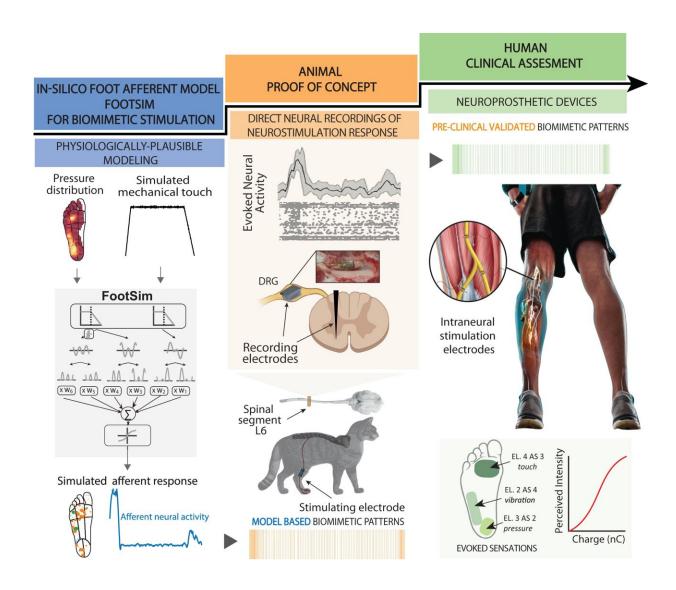


Bio-inspired neuroprosthetics: Sending signals the brain can understand

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Neuroscience-driven development of a biomimetic neuroprosthetic device. The successful development of a somatosensory neuroprosthesis is based on three main pillars: (1) In-silico models of the biological sensory processing have to be



exploited for emulating the natural neural activation of the nervous system to external tactile stimuli (blue segment); (2) animal proof of concept allows for experimental validation of the mechanisms behind the use of specific neurostimulation strategies defined with the use of modeling (orange segment); (3) A rigorous clinical validation of the biomimetic technology with implanted humans has to be performed in order to assess the functional outcomes in real-life scenarios (green segment). Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-45190-6

A few years ago, a team of researchers working under Professor Stanisa Raspopovic at the ETH Zurich Neuroengineering Lab gained worldwide attention when they announced that their prosthetic legs had enabled amputees to feel sensations from this artificial body part for the first time.

Unlike commercial leg prostheses, which simply provide amputees with stability and support, the ETH researchers' prosthetic device was connected to the sciatic nerve in the test subjects' thigh via implanted electrodes.

This electrical connection enabled the neuroprosthesis to communicate with the patient's brain, for example relaying information on the constant changes in pressure detected on the sole of the prosthetic foot when walking. This gave the test subjects greater confidence in their prosthesis—and it enabled them to walk considerably faster on challenging terrains.

"Our experimental leg prosthesis succeeded in evoking natural sensations. That's something current neuroprostheses are mainly unable to do; instead, they mostly evoke artificial, unpleasant sensations," Raspopovic says.



This is probably because today's neuroprosthetics are using time-constant electrical pulses to stimulate the nervous system. "That's not only unnatural, but also inefficient," Raspopovic says.

In a recently published <u>paper</u> in *Nature Communications*, he and his team used the example of their leg prostheses to highlight the benefits of using naturally inspired, biomimetic stimulation to develop the next generation of neuroprosthetics.

Model simulates activation of nerves in the sole

To generate these biomimetic signals, Natalija Katic—a doctoral student in Raspopovic's research group—developed a computer model called FootSim. It is based on data collected by collaborators in Canada, who recorded the activity of natural receptors, named mechanoreceptors, in the sole of the foot while touching different points on the feet of volunteers with a vibrating rod.

The model simulates the dynamic behavior of large numbers of mechanoreceptors in the sole of the foot and generates the <u>neural signals</u> that shoot up the nerves in the leg towards the brain—from the moment the heel strikes the ground and the weight of the body starts to shift forward to the outside of the foot until the toes push off the ground ready for the next step.

"Thanks to this model, we can see how sensory receptors from the sole, and the connected nerves, behave during walking or running, which is experimentally impossible to measure," Katic says.

Information overload in the spinal cord

To assess how closely the biomimetic signals calculated by the model



correspond to the signals emitted by real neurons, Giacomo Valle—a postdoc in Raspopovic's research group—worked with colleagues in Germany, Serbia and Russia on experiments with cats, whose nervous system processes movement in a similar way to that of humans. The experiments took place in 2019 at the Pavlov Institute of Physiology in St. Petersburg and were carried out in accordance with the relevant European Union guidelines.

The researchers implanted electrodes, connecting some to the nerve in the leg and some to the <u>spinal cord</u> to discover how the signals are transmitted through the nervous system. When the researchers applied pressure to the bottom of the cat's paw, thereby evoking the natural neural response that occurs when a cat takes a step, the peculiar pattern of activity recorded in the spinal cord did indeed resemble the patterns that were elicited in the spinal cord when the researchers stimulated the leg nerve with biomimetic signals.

By contrast, the conventional approach of time-constant stimulation of the sciatic nerve in the cat's thigh elicited a markedly different pattern of activation in the spinal cord. "This clearly shows that the commonly used stimulation methods cause the neural networks in the spine to be flooded with information," Valle says. "This information overload could be the reason for the unpleasant sensations or paraesthesia reported by some users of neuroprosthetics," Raspopovic adds.

Learning the language of the nervous system

In their clinical trial with leg amputees, the researchers were able to show that biomimetic stimulation is superior to time-constant stimulation. Their work clearly demonstrated how the signals that mimicked nature produced better results: not only were the test subjects able to climb steps faster, they also made fewer mistakes in a task that required them to climb the same steps while spelling words backwards.



"Biomimetic neurostimulation allows subjects to concentrate on other things while walking," Raspopovic says, "so we concluded that this type of stimulation is more naturally processed and less taxing on the brain."

Raspopovic, whose lab forms part of the ETH Institute of Robotics and Intelligent Systems, believes that these new findings are not only relevant to the limb prostheses he and his team have been working on for over half a decade. He argues that the need to move away from unnatural, time-constant stimulation towards biomimetic signals also applies to a whole series of other aids and devices, including spinal implants and electrodes for brain stimulation.

"We need to learn the language of the nervous system," Raspopovic says. "Then we'll be able to communicate with the brain in ways it really understands."

More information: Giacomo Valle et al, Biomimetic computer-to-brain communication enhancing naturalistic touch sensations via peripheral nerve stimulation, *Nature Communications* (2024). DOI: 10.1038/s41467-024-45190-6

Provided by ETH Zurich

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