bacteria are applied to all liquid manure systems in Europe, the total human-associated N_2O emissions from the region would decrease by 2.7%. The decrease would be 4% for the 27 member countries of the European Union, which have a higher share of liquid manure systems than do European countries outside the EU. If the bioaugmentation approach of bacterial supplementation could be extended to all types of mineral and natural fertilizer applied to agricultural fields, the authors estimate that Europe could decrease its N_2O emissions by 24%.

As a proof of concept, the authors demonstrate the utility of bioaugmentation with *Cloacibacterium* sp. strain CB-01 grown in digestate used as a nitrogen fertilizer. The effectiveness of the approach was validated using four soils that have different physical and geochemical properties. To achieve the projected 2030 emission reductions, the bioaugmentation agent must be grown in manure and other forms of mineral and natural fertilizers before application to agricultural fields. In addition, a variety of factors will affect the success of this approach – for example, the method should be suitable for a range of soil types, management practices, dynamic biogeochemical properties (such as pH)[8] and fluctuating climate and weather patterns. Given the factors that might influence performance of the bioaugmentation approach, a suite of N_2O-reducing microorganisms adapted to various environmental conditions and fertilizers will be needed to achieve effective and cost-efficient soil inoculation on a large scale.

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Robotics

Leg exoskeleton trained through simulation alone

Alexandra S. Voloshina

A strategy for training a robotic exoskeleton through simulation takes the user out of the equation – saving users of wearable devices time and energy, and smoothing the transition between different types of movement. **See p.353**

Wearing a robotic exoskeleton can restore mobility for individuals with motor disabilities, or enhance a person's ability to perform daily activities. The ways that humans move are both complex and varied, yet these devices[1] are often designed to assist with only one activity, such as walking or running, and can require extensive tuning for each wearer. On page 353, Luo *et al.*[2] introduce a framework for developing more-versatile and adaptable devices. It relies on simulating human–device interactions without the need for copious data amassed from a human using the device. The authors show that this simulation-based approach leads to effective assistance for a range of tasks and can be adapted to different individuals – paving the way towards the integration of robotic exoskeletons into everyday life.

Robotic devices designed to improve a person's gait can be worn on one or more joints of the leg, and usually have embedded motors that apply torques to either bend or extend the joint. This assistance – when applied properly – reduces the energy that the wearer expends when using their muscles. The device moves in sync with the joint, enabling the leg muscles to relax and allowing the device to assume their workload. However, for the device to offer optimal assistance and save maximum energy for the wearer, it must provide the right amount of assistive torque at the correct time.

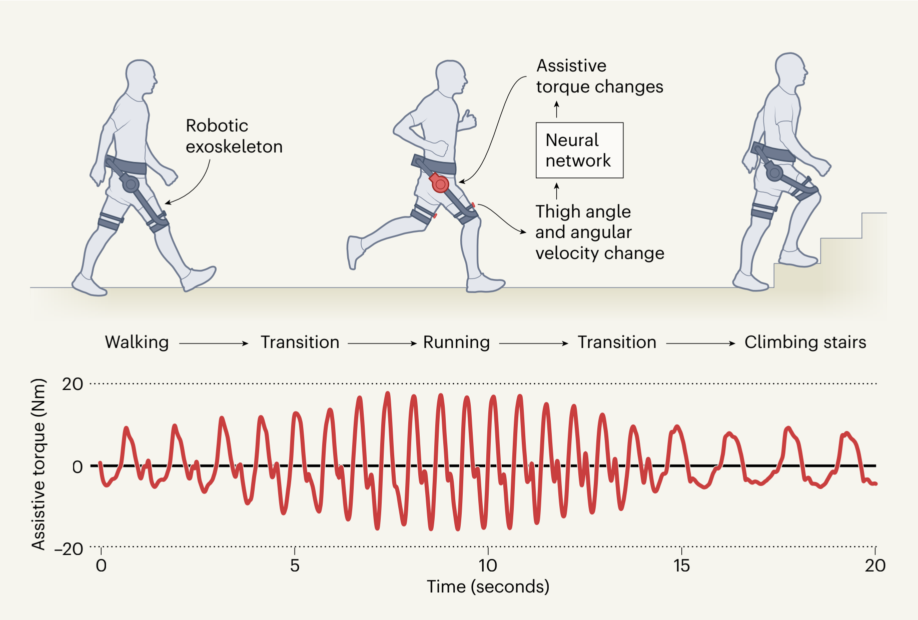

Figure 1 | A multitasking robotic exoskeleton. Luo *et al.*[2] developed a strategy for programming the assistive torque (measured in Newton metres, Nm) that a robotic leg exoskeleton provides while its wearer is walking, running and climbing stairs. The method trains the device controller using simulations, in contrast to other approaches, which often rely on hand-tuned controllers. Basic kinematic measurements, such as the angle and angular velocity of the thigh, are fed into a set of interconnected neural networks that enable the trained controller to calculate the required torque for each type of movement. Luo *et al.* showed that this strategy allows the controller to transition smoothly between the three locomotive tasks and saves energy for the wearer. (Adapted from Fig. 4 of ref. 2.)

Failure to do so can make the user resist the assistance offered by the device, increasing their muscle activity and making movement more difficult.

Developing precise and adaptive control for these devices therefore remains a key challenge in exoskeleton research. It involves formulating control laws, which are sets of instructions that guide the device along a trajectory from one state to another. Controllers for lower-limb exoskeletons often follow pre-defined torque assistance profiles[3,4] that stipulate how much torque to apply over the course of a single step. These profiles are adjusted manually, sometimes while the device is in use. This process can be cumbersome and subjective, often resulting in suboptimal assistance profiles.

One way around this problem involves a strategy known as human-in-the-loop optimization[5]. In this approach, the wearer's physiological measures are used to iteratively and systematically adjust the control laws to achieve a given objective, such as reducing the energy consumption of the user. A similar data-driven method[6] can train an exoskeleton while its wearer walks around outside, by relating kinematic measurements to energy consumption. These methods can lead to personalized and highly effective assistive torque profiles, but require a lot of user training, which limits their practicality.

Another issue is that assistive device controllers are typically designed to help with one specific task[3], which means that separate controllers are required for each task. Multiple controllers can be implemented in a single device, but this can create abrupt transitions between assistive torque profiles, causing discomfort for the user. Moreover, control laws are often largely fixed once defined, and this limits the controller's ability to adapt to changes in the way that the wearer interacts with the device, or in their biomechanics.

Luo *et al.* tackled these problems by simulating a musculoskeletal human model combined with a physics-based exoskeleton model. Specifically, the authors used three interconnected neural networks to generate human movement, muscle coordination and exoskeleton control. The networks learnt from kinematic trajectory data that were collected through experiments involving humans walking, running and climbing stairs. Implementing reinforcement learning, a type of machine learning that improves its decision-making on the basis of interactions with the environment, Luo *et al.* conducted millions of simulations of desired movements using their human–exoskeleton model. After about 8 hours of simulation, they were able to decrease muscle activation and energy expenditure in the model by manipulating the exoskeleton and identifying the most effective controller.

Once the controller had been trained in the simulation, Luo and colleagues then demonstrated that it could be implemented in a custom-designed hip exoskeleton (Fig. 1). By using basic kinematic measurements collected from sensors on the wearer, specifically the angle and angular velocity of their thigh, the trained controller was able to produce assistive torques and seamless transitions between walking, running and climbing stairs. The assistance provided by the device also substantially decreased the energy expended by its wearers during all three of these activities.

It is important to note that the three gait tasks studied here are cyclical in nature, composed of repeated, similar movements, which helps to identify an effective exoskeleton controller. However, it remains to be seen how the simulation-based approach would perform in response to more-discrete movements, such as stepping over a puddle or changing direction, which occur frequently in everyday life.

> **"The trained controller was able to produce seamless transitions between walking, running and climbing stairs."**

Furthermore, the authors focused on developing a controller for reducing energy expenditure. But many individuals, such as elderly people or individuals with motor impairments, might not prioritize energetic cost when generating movement and might instead prefer assistance that provides other benefits, such as improved balance, faster walking speeds or gait symmetry. Future studies could explore how the authors' learning-in-simulation framework could help to generate exoskeleton behaviours that produce those outcomes.

The strategy presented by Luo and colleagues streamlines the development of controllers for robotic exoskeletons by eliminating the need for human experiments and transitioning the training process into simulation. The controllers developed through this approach are adaptable, depend on minimal user input and do not need to be tuned individually for a specific activity. Further work will broaden the applicability of these controllers and bring assistive exoskeletons to a wider range of individuals and tasks, treading the path that Luo and co-workers have paved towards natural and interactive wearable assistive devices.

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Developmental biology

Nuclear position matters for tissue development

Tanvi Kulkarni & Asifa Akhtar

Using tissue from the developing fruit-fly wing, researchers show that a nucleus's location in the cell determines how it experiences signals that regulate genes needed for proper wing formation. **See p.466**

The development of specialized tissues relies on the intricate interplay between various cellular mechanisms, and the careful control over the timing and location of these processes. On page 466, Willnow and Teleman[1] uncover a developmental process that is influenced by a cell's nuclear position with respect to the tissue's surface.

Epigenetic regulation – the chemical modification of DNA or the histone proteins around which DNA is packaged – has a central role in determining the identity and function of cells in tissues, by dictating which genes are turned on and off. These reversible epigenetic modifications, and the enzymes that add or remove them, depend heavily on the metabolic status