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The current state of bionic limbs from the surgeon's viewpoint

Marko Bumbaširević[1,2]
Aleksandar Lesic[1,2]
Tomislav Palibrk[1,2]
Darko Milovanovic[1,2]
Milan Zoka[3]
Tamara Kravić-Stevović[4]
Stanisa Raspopovic[5]

- Amputations have a devastating impact on patients' health with consequent psychological distress, economic loss, difficult reintegration into society, and often low embodiment of standard prosthetic replacement.
- The main characteristic of bionic limbs is that they establish an interface between the biological residuum and an electronic device, providing not only motor control of prosthesis but also sensitive feedback.
- Bionic limbs can be classified into three main groups, according to the type of the tissue interfaced: nerve-transferred muscle interfacing (targeted muscular reinnervation), direct muscle interfacing and direct nerve interfacing.
- Targeted muscular reinnervation (TMR) involves the transfer of the remaining nerves of the amputated stump to the available muscles.
- With direct muscle interfacing, direct intramuscular implants record muscular contractions which are then wirelessly captured through a coil integrated in the socket to actuate prosthesis movement.
- The third group is the direct interfacing of the residual nerves using implantable electrodes that enable reception of electric signals from the prosthetic sensors. This can improve sensation in the phantom limb.
- The surgical procedure for electrode implantation consists of targeting the proximal nerve area, competently introducing, placing, and fixing the electrodes and cables, while retaining movement of the arm/leg and nerve, and avoiding excessive neural damage.
- Advantages of bionic limbs are: the improvement of sensation, improved reintegration/embodiment of the artificial limb, and better controllability.

Keywords: bionic limbs; limb amputation; prosthetics

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Introduction

Amputations and, consequently, prostheses as their most immediate solution, have a long history, starting with hooks and other prosthetic replacements of the Middle Ages, continuing to Ambroise Paré's mechanical hand (Fig. 1),[1] to modern robotic, osteointegrated[2] and bionic limbs,[2–9] which are the results of both medical and technological progress. Modern-age prosthesis development was boosted as a consequence of the World Wars – first in Germany[10] and then in the former USSR.[11]

There are around 2 million limb amputees in the USA with 185,000 amputations performed annually.[12] Inferred from statistics for Germany, Italy, Ireland and the USA, the EU has approximately 3.18 million limb amputees (4.66 million for all of Europe) and around 295,000 amputations are performed each year (431,000 for all of Europe).[12–16] This poses a huge medical and economic problem. Amputations have a devastating impact on a patients' health and produce psychological distress with consequent economic loss. Patients have difficulties being fully reintroduced to

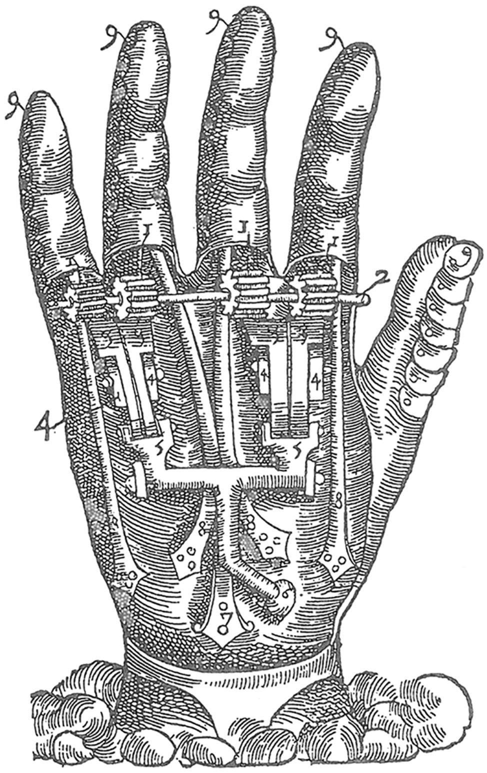

Fig. 1 Articulated hand by AmbroiseParé from1579.

their workplaces in the post-amputation period.[3,17] They usually feel the prosthesis as a foreign body (low embodiment), therefore there is a need to provide new prosthetic solutions, which should be more efficient and more easily accepted/embodied by patients.[18,19]

In the case of a traumatic amputation and if there is an indication for it to be performed, replantation is always the treatment of choice.[20,21] From our experience, in cases of severe limb trauma with mangled extremities, microsurgical reconstruction, if indicated and successful, gives much better results than any other possible solution. Alternatively, we have recently witnessed a successful cadaveric limb transplantation, [22–24] albeit followed by a requirement for life-long immunosuppressive therapy and the patient's difficult psychological acceptance of the dead-donor hand.

Yet, prostheses are still an important aspect of orthopaedic practice, since traffic accidents, tumours and especially diabetes are widely present and these patients very often have non-reconstructable limbs. Prostheses try to replicate the appearance and functionality of limbs to the finest detail. We may have reached the pinnacle of prosthetic aesthetics, but the patient's control and 'feeling' of these artificial replacements is still very problematic.[2–9] Therefore, the need for modern, intuitively controllable and naturally perceived prosthesis is nowadays even more pronounced. Thus, the aim of many research projects both in the United States[25,26] (Revolutionizing Prosthetics and HAPTIX program from Defence Advanced Research Projects Agency) and in Europe[18,27] (Cyberhand and NEBIAS from the EU commission) has been to restore the motor control of the device, but also sensation flow from the prosthesis to the body. In the recent past, several research groups have shown the benefits of restoring sensory feedback together with motor control of the prosthesis in upper[2,8,9,28–31] and lower limb amputees.[6,32,33] These approaches have the scope to replicate the near-to-natural motor and sensory limb functionalities of an intact limb, replacing it with an active and sensorized prosthetic device. As a result of these innovations, 'bionic limbs' were developed and represent the newest achievement in prosthetics.

This article describes and compares data from literature on bionic limbs, the available technological solutions and limitations, future perspectives and possibilities for further clinical applications. Related surgical procedures are also described and derived from the authors' personal experience.

Bionic limbs terminology, existing solutions and current pains

The term 'bionics' was first used by Jack E. Steele in the US TV show – 'The Six Million Dollar Man and Bionic Woman', in which superpowers were imparted to the protagonists by electromechanical implants. Afterwards, this term earned widespread use in literature and television.[34] In current terminology, it mainly addresses devices that make a direct connection with the residual nervous or muscular system of the impaired individuals.

There is a difference in the role and, consequently, construction of bionic limbs for the upper (including hand) and the lower extremities. The functions of the upper limbs (UL) and the lower limbs (LL) differ, and the role of and need for limb replacement in these cases are different; therefore, careful evaluation of the needs and the remaining capacity of patients must be considered during the construction of aprobable bionic limb. The situation in upper limb amputation, hand or forearm, is the most complex, since the hand represents the highest level of evolution with sophisticated and unique functions. Its control of 40 muscles and the involvement of a large surface of the brain cortex, suggests its significant role and importance in human performance. Present commercial prostheses are failing in replicating such control of the actuation or sensing capability.[3,4,35,36] Conversely, the LLs are used for standing, walking, ensuring stability and balance. This is made possible after a transtibial amputation, using the modern below-the-knee prostheses.[6,25] Such patients can walk, dance, and play sports at near-normal levels. However, those undergoing high transfemoral (thigh-level) amputations do not regain normal gait and balance, and are at risk of falling and overloading the opposite, healthy leg. Several long-term problems, including osteoporosis, arthritis, back pain, and increased metabolic consumption (with possible disastrous outcomes) frequently occur in these patients.[37,38]

Bidirectional control

Many efforts have been made to solve a number of technical problems, which were present in prosthetic devices. Batteries are today long-lasting and energy consumption for these limbs is lower.[3,39,40] Biological residuum and electronic devices interface through the placement of parts of a machine in direct connection with the human body in order to enable bidirectional communication between the electronic signals and ionic currents within the living organism.[34] Actually, a bionic limb is denominated as such, thanks to the inclusion of the hardware that acts as an interface between the residual human nervous system and the device (such as a robotic hand or leg). Novel surgical techniques have improved the efficacy of these technologies interfacing them with several muscular [41–44] and nervous structures,[2,8,9,27,28–31,45,46] in a more intimate way. These include the muscle direct approach through the injections of small implants,[42,47] nerve rerouting for the muscular reinnervation,[18,41,43,44,48–50] and nerve interfacing around,[2,9] or within[8,27,28–31,45] the fascicular structures.

A bionic limb is controlled by the electric signals from the muscle and/or nerves above the level of the amputation. Bidirectional control is then completed via sensation restoration through the connection of the remaining nerves or muscles above the level of amputation to the prosthetic device sensors.Therefore these devices enable both intuitive control and natural flow of sensation from the artificial device to the user (Fig. 2). The first successful proof of concept was achieved with bionic hands.[7–9,41,42,45,48] Modern hand prostheses are actuated by advanced motors, enabling the restoration of sophisticated

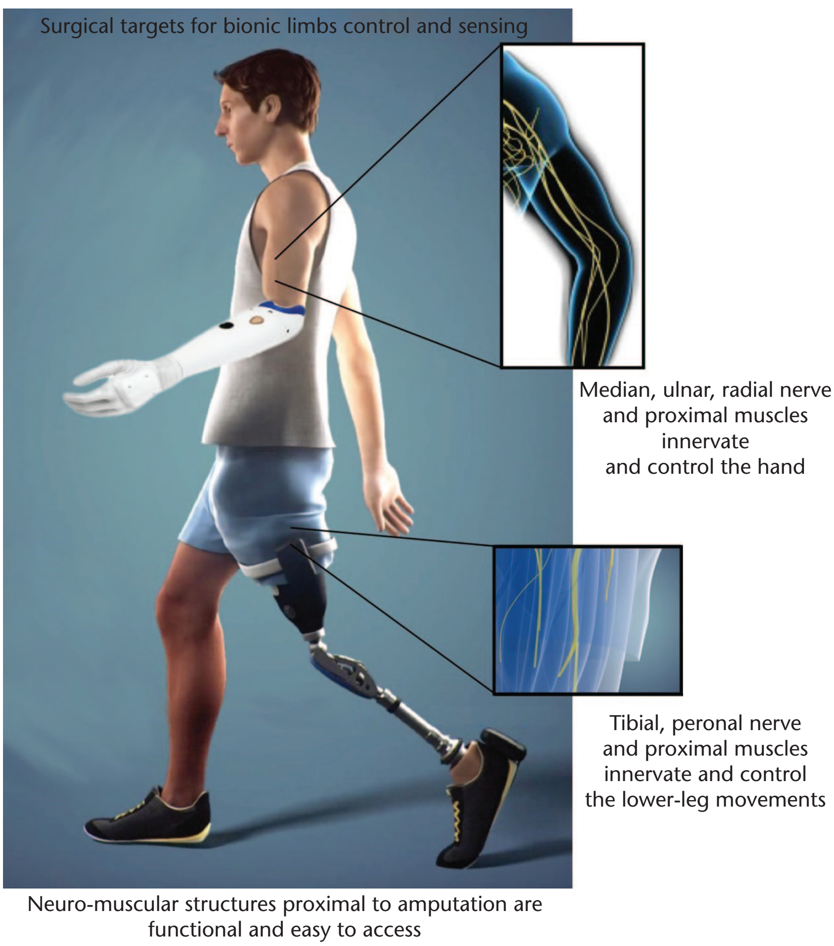

Fig. 2 Surgical targets for bionic limb control andsensing.

hand movements, through the connection with direct muscular signals.[31,42,50]

In order to restore the sensory information flow, the signals from tactile and position sensors embedded in the prosthesis are converted into electrical impulses by sensory encoding algorithms implemented on a system controller.[8,9,28,30,46] Then, the stimulation trains are delivered to the nerve, using a neural stimulator by means of microelectrode implants previously fixed into or around the somatosensory nerves. In this way, users could perceive sensations directly on the phantom limb according to the interactions between prosthesis and external world, being again masters of the space around them.

Implants, nerve and muscles transferring

The neural signal pick-up can be achieved by exploiting the natural nerve motor signal amplification that is obtained on the neuromuscular junction, therefore placing the recording electrode on the surface of the muscle[50,51] (surface electromyography (EMG)) or inside the muscle[42,52] (intramuscular EMG). Moreover, the motor intentions potentially could be also recorded directly from the peripheral nerves[27,31,53] (electoroneurography (ENG)) in order to be more selective. Yet the last approach suffers from difficulties with long-term stability and reliability.[4,5,27,31]

Bionic limbs can be divided into three main groups, according to the implant used, the type and the tissue interfaced:

1. Nerve and muscle transferring
2. Direct muscleinterfacing
3. Direct nerveinterfacing

Nerve and muscle transferring

Targeted muscular reinnervation (TMR) invented by Kuiken[41,43] involves the transfer (rerouting) of the remaining nerves (e.g. median and ulnar nerve) of the amputated stump to the available muscles (e.g. chest muscles), thus amplifying neural control signals via their natural muscular amplifier. Those signals are then registered by the electrodes and transferred to the prosthesis to control its action.[41,43] Indeed, when a subject thinks of moving his/her missing hand, the reinnervated chest muscles are stimulated and the signal is then captured by recording electrodes and used to drive the movement of the robotic arm.[41,50] The same approach was also applied to lower limb amputees.[44] Additionally, tactile stimulation over the reinnervated areas (e.g. chest) can induce the sense of touch of the missing arm/fingers.[18,48] However, when trying to implement real bidirectional control, it is yet impossible to record the signals from the innervated muscle and, at the same time, implement the sensory touch-feedback, since the same area needs to be approached, possibly due to the sensory gating problem.[52] Recently, this issue was tackled, achieving reinnervation of separated motor and sensory fascicles over different muscles.[18] This approach shows promise for the success of such a bidirectional system. The targeted muscle reinnervation approach is an excellent solution, especially for very high amputees (e.g. shoulder disarticulation or transhumeral amputation of the arm).

Recently, an elective amputation, combined with the techniques of selective nerve and muscle transfers and prosthetic rehabilitation to regain hand function, have also been proposed in three patients with brachial plexus injuries.[7] On a similar track, Herr and colleagues[6], recently proposed the so-called agonist-antagonist myoneural interface (AMI). AMI is a new idea encompassing a surgical construct made up of two muscle tendons – an agonist and an antagonist – surgically connected in a series so that contraction of one muscle stretches the other. The idea of the AMI is to recreate the dynamic muscle relationship that existed within the pre-amputation anatomy, thereby allowing proprioceptive signals from both muscles to be transferred to the central nervous system. Herr and his team surgically constructed two AMIs within the residual limb of a subject with a transtibial amputation, achieving very promising results.[6] Such an elegant surgical approach appears to be very promising in transtibial amputees, while it could be more difficult to apply in transfemoral patients.

Direct muscleinterfacing

In the second type of bionic limbs, the approach to the control signal captured from the residual muscular tissue is made through direct intramuscular implants.[42,47] Intramuscular implant-based control consists of small recording devices implanted into the residual muscle to record muscular contractions, which are then wirelessly captured through a coil integrated in the socket. Muscular contractions then actuate the prosthesis movement. In the case of upper limb amputees,[42] control has been achieved over simultaneous grasp and wrist movements; whereas a previously unseen, voluntary control of the ankle motion has been achieved in lower limb amputees.[47] Yet, sensory feedback is not available with this solution. The drawback is that this approach can work better in the case of more distal amputations (low transradial or transtibial), when many of the extrinsic muscles have been preserved, while in more proximal amputations (were muscles are missing) it would be difficult to implement. However, in higher (more proximal) amputations it could possibly be combined with the surgical techniques described above.

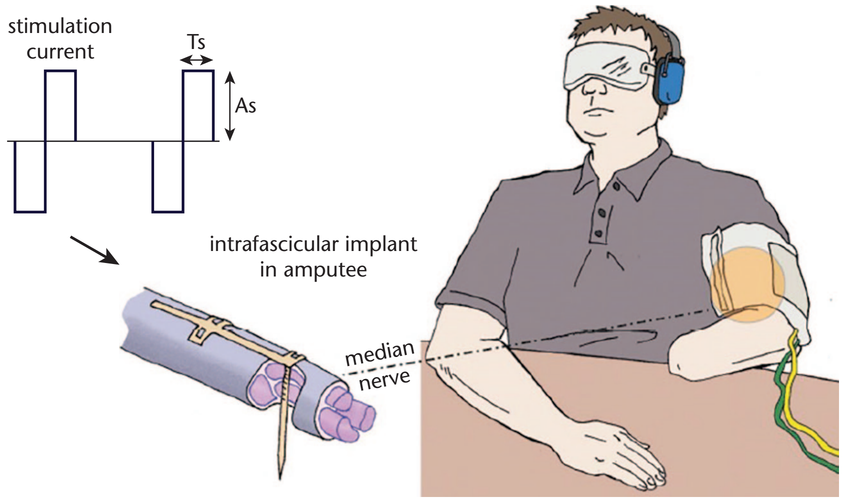

Fig. 3 Position of the electrodes in the nerves (Adapted from: Oddo CM, Raspopovic S, Artoni F, et al. Intraneural stimulation elicits discrimination of textural features by artificial fingertip in intact and amputee humans. *eLife* 2016;5:e09148 (https://doi.org/10.7554/eLife.09148.003)).[57]

Note. As (Amplitude), Ts (Pulse duration)

Direct nerveinterfacing

The third option involves the direct interfacing of the residual nerves using implantable peripheral neural interfaces.[35,36] This may be achieved by means of the neural electrodes going around or through the nerve. It is thus possible to enable control of the device[41] or to impart a sensation from the device.[8,9,54,55] Actually, transformed electric signals from prosthetic sensors stimulate the nerves in the stump, restoring sensation in the phantom limb, and thus allowing the patient to 'feel' once more.[27,45] The third group of bionic limbs incorporates the sense of the absent extremity via electrodes implanted surgically in the residual nerves, which innervate the UL or LL. To regain and improve bionic limb sensibility[28–31,56] the electrodes are introduced and placed intraneurally through the fascicles,[5,8,28–31,45] or around the nerves by means of an epineural cuff.[2,9,46] This has its rationale, since the peripheral nerve is positioned transversally from the topographic aspect, thus enabling different structures to be successfully stimulated through the device pinching the nerve transversally. Investigations suggest that intraneural stimulation can revive neural paths and improve control of an artificial limb through very short learning and training processes.[8,28,30] This is achieved by the process of decoding motor intention from the remaining muscles and encoding the sensation with electric nerve stimulation through the electrodes,[8,28] which are placed through the nerve during the intraoperative procedure.[8,27,28] In specific studies,[8,28–30] the intraneural implants (two in each median and ulnar nerve) bear external wires that are connected to the artificial touch sensors and a neural stimulator of the bionic limb. This enables them to send impulses to the brain by a process of mapping what patients feel and detect when touch is executed over a certain area of the sensorized prosthesis. These patients exhibit remarkable dexterity[8,28–30] and even texture recognition.[57] Simultaneously, due to the physiologically plausible afferent drive restoration, phantom pain decreased.[28,56,58–60]

Preliminary trials seeking to combine osteointegration and neural interfacing into a fully portable and self-contained bionic device have also been performed.[2]

Surgical procedures

Correct interfacing of residual nerves (Fig. 3) is critical. In such case, the surgeon must take extreme care to do the following:

a) Target the proximal nerve area, free of any neuro degeneration (e.g. the valerian nerve).
b) Competently place and fix the interface and cables,while retaining movement of the arm/leg and nerve.
c) Avoid excessive neural damage.

The surgical procedure for electrode implantation is performed in a limited number of cases.[2,8,9,27,28,31] We have trained in the implantation of TIMEs[61] (transversal intra-fascicular multichannel electrodes) in the median and ulnar nerve of the upper and sciatic nerve of the lower limb of cadavers. The surgical approach to the both UL and LL nerves is direct. The nerves of interest are the median and the ulnar nerve of UL and the sciatic nerve (tibial nerve) for LL. Skin incision and separation of

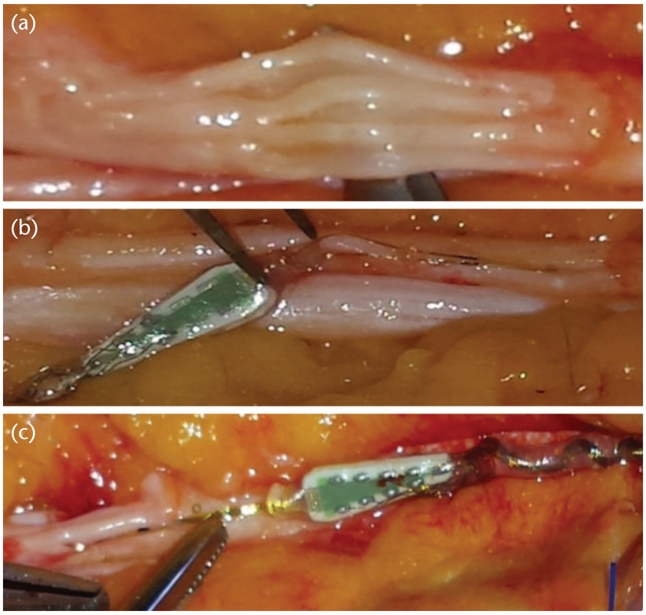

Fig. 4 Intraneural electrode placement (cadaveric preparation): (a) fascicles structures access, (b) electrode placement through different fascicles, (c) electrode fixation.

muscles from other soft tissues should be gentle in order to prevent scarring and fibrosis.

Haemostasis must be meticulous to reduce interference with electronic signalling, oedema and infection. Also, special attention must be paid to nerve preparation. As it is crucial to preserve the epineural tissue and fine vascular structure, electrodes must be placed only after mapping the fascicular structure. After a gentle opening of an external neural sheet, it is advised to access fascicular structures (Fig. 4a). Electrodes should be perpendicularly inserted into the nerve through as many fascicules as possible to obtain contact with the active sites of the electrodes (Fig. 4b). By pulling the straight needle with an 8-0 suture the electrode could be placed into the nerve. Then the electrode is fixed with sutures through the fixation tabs with holes to the surrounding epineural tissue (Fig. 4c). The electrode structure is fragile and breakage must be avoided so technique must be meticulous. After electrodes are placed and secured at three levels, a subcutaneous tunnel should be created for the cable and connector towards the neurostimulator. This surgical procedure is a demanding one, and requires an experienced microsurgeon to perform it properly. It enables stable fixation of electrodes and cables, and is suitable therefore for long-term use.

Discussion and conclusion

Advantages observed in the use of bionic limbs are: the restoration of sensation, improved reintegration/embodiment of the artificial limb and better controllability. For future applications to LLs, we envision the possibility of achieving better balance and a close to normal gait, which will decrease the number of falls and energy consumption.

Despite several promising aspects offered by innovative bionic solutions, there are still several limitations, which must be faced prior to the widespread use of similar devices. The main limitation of the majority of studies presented in this article is that these were mainly time-limited studies; therefore, long-term research regarding the behaviour of electrodes in muscles and nerves must be performed in view of their safety and functionality. In the majority of clinical trials, transcutaneous cables were used. The exit points on the skin for the cables are a matter of concern, both from a mechanical standpoint and in terms of preventing infection. Fully implantable solutions must be developed and tested.

The presence of microelectrodes for recording or/and stimulation inside the body makes the overall approach prone to stress-induced mechanical failures.[28] For future clinical practices, though, the solution should be represented by a fully implantable system, which will avoid any daily connection and disconnection between the electrode cables and the neural stimulator.

Bionic limb replacement promises to be available as a fully implantable, bidirectional device for the upper limb, controlled via implanted electrodes to obtain muscular or nerve signals and with sensory feedback achieved through nerve stimulation. In the future, it would be interesting to implement such bionic solutions to lower limb amputees as well, especially for highly disabling transfemoral amputations, since they hold promise for tremendous health improvements and an overall increase in quality of life. Research efforts are still needed to investigate the long-term presence of electrodes, their fixation, cable fixation, and fully implantable and portable electronics.

AUTHOR INFORMATION

[1]School of Medicine, University of Belgrade, Serbia.
[2]University Clinic for Orthopaedic Surgery and Traumatology, Clinical Centre of Serbia, Serbia.
[3]King's College Hospital, London, UK.
[4]University of Belgrade, Department of Histology and Embryology, Serbia.
[5]ETH Zürich, Department of Health Sciences and Technology, Institute for Robotics and Intelligent System, Zurich, Switzerland.

Correspondence should be sent to: Marko Bumbaširević, StojanaNovakovića 25, 11000 Belgrade, Serbia.
Email: marko.bumbasirevic@gmail.com

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The authors declare no conflict of interest relevant to this work.

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