quickly, a response based on a past state can be inappropriate for its current state [1–5]. Animals can compensate for sensorimotor delays to some extent by relying on mechanical self-stabilization to help compensate for disturbances [3,4,6–10], or using prediction to provide an estimate of their future state [5,11,12]. But if all other factors are equal, an animal with shorter sensorimotor delays can more effectively respond to disturbances and control its movement.

An animal's size may have a substantial effect on its sensorimotor delays. For example, we previously found that one sensorimotor delay—nerve fibre conduction velocity—remains nearly constant across the full size range of terrestrial mammals, indicating that the time required for a nerve fibre to transmit information increases in direct proportion to the length of the fibre [13]. Larger animals have longer peripheral nerve fibres due to their longer limbs and thus are faced with longer nerve conduction delays. These longer delays are partially offset by the longer movement durations of larger animals—they have more time available to respond to a disturbance during the stance phase of a step, within a stride or before they fall to the ground. But movement durations do not increase as sharply as nerve conduction delay,

changing only with the square root of limb length [14–16]. Consequently, the ratio between nerve conduction delay and movement duration is about 10 times higher in an elephant than in a shrew [13]. The scaling of other sensorimotor delays with animal size has not previously been studied, but if they were all size-independent, our observed scaling of nerve conduction delay would result in total delays that increase strongly with animal size and outpace increases in movement duration. This would place large animals at a significant disadvantage for effective feedback control.

Given the importance of feedback control for movement, the implications of sensorimotor delays for effective feedback control and the potential size dependence of delays, we sought to determine how total sensorimotor delay scales with size in terrestrial mammals. Here, we define total delay as the time elapsed between a stimulus that evokes a stretch reflex and the resulting peak twitch force (we use the terms total delay and total sensorimotor delay interchangeably in this paper). We chose to focus on stretch reflexes because they govern the fastest neural response to peripheral stimuli in terrestrial mammals of all sizes, providing a useful means to benchmark these animals' minimum sensorimotor delay. Stretch reflexes use the fastest peripheral nerve fibres to conduct information and employ only a single synapse within the spinal cord to transform a sensory signal into a motor command [17]. Although more complex pathways involving multiple spinal synapses and higher-level brain centres also play important roles in responding to disturbances [18,19], they always require more time than that for a simple stretch reflex. The total sensorimotor delay, as we have defined it here, has contributions from six main sources. We refer to these sources as component delays, and term them sensing delay, nerve conduction delay, synaptic delay, neuromuscular junction delay, electromechanical delay and force generation delay (figure 1).

Based on our previous findings for nerve conduction delay, we hypothesized that not only would total delay increase in larger animals in an absolute sense, but that it would also increase when expressed relative to movement duration. This hypothesized scaling is not inevitable, because distinct physiological processes underlie the component delays. Consequently, their contributions to total delay may scale differently than what we previously observed for nerve conduction delay [13], offsetting or adding to its effect. We focused on two characteristic movement durations: stride duration, because it is the maximum time available for the nervous system to make adjustments for the next step [20]; and stance duration, because it is the maximum time available to respond to a disturbance within the same step. To test our hypothesis, we combined our findings from previous studies with existing literature data to determine component delays and their total combined delay as function of animal size. We then calculated changes in stride duration and stance duration as a function of animal size, and compared these to our results for total delay. To better understand the mechanisms underlying component delays, and to test our identified scaling relationships, we examined the behaviour of established biophysical models as we incorporated size-dependent model parameters. Our analysis focused exclusively on terrestrial mammals. Owing to the availability of reliable data that met our inclusion criteria, the sizes of our datasets varied between

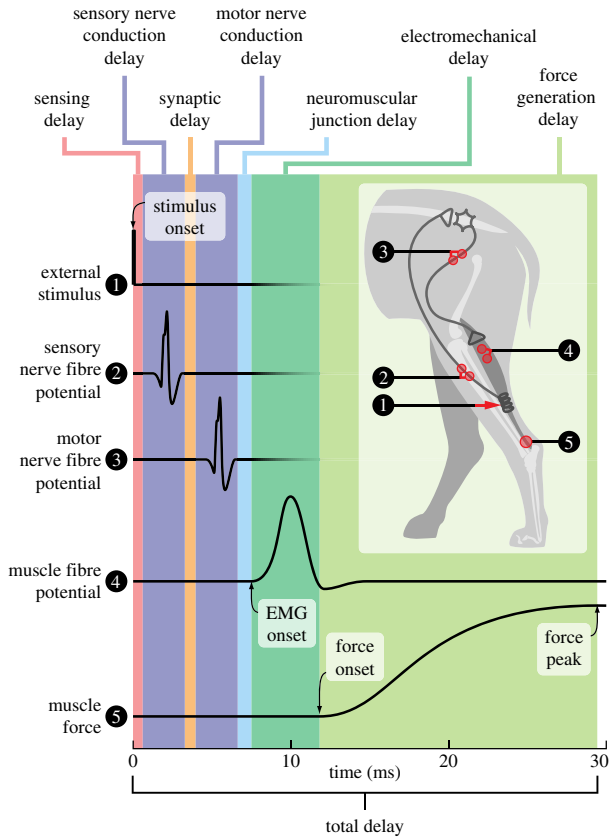


**Figure 1.** Component delays superimposed on example recordings of nerve fibre activity, muscle activity and muscle force. The total time between stimulus onset and peak muscle force, termed total delay, incorporates several sources of delay, termed component delays. Here, we conceptually illustrate component delays by showing their predicted durations for a hypothetical 1 kg animal (coloured areas), calculated from the results of our systematic review (table 1). We considered component delays in the context of the simple monosynaptic reflex pathway initiated by an external stimulus such as a tendon tap. We defined sensing delay as the time from the onset of a stretch in the ankle extensor muscles to the generation of an action potential in a stretch-sensitive sensory receptor, nerve conduction delay as the time to transmit the action potential along the length of the sensory and motor nerve fibres, synaptic delay as the time for the action potential to be transferred from the sensory nerve fibre to the motor nerve fibre at a single synapse in the spinal cord, neuromuscular junction delay as the time for the action potential to be transferred from the motor nerve fibre to muscle fibres at the neuromuscular junction in the muscle, electromechanical delay as the time for the action potential to be conducted along muscle fibres and for molecular mechanisms involved in cross-bridge formation to be activated, and force generation delay as the time for the muscle to develop peak twitch force. We include the time lag to the peak force response as part of the total sensorimotor delay, with the understanding that the first onset of force precedes peak force. Electromyography (EMG) onset = the onset of electrical activity in the muscle, as detected by EMG.

component delays. While it was as small as three data points in a single species for one component delay, it spanned six orders of magnitude in mass, ranging from shrews to elephants, for another.

## 2. Material and methods

First, we searched the literature for component delays of the monosynaptic stretch reflex in the medial gastrocnemius, measured in terrestrial mammals across their full range of

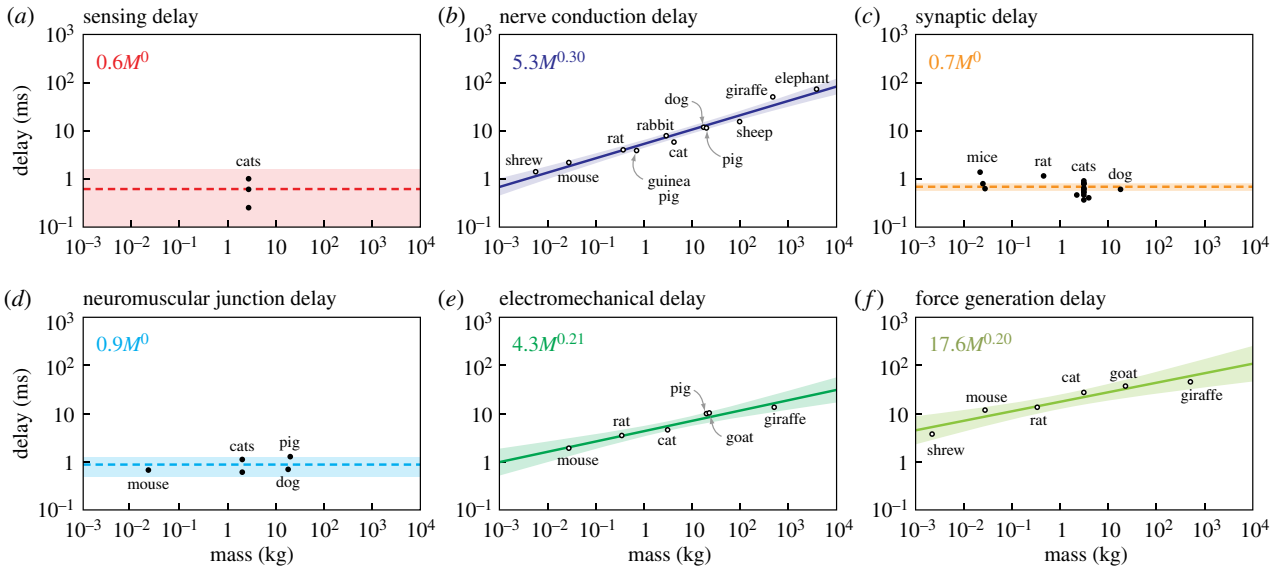


**Figure 2.** Component delay scaling relationships. Each plot shows one scaling relationship from table 1 (coloured lines and coloured text). Dashed lines in (*a*), (*c*) and (*d*) are averages of all data points (filled circles); solid lines in (*b*), (*e*) and (*f*) are regressions of species averages (open circles). Shaded areas are 95% confidence intervals for mean delay at a given mass. All plots have the same axis units.

masses. We used the resulting data to determine the power law relationship describing the scaling of each component delay with body mass; a phylogenetically independent contrasts analysis indicated that our data were not significantly affected by evolutionary history. Next, we calculated the scaling relationship for total delay by numerically adding predicted component delays for hypothetical animals spanning the range of masses in our systematic review, then fitting a power law to the results. We calculated relative delay by normalizing total delay by stride duration and by stance duration at two equivalent speeds: trot–gallop transition speed, because it is physiologically similar for animals of different sizes [15,16], and maximum sprint speed, because it represents a lower bound on stride and stance duration. Monte Carlo simulations propagated uncertainties in the individual component delay estimates and gait parameter estimates through our entire calculations. Finally, we simulated the size dependence of key mechanisms—neurotransmitter diffusion delay, muscle fibre conduction delay and the dynamics of muscle's force production—involved in four component delays. Additional details of our methods, and data from our systematic reviews, are given in the electronic supplementary material.

## 3. Results

We assume that some component delays are constant and found that others increase with animal size (figure 2 and table 1). We did not measure sensing delay, synaptic delay and neuromuscular junction delay here or in our prior experiments, and these three delays were too sparsely reported in the literature to determine whether they changed with size in terrestrial mammals (figure 2*a*,*c*,*d*). We preliminarily considered these three component delays as size-independent (see Discussion). For our calculations of total delay, we set each of these delays equal to its average value from the literature—approximately 0.6 ms for sensing delay, 0.7 ms for synaptic delay and 0.9 ms for neuromuscular junction delay (table 1). By contrast, nerve conduction delay, electromechanical delay and force generation delay increase with animal size (figure 2*b*,*e*,*f*). Of these three increasing delays, nerve conduction delay increased most strongly, in proportion to $M^{0.30\pm0.04}$, while electromechanical delay and force generation delay increased in proportion to $M^{0.21\pm0.07}$ and $M^{0.20\pm0.08}$, respectively (table 1; all exponents are shown as their mean ± 95% confidence interval). The scaling exponent for nerve conduction delay was significantly larger than the exponent for force generation delay but not for electromechanical delay ($p = 0.02$ and $p = 0.10$, respectively; multiple comparison test with Tukey's honestly significant difference criterion), while the exponents for electromechanical delay and force generation delay were not significantly different from each other ($p = 0.91$). As a consequence of its relatively strong dependence on size, nerve conduction delay was one of the shortest component delays in small animals, at about 1 ms, but in large animals it became one of the longest, at about 70 ms. Force generation delay was the longest component delay in animals of all sizes and measured about four times as long as electromechanical delay—in a 5 g shrew, electromechanical delay and force generation delay are approximately 1 ms and 6 ms, respectively, whereas in a 5000 kg elephant they are approximately 25 ms and 95 ms, respectively (table 1).

Owing to the size dependence of some component delays, total delay increases with animal size (figure 3*a* and table 1). This increase is in proportion to $M^{0.21\pm0.06}$, giving a shrew a total delay of just 10 ms while an elephant has a total delay of about 180 ms. As animal size increases, nerve conduction delay makes up a larger fraction of total delay, while the contributions of the constant component delays (sensing, synaptic and neuromuscular junction delay) decrease (figure 4). For terrestrial mammals of all sizes, the combined contributions of electromechanical delay and force generation delay to total delay remain approximately constant (figure 4). Most of total delay is due to delays within the muscle, rather than within the nervous system—muscle delay, calculated as the sum of electromechanical and force generation delay, comprised approximately 70% of total delay across all animals, with neural delays responsible for the remainder.

Relative delay is nearly constant across animal size. To calculate relative delay, we normalized total delay by stride duration and by stance duration at two different speeds: trot–gallop transition speed and maximum sprint speed.

**Table 1.** Delay scaling relationships and statistics. The magnitude in milliseconds of each delay is given by $aM^b$, where $a$ is the coefficient, $b$ is the exponent and $M$ is animal mass in kilograms. Sensing, synaptic and neuromuscular junction delays have exponents equal to zero, and no regression statistics, because they were determined by averaging all data points for each delay. 95% confidence intervals (CIs) for mean sensing, synaptic and neuromuscular junction delays are given as +/− intervals, because they were calculated using a standard formula based on the standard deviations of data points (electronic supplementary material). CIs for the coefficients of nerve conduction, electromechanical and force generation delays are given as ×/÷ intervals, because they were determined by transforming CIs for regression intercepts calculated from logarithmically transformed data. Total delay and relative delays have no regression statistics, because they were calculated from scaling relationships rather than from data points; 95% CIs for their coefficients and exponents were determined using Monte Carlo simulations (electronic supplementary material).

| | coefficient ($a$) | | exponent ($b$) | | regression statistics | |
|---|---|---|---|---|---|---|
| delay | value | 95% CI | value | 95% CI | $p$-values | $R^2$ |
| sensing | 0.6 | +/− 0.9 | 0 | | | |
| nerve conduction | 5.3 | ×/÷ 1.2 | 0.30 | +/− 0.04 | <0.001 | 0.96 |
| synaptic | 0.7 | +/− 0.1 | 0 | | | |
| neuromuscular junction | 0.9 | +/− 0.4 | 0 | | | |
| electromechanical | 4.3 | ×/÷ 1.3 | 0.21 | +/− 0.07 | 0.001 | 0.94 |
| force generation | 17.6 | ×/÷ 1.4 | 0.20 | +/− 0.08 | 0.003 | 0.91 |
| total | 31.0 | ×/÷ 1.3 | 0.21 | +/− 0.06 | | |
| *total relative to stride duration* | | | | | | |
| at trot–gallop transition | 0.14 | ×/÷ 1.3 | 0.07 | +/− 0.05 | | |
| at maximum sprint | 0.16 | ×/÷ 1.3 | 0.04 | +/− 0.05 | | |
| *total relative to stance duration* | | | | | | |
| at trot–gallop transition | 0.33 | ×/÷ 1.3 | 0.07 | +/− 0.05 | | |
| at maximum sprint | 0.70 | ×/÷ 1.3 | 0.07 | +/− 0.06 | | |

All four of these movement duration measures increase proportional to approximately $M^{0.14}$. Total delay increases with size in proportion to $M^{0.21}$, comprising nearly constant fractions of stride and stance duration and resulting in a weak dependence of relative delay on animal size (approx. $M^{0.07\pm0.05}$ for all speeds and durations; figure 3*b* and table 1). Consequently, relative delays only double in large animals when compared to their smaller counterparts. In a 5 g shrew, for example, total delay would comprise approximately 25% of stance duration at the trot–gallop transition speed, whereas in a 5000 kg elephant it would require approximately 60%. While the duration of relative delay may be more problematic for large animals, sensing and responding to a stimulus requires a substantial fraction of movement duration in animals of all sizes. This is especially the case at fast speeds, where the minimum sensorimotor delay between stimulus and response consumes most of the time that a foot spends in contact with the ground (figure 3*b*, black dashed line).

## 4. Discussion

Remarkably, and in contradiction to our hypothesis, increases in total delay with increases in animal size are mostly offset by the longer movement durations of larger animals. Thus, despite a 1-million-fold range in mass, a 100-fold change in leg length and a more than 15-fold difference in absolute delay, relative delays in the largest terrestrial mammals are only double the duration of those in the smallest. Nerve conduction delay increases most sharply with size, but does not result in exceptionally long relative delays for large animals because it is balanced by sensing, synaptic and neuromuscular junction delays, which we have assumed do not depend on size. The sum of these four component delays increases with mass less sharply than nerve conduction delay alone and with approximately the same exponent as electromechanical delay and force generation delay. As a consequence, the sum of all six component delays increases with about the same exponent as stance duration, and other measures of movement duration such as stride period and the time it takes to fall to the ground (figure 3) [14–16].

### (a) Sensing, synaptic and neuromuscular junction delays

The durations of component delays, and how these durations scale with size, depend on their underlying physiological processes. Synaptic delay and neuromuscular junction delay are governed by fast biophysical processes that begin with the release of neurotransmitter molecules from the presynaptic neuron, which then diffuse across a narrow gap to the postsynaptic cell and bind to receptors, changing the conductance of the postsynaptic membrane and eventually generating an action potential in the postsynaptic cell [21–23]. For these delays to change substantially with animal size requires changes to the speed of neurotransmitter release from the presynaptic cell, the distance between cells or the function of ion channels in the postsynaptic cell. Our data for synaptic and neuromuscular junction delays were too sparse to determine their scaling relationships, but major size-dependent changes seem unlikely given that presynaptic and postsynaptic

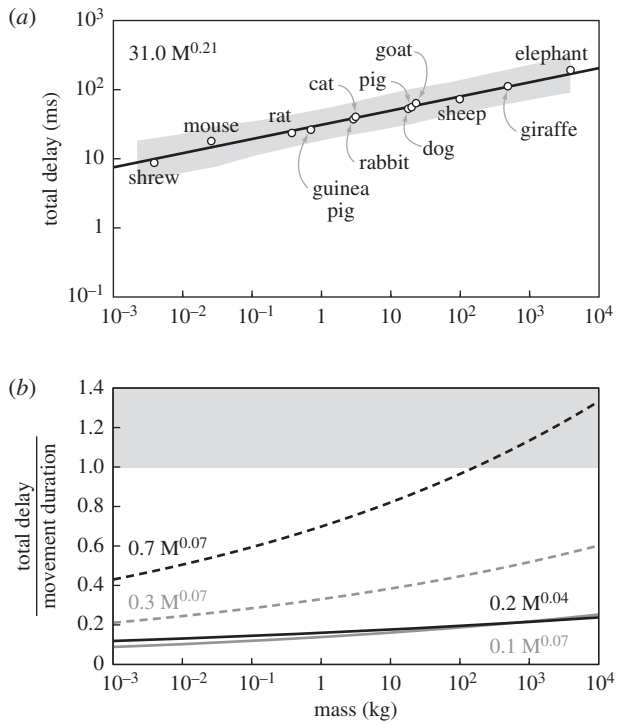


**Figure 3.** Total delay and relative delay. (*a*) Total delay, calculated by least-squares regression of the sum of scaling relationships in figure 2 (black line). We estimated total delay for each species (open circles) by adding the species' component delays; we used data points from figure 2 where possible, and predictions from the power law relationships in table 1 where the species had no data points. Monte Carlo simulations determined the uncertainty in our total delay relationship by propagating the error from each component delay; the shaded area encloses 95% of simulation values. (*b*) Total delay relative to stride duration (solid lines) and stance duration (dashed lines) at trot–gallop transition speed (grey) and maximum sprint speed (black). We calculated relative delay by dividing total delay by each movement duration at each speed. The shaded area indicates the region where total delay exceeds movement duration. Scaling relationships for all delays are given in table 1.

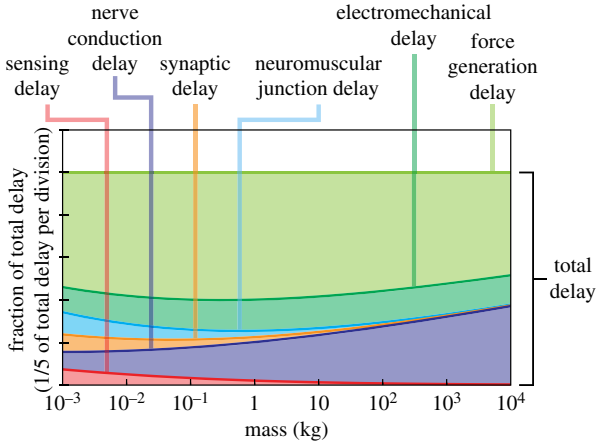


**Figure 4.** Component delays (coloured areas) expressed as fractions of total delay. The fraction of an animal's total delay required by each component delay is represented by the vertical thickness of the corresponding coloured area at the horizontal location appropriate for the animal's mass.

cell size, as well as the general structure of ion channels, remain relatively constant across a wide size range of animals [13,24–26]. It is not known how the distance between cells scales with animal size, but simulations conservatively assuming that it scales proportional to $M^{1/3}$ predict negligible increases to neurotransmitter diffusion times (electronic supplementary material). Sensing delay shares some of the same fast biophysical processes as synaptic delay—a physical stimulus changes the conductance of the receptor membrane to specific ions, allowing ions to flow across the membrane and generate an action potential in the sensory nerve fibre [27]. Sensing delay has only been measured in a single species, indicating that it is short but preventing us from estimating a scaling relationship from literature values. However, a strong dependence on size seems unlikely given that the structures of several types of mechanoreceptors are size-independent [28,29]. Combining our findings with insights based on the underlying biophysical mechanisms suggests that sensing, synaptic and neuromuscular junction delays are relatively short for most animals. We suspect that expanding the datasets for these three delays is unlikely to substantially affect our conclusions regarding total delay, particularly for animals rat-sized and larger, for two reasons. First, we based our estimates of these component delays in part on measurements from animals with masses similar to rats. Second, even if these delays increase with animal size, the likelihood that they remain relatively short means that they will contribute only slightly to total delay in large animals (figure 4).

## (b) Nerve conduction delay

Unlike synaptic delay, nerve conduction delay increases rapidly with animal size. To conduct information along a nerve fibre, an electrical current flows quickly down the fibre in areas insulated by myelin, slowing only periodically at gaps in the myelin to regenerate itself by triggering action potentials [30]. We previously found that the conduction velocity of nerve fibres is relatively constant regardless of animal size [13], making nerve conduction delay almost entirely dependent on conduction distance. In the case of the hindlimb stretch reflex, increases in animal size lead to longer legs, which increases conduction distance and thereby lengthens nerve conduction delay. Synaptic delay appears to lack this strong size dependence, and consequently the delays associated with nerve conduction in an elephant are equivalent to the time required to cross almost 100 synapses. By contrast, it takes about the same time for a signal to cross one shrew synapse as it does for the signal to travel from a shrew's ankle extensor muscle to its spinal cord. The time required for more complex pathways involved in thinking, approximated by synaptic delay, is therefore relatively short for large animals and relatively long for small animals.

## (c) Electromechanical delay

Electromechanical delay increases with size, but less steeply than nerve conduction delay. For a muscle to initiate force generation after a signal crosses the neuromuscular junction, action potentials must be propagated along muscle fibre membranes until they reach and stimulate specialized regions of the membrane that are coupled to calcium-containing structures inside the muscle fibre; upon stimulation, these structures release calcium ions which then quickly diffuse throughout the cytoplasm, activating contractile proteins within the muscle fibre [31,32]. The speed of propagation in muscle fibres, like unmyelinated nerve fibres, depends on the square root of their diameter [33,34]. Muscle fibres have

nearly constant diameters and hence conduction velocities, regardless of animal size [35]. But their length, and hence conduction distance, is longer in larger animals [36]. Simulations combining scaling relationships for these properties predict that muscle fibre conduction delay increases in proportion to $M^{0.21}$ (electronic supplementary material). This exponent is similar to that of our electromechanical delay power law, indicating that our identified scaling relationship is consistent with established biophysical mechanisms while helping to explain why electromechanical delay increases with body size. While the mechanisms underlying the scaling of electromechanical and nerve conduction delay are similar, electromechanical delay increases less steeply with size because muscle fibre lengths increase less steeply with size than nerve fibre lengths [13,36]. This analysis is suggestive rather than complete, because factors such as calcium release also contribute to electromechanical delay and their scaling is difficult to predict without improving our understanding of the scaling of their underlying processes.

## (d) Force generation delay

Force generation delay also scales less steeply with size than nerve conduction delay, but nevertheless comprises the largest component delay for all terrestrial mammals. To generate force, activated contractile proteins within muscle fibres repeatedly change shape and slide past each other, shortening the muscle [32]. Our identified scaling relationship for force generation delay is consistent with our simulations of the time to peak tetanic force, which increased in proportion to $M^{0.24}$ (electronic supplementary material), even though these two analyses used different sources of data and relied on different assumptions. Our simulations, which parametrized Hill-type muscle models with established scaling relationships for muscles and tendons, indicate that the scaling relationship for force generation delay is due partly to muscles in larger animals being relatively shorter and stronger than those in smaller animals, while the relative length and stiffness of tendon are size-independent [36]. Muscles in large animals must therefore shorten by a greater fraction of their lengths before their maximum force is balanced by the force in the tendons. Maximum muscle shortening velocity also decreases with increasing animal size [35], further increasing the time required to reach maximum force and fully stretch the tendon. Thus, larger animals appear to suffer longer force generation delays because stretching their elastic tissue requires their muscle to shorten by relatively longer distances at relatively slower speeds [37].

## (e) Component delay trade-offs

Given the importance of rapid feedback control, why are component delays not shorter? One possible explanation is that there are detrimental effects to decreasing latency. Consider, for example, decreases to nerve conduction delays by increasing nerve fibre conduction velocity. For a nerve fibre with a given diameter, its conduction velocity is determined by its internodal distance and the ratio of axon diameter to myelin thickness [34]. Speed gains are not possible through further refinement of these parameters, because their current values already achieve the fastest conduction velocities [34]. Conduction velocity can, however, be increased by enlarging nerve fibre diameter [34], but only with an energetic penalty as indicated by the greater number of mitochondria in larger nerve fibres [38]. Furthermore, fewer nerve fibres could be contained in a nerve of a given size, which would decrease the number of innervated sensory receptors and motor units and, consequently, the precision at which an animal could sense and respond to stimuli [13]. While peripheral nerve area does increase with animal size, it cannot increase enough to maintain both nerve conduction delay and nerve fibre number [13]. Similar trade-offs exist in muscles—electromechanical and force generation delay could be shortened by shifting towards faster motor units or faster cross-bridge dynamics, but only with associated penalties of increased fatigability, higher energetic cost or weaker muscles [39,40].

## (f) Total delay

Our measure of minimum sensorimotor delay is based on several simplifications and assumptions. While we investigated the simple monosynaptic stretch reflex, animals respond to stimuli during most behaviours using more sophisticated control mechanisms [18,19]. The actual delay that an animal experiences likely also depends on the disturbance, and neurally mediated responses may be considerably longer if the animal's response is generated via feedback pathways with slower nerve fibres and multiple synapses. The stretch reflex is nevertheless relevant for our purpose because its duration approximates the minimum neural delay between an unpredictable disturbance and an animal's controlled response. We have also assumed that the end of total delay is well defined by the production of peak twitch force during isometric contraction. This assumption may overestimate total delay if useful forces are generated prior to the peak twitch force, when the muscle is still at submaximal levels, or if an already active muscle modulates its force in a shorter time. Indeed, muscle that is being stretched, such as during a stretch reflex, generates force more rapidly than isometric muscle [41]. Alternatively, this assumption may underestimate total delay if useful forces require the summation of multiple twitch forces or the recruitment of slower motor units with their correspondingly slower force generation dynamics [39,42]. Here, we chose to use peak twitch force to define the conclusion of total delay for three reasons: it represents a compromise between mechanisms that may shorten or lengthen force generation delay, it is correlated with other possible definitions of force generation delay such as time to tetanus [39], and it is commonly measured and therefore facilitates comparisons across different species. Of all the component delays, we suspect that the scaling relationship for force generation delay is most sensitive to our underlying assumptions, and thus should be treated with the least confidence. Because it also appears to be the largest contributor to total sensorimotor delay, we suggest that further studies aim to understand how force generation delay depends on muscle activation level, muscle and tendon dynamics, and animal size.

For all terrestrial mammals in our study, regardless of size, total delay comprises a substantial fraction of movement duration. While these fractions are relatively smaller for smaller animals, and for all animals moving at slower speeds, they are nevertheless likely to remain a challenge for effective feedback control [10]. For example, the smallest mammal—a shrew—requires almost half of its stance duration to sense

and respond to a disturbance when sprinting. Because relative delay approximately doubles over the size range of terrestrial mammals, delays become even more of a challenge for larger animals. Indeed, for animals that weigh about 200 kg, like large deer, total delay approaches the duration of the entire stance phase when moving quickly (figure 3*b*). If these animals were to step into a hole while sprinting, they would not be able to use the same leg to generate a corrective response. Instead, they would have to rely either on passive mechanical stabilization [4,6–10] or on control strategies that coordinate the other legs to generate corrective responses during subsequent ground contact phases. Such intermittent control appears to be possible for all animal sizes at all speeds—even in large sprinting animals, stride duration is about fourfold longer than the total sensorimotor delay (figure 3*b*). However, waiting to respond to a disturbance is not without drawbacks, the most notable of which is that a large perturbation could cause an animal to fall before the next stride even begins. Elephants and other very large animals do not run as fast as predicted from trends in smaller animals. But even at the slower maximum speeds that they actually use, total delay still requires about half of the time that their foot is on the ground [43]. That is, a trotting elephant experiences similar relative delays as a galloping shrew. Importantly, biomechanically meaningful responses are further delayed by inertia—an appropriate response to a disturbance may require an animal to not only generate muscle force, but to use that force to redirect its motion, or to move a limb to a new position. While it is unknown how inertial delays scale with animal size, they certainly add to the total sensorimotor delay that we have estimated here, lengthening minimum response times for all animals.

Given the importance of feedback for controlling movement, and the importance of time delays for effective feedback, how do animals cope with their long total delays? We suspect that there is no single answer, but a suite of strategies employed by animals to help mitigate the effects of sensorimotor delays. One such strategy is to reduce the maximum speed of locomotion below that predicted based on the scaling of movement duration—simply moving more slowly provides more time to respond to disturbances. Large terrestrial mammals appear to benefit from this strategy—elephants, for example, move almost 90% slower at their top speed than predicted based on smaller animals [44]. This is not to say that sensorimotor delays are the only limit to maximum speed. Indeed, other physiological limits, including muscle strength and bone stress, have been convincingly demonstrated [45,46]—perhaps we can now count sensorimotor delays among them. A second strategy is to use innate biomechanics to rapidly reject disturbances, thereby relying less on the relatively slow neural control of muscles. For example, animals stabilize their motion using the passive dynamics of their moving body [3,47], the geometry of their legs [48] and the intrinsic properties of muscle [4,6–8,10]. A third strategy for coping with long sensorimotor delays is to use neural prediction rather than feedback. The human nervous system, and perhaps that of other animals, compensates for delays using an internal model of the body's dynamics that takes delayed and incomplete sensory information and predicts the best future motor response [5,11,12]. This may only be a useful strategy for comparatively large animals, in which the synaptic delays associated with neural computation are short relative to movement durations [20]. When viewed through the lens of feedback control, many fundamental characteristics of animal physiology appear as solutions for the detrimental effects of sensorimotor delays.

Data accessibility. Our systematic review datasets are included in the electronic supplementary material.

Authors' contributions. H.L.M. led the literature review. J.M.D. led the modelling. H.L.M. and J.M.D. jointly designed the study, conducted the statistical analyses and wrote the manuscript.

Competing interests. We have no competing interests.

Funding. This work was supported by the Natural Sciences and Engineering Research Council of Canada with a Canada Discovery Grant (J.M.D.) and a Canada Graduate Scholarship D (H.L.M.), and by Simon Fraser University with a President's PhD Scholarship and a Graduate Fellowship (H.L.M.).

Acknowledgements. We thank Noah Cowan, John Hutchinson, Devin Jindrich, Jerry Loeb, Carl Schwarz and James Wakeling for their helpful suggestions and discussions throughout this project, and Sabrina Lee for providing goat electromechanical delay data.

## References

1. Cowan NJ, Lee J, Full RJ. 2006 Task-level control of rapid wall following in the American cockroach. *J. Exp. Biol.* **209**, 1617–1629. (doi:10.1242/jeb.02166)
2. Elzinga MJ, Dickson WB, Dickinson MH. 2012 The influence of sensory delay on the yaw dynamics of a flapping insect. *J. R. Soc. Interface* **9**, 1685–1696. (doi:10.1098/rsif.2011.0699)
3. Jindrich DL, Full RJ. 2002 Dynamic stabilization of rapid hexapedal locomotion. *J. Exp. Biol.* **205**, 2803–2823.
4. Loeb GE. 1995 Control implications of musculoskeletal mechanics. In *17th Int. Conf. of the Engineering in Medicine and Biology Society*, Montreal, Canada, 20–23 September 1995, pp. 1393–1394. Montreal, Canada: IEEE.
5. Wolpert DM, Ghahramani Z. 2000 Computational principles of movement neuroscience. *Nat. Neurosci.* **3**, 1212–1217. (doi:10.1038/81497)
6. Daley MA, Biewener AA. 2006 Running over rough terrain reveals limb control for intrinsic stability. *Proc. Natl Acad. Sci. USA* **103**, 15 681–15 686. (doi:10.1073/pnas.0601473103)
7. Daley MA, Biewener AA. 2011 Leg muscles that mediate stability: mechanics and control of two distal extensor muscles during obstacle negotiation in the guinea fowl. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **366**, 1580–1591. (doi:10.1098/rstb.2010.0338)
8. Daley MA, Usherwood JR, Felix G, Biewener AA. 2006 Running over rough terrain: guinea fowl maintain dynamic stability despite a large unexpected change in substrate height. *J. Exp. Biol.* **209**, 171–187. (doi:10.1242/jeb.01986)
9. Dickinson MH, Farley CT, Full RJ, Koehl MA, Kram R, Lehman S. 2000 How animals move: an integrative view. *Science* **288**, 100–106. (doi:10.1126/science.288.5463.100)
10. Grillner S. 1972 The role of muscle stiffness in meeting the changing postural and locomotor requirements for force development by the ankle extensors. *Acta Physiol. Scand.* **86**, 92–108. (doi:10.1111/j.1748-1716.1972.tb00227.x)
11. Kuo AD. 2002 The relative roles of feedforward and feedback in the control of rhythmic movements. *Motor Control* **6**, 129–145. (doi:10.1123/mcj.6.2.129)
12. Milton JG. 2011 The delayed and noisy nervous system: implications for neural control. *J. Neural Eng.* **8**, 065005. (doi:10.1088/1741-2560/8/6/065005)
13. More HL, Hutchinson JR, Collins DF, Weber DJ, Aung SKH, Donelan JM. 2010 Scaling of sensorimotor control in terrestrial mammals. *Proc. R. Soc. B* **277**, 3563–3568. (doi:10.1098/rspb.2010.0898)
14. Alexander RM. 2002 Stability and manoeuvrability of terrestrial vertebrates. *Integr. Comp. Biol.* **42**, 158–164. (doi:10.1093/icb/42.1.158)

15. Heglund NC, Taylor CR. 1988 Speed, stride frequency and energy cost per stride: how do they change with body size and gait? *J. Exp. Biol.* **138**, 301–318.
16. Heglund NC, Taylor CR, McMahon TA. 1974 Scaling stride frequency and gait to animal size: mice to horses. *Science* **186**, 1112–1113. (doi:10.1126/science.186.4169.1112)
17. Lloyd DPC. 1943 Conduction and synaptic transmission of the reflex response to stretch in spinal cats. *J. Neurophysiol.* **6**, 317–326. (doi:10.1152/jn.1943.6.4.317)
18. Prochazka A, Gritsenko V, Yakovenko S. 2002 Sensory control of locomotion: reflexes versus higher-level control. *Adv. Exp. Med. Biol.* **508**, 357–367. (doi:10.1007/978-1-4615-0713-0_41)
19. Zehr EP, Stein RB. 1999 What functions do reflexes serve during human locomotion? *Prog. Neurobiol.* **58**, 185–205. (doi:10.1016/S0301-0082(98)00081-1)
20. Hooper SL. 2012 Body size and the neural control of movement. *Curr. Biol.* **22**, R318–R322. (doi:10.1016/j.cub.2012.02.048)
21. Ceccarelli B, Hurlbut WP. 1980 Vesicle hypothesis of the release of quanta of acetylcholine. *Physiol. Rev.* **60**, 396–441. (doi:10.1152/physrev.1980.60.2.396)
22. Hubbard JI. 1973 Microphysiology of vertebrate neuromuscular transmission. *Physiol. Rev.* **53**, 674–723. (doi:10.1152/physrev.1973.53.3.674)
23. Katz B, Miledi R. 1967 A study of synaptic transmission in the absence of nerve impulses. *J. Physiol.* **192**, 407–436. (doi:10.1113/jphysiol.1967.sp008307)
24. Changizi MA. 2001 Principles underlying mammalian neocortical scaling. *Biol. Cybern.* **84**, 207–215. (doi:10.1007/s004220000205)
25. Olivera BM, Miljanich GP, Ramachandran J, Adams ME. 1994 Calcium channel diversity and neurotransmitter release: the omega-conotoxins and omega-agatoxins. *Annu. Rev. Biochem.* **63**, 823–867. (doi:10.1146/annurev.bi.63.070194.004135)
26. Phalen G, Davenport HA. 1937 Pericellular end-bulbs in the central nervous system of vertebrates. *J. Comp. Neurol.* **68**, 67–81. (doi:10.1002/cne.900680104)
27. Delmas P, Hao JZ, Rodat-Despoix L. 2011 Molecular mechanisms of mechanotransduction in mammalian sensory neurons. *Nat. Rev. Neurosci.* **12**, 139–153. (doi:10.1038/nrn2993)
28. Banks RW, Hulliger M, Saed HH, Stacey MJ. 2009 A comparative analysis of the encapsulated end-organs of mammalian skeletal muscles and of their sensory nerve endings. *J. Anat.* **214**, 859–887. (doi:10.1111/j.1469-7580.2009.01072.x)
29. Straile WE. 1969 Encapsulated nerve end-organs in the rabbit, mouse, sheep and man. *J. Comp. Neurol.* **136**, 317–335. (doi:10.1002/cne.901360305)
30. Huxley AF, Stampfli R. 1949 Evidence for saltatory conduction in peripheral myelinated nerve fibres. *J. Physiol.* **108**, 315–339. (doi:10.1113/jphysiol.1949.sp004335)
31. Fleischer S, Inui M. 1989 Biochemistry and biophysics of excitation-contraction coupling. *Annu. Rev. Biophys. Biol.* **18**, 333–364. (doi:10.1146/annurev.biophys.18.1.333)
32. Rayment I, Holden HM, Whittaker M, Yohn CB, Lorenz M, Holmes KC, Milligan RA. 1993 Structure of the actin-myosin complex and its implications for muscle-contraction. *Science* **261**, 58–65. (doi:10.1126/science.8316858)
33. Loeb GE, Pratt CA, Chanaud CM, Richmond FJR. 1987 Distribution and innervation of short, interdigitated muscle fibers in parallel-fibered muscles of the cat hindlimb. *J. Morphol.* **191**, 1–15. (doi:10.1002/jmor.1051910102)
34. Rushton WAH. 1951 A theory of the effects of fibre size in medullated nerve. *J. Physiol.* **115**, 101–122. (doi:10.1113/jphysiol.1951.sp004655)
35. Seow CY, Ford LE. 1991 Shortening velocity and power output of skinned muscle fibers from mammals having a 25 000-fold range of body mass. *J. Gen. Physiol.* **97**, 541–560. (doi:10.1085/jgp.97.3.541)
36. Pollock CM, Shadwick RE. 1994 Allometry of muscle, tendon, and elastic energy storage capacity in mammals. *Am. J. Physiol.* **266**, R1022–R1031.
37. Hill AV. 1951 The effect of series compliance on the tension developed in a muscle twitch. *Proc. R. Soc. Lond. B* **138**, 325–329. (doi:10.1098/rspb.1951.0025)
38. Perge JA, Niven JE, Mugnaini E, Balasubramanian V, Sterling P. 2012 Why do axons differ in caliber? *J. Neurosci.* **32**, 626–638. (doi:10.1523/JNEUROSCI.4254-11.2012)
39. Burke RE, Levine DN, Tsairis P, Zajac F. 1973 Physiological types and histochemical profiles in motor units of the cat gastrocnemius. *J. Physiol.* **234**, 723–748. (doi:10.1113/jphysiol.1973.sp010369)
40. Rome LC, Cook C, Syme DA, Connaughton MA, Ashley-Ross M, Klimov A, Tikunov B, Goldman YE. 1999 Trading force for speed: why superfast crossbridge kinetics leads to superlow forces. *Proc. Natl Acad. Sci. USA* **96**, 5826–5831. (doi:10.1073/pnas.96.10.5826)
41. Roberts TJ, Azizi E. 2010 The series-elastic shock absorber: tendons attenuate muscle power during eccentric actions. *J. Appl. Physiol.* **109**, 396–404. (doi:10.1152/japplphysiol.01272.2009)
42. Burke RE, Levine DN, Zajac III FE. 1971 Mammalian motor units: physiological-histochemical correlation in three types in cat gastrocnemius. *Science* **174**, 709–712. (doi:10.1126/science.174.4010.709)
43. Hutchinson JR, Schwerda D, Famini DJ, Dale RHI, Fischer MS, Kram R. 2006 The locomotor kinematics of Asian and African elephants: changes with speed and size. *J. Exp. Biol.* **209**, 3812–3827. (doi:10.1242/jeb.02443)
44. Iriarte-Díaz J. 2002 Differential scaling of locomotor performance in small and large terrestrial mammals. *J. Exp. Biol.* **205**, 2897–2908.
45. Biewener AA. 1989 Scaling body support in mammals: limb posture and muscle mechanics. *Science* **245**, 45–48. (doi:10.1126/science.2740914)
46. Hutchinson JR, Garcia M. 2002 Tyrannosaurus was not a fast runner. *Nature* **415**, 1018–1021. (doi:10.1038/4151018a)
47. McGeer T. 1992 Principles of walking and running. In *Advances in comparative and environmental physiology* (ed. RM Alexander), pp. 113–139. Berlin, Germany: Springer.
48. Farley CT, Houdijk HH, Van Strien C, Louie M. 1998 Mechanism of leg stiffness adjustment for hopping on surfaces of different stiffnesses. *J. Appl. Physiol.* **85**, 1044–1055. (doi:10.1152/jappl.1998.85.3.1044)