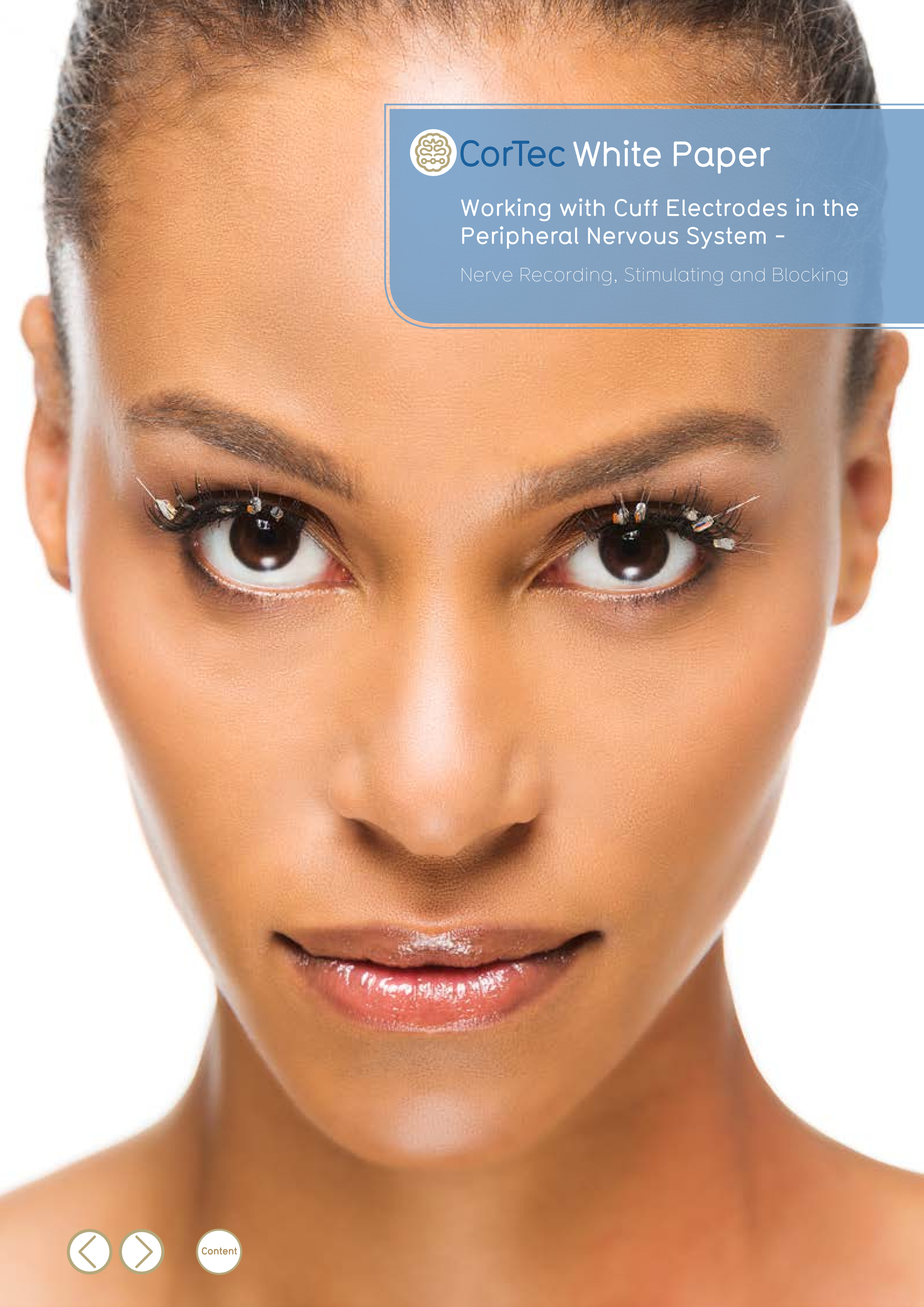
CorTec White Paper

Working with Cuff Electrodes in the Peripheral Nervous System –

Nerve Recording, Stimulating and Blocking



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>> Welcome! <<

Our White Paper on Nerve Cuffs represents a basic guideline for working with cuff electrodes in the peripheral nervous system.

It gives an overview about

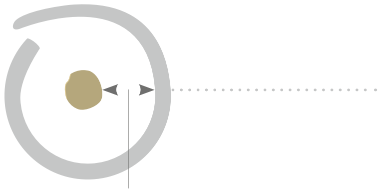
- the important factors for selecting the right electrodes,
- the preparation of the electrode before implantation,
- the basic conditions of a successful implantation,
- the use of cuff electrodes in your experiment.

CorTec is producing a variety of cuff electrodes made from minimal traumatic flexible silicone.

AirRay research Micro Cuff Tunnel and
AirRay research Micro Cuff Sling

AirRay research Micro Cuff form our standard product portfolio available for applications in pre-clinical research.

The standard configurations start at 100 µm of inner diameter with 2 mm of electrode length going up to inner diameters of several millimeters. Individual contact configurations and other customized specifications are available.



Recommended
Cuff Inner Diameter
20%
LARGER
THAN THE NERVE

›› At a pressure of 20 mmHg the venal blood flow inside the nerve starts to get disturbed with the potential effect of nerve damage.‹‹

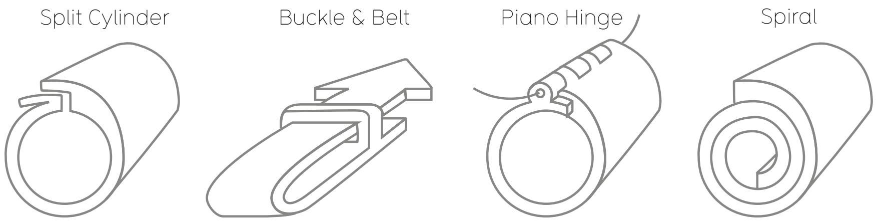
1. Selecting the Right Cuff

1.1 Diameter

The cuff should fit snuggly around the peripheral nerve permitting an intimate contact between the electrodes and the neural tissue and minimizing the body liquid inside the cuff, which otherwise can lead to current shorting with the effect of less efficient electrical stimulation and reduced recording amplitudes.
However, especially in chronic implants, the nerve should be allowed to swell, which is often observed after or during implantation, induced by mechanical nerve irritation. As a compromise, either the cuff inner diameter is commonly selected to be some 10% larger than the initial diameter of the nerve (no swelling). As an alternative, a self-sizing cuff (e.g. spiral cuff) can be used.

1.2 Closure Mechanisms

There are numerous mechanisms that allow opening of the cuff, inserting the nerve, and closing of the cuff. Some of the mechanisms result in a fixed cuff diameter (e.g. piano hinge closure, and buckle-and-belt closure e.g. used for **CorTec's** Micro Cuff Sling closure), some allow for cuff diameter adjustment (e.g. spiral cuff closure, helical cuffs, split cylinders e.g. used for **CorTec's** Micro Cuff Tunnel closure). Adjustable diameter closures are associated with the risk of the nerve escaping from the cuff or connective tissue growing into the cuff and effectively opening it. An opened cuff results in less effective stimulation or even cross activation of adjacent (nerve) tissue. Even worse, it dramatically compromises nerve cuff recording quality and amplitude because the electrical insulation against the environment is affected.



As a rule of thumb, spiral cuffs should wrap around the nerve at least with 2.5 turns in order to avoid cuff nerve escape and electrical insulation issues. Self-adjusting diameter cuffs can compensate for nerve swelling to some extent. However one has to ensure that these cuffs do exert a pressure on the nerve that remains well below 20 mm Hg, the pressure at which venal blood flow inside the nerve starts to get disturbed with the potential effect of nerve damage.

1.3 Cable

Cables should be made from wires that provide low electrical resistance between cuff and electronic equipment and good electrical insulation against the environment. Cables should be mechanically very flexible and at the same time very strong.

For acute experiments, straight wires provide sufficient mechanical robustness. Litz wires (multi strand solid wires) provide higher mechanical flexibility than a single solid wire of similar total diameter. For chronic experiments, wires are often coiled inside a silicone or polyurethane hose, enduring bending- and stretchingloads.

Typical wire materials are MP35N[1] or Platinum-Iridium (PtIr) with diameters between 25 µm up to 120 µm. These materials provide good robustness but have poor electrical conduction properties.

[1] MP35N is an alloy of Ni-Co-Cr-Mo, commonly used for implantable devices.

›› Tri-polar cuff arrangements can avoid currents leaving the cuff causing side effects on adjacent tissue.‹‹

In order to reduce the wire resistance, these materials are available as tubing filled with silver (so-called Drawn Filled Tubing, DFT, technology).
A good option for acute cuff wires are 7-stranded MP35N-DFT wires (each 25 µm in diameter) coated in a fluoro-polymer. Chronic implant cables are often made from MP35N-DFT or PtIr wires of up to 100 µm diameter, insulated with polyesterimide or fluoropolymer and coiled inside a silicone or polyurethane hose of 1-2 mm outer diameter.The wires can be connected to many metal connectors by welding (resistance welding or laser welding) or by soldering. Therefore the wires have to be cut to length and the insulator as to be stripped e.g. by using cutting tweezers before soldering.

Although soft soldering of PtIr is easy to do using conventional soldering materials, soldering of MP35N is more demanding. **CorTec** recommends using lead based solder in combination with aggressive flux (e.g. ALUSOL solder wire).
Please contact CorTec if you need more detailed advice or alternative solutions for connecting wires to your equipment!

1.4 Electrode Contacts

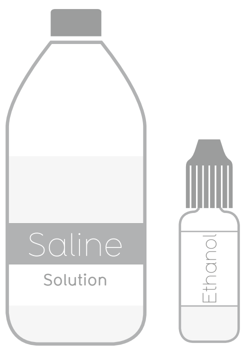
Typically, the electrode contacts of the cuff are shaped as rings wrapped around the nerve or disk or rectangular shaped contacts; or a combination of both.
The function of the cuff determines size, shape and material of electrode contacts. If the cuff shall be very flexible and allow stretching or bending to a limited degree, solid contact areas (much stiffer than the cuff elastomer body) should be avoided by either breaking them up in several small contacts or by using **CorTec's** meander electrode contacts.

In case of electrical stimulation, DC or AC blocking, one has to take the electrical charge per phase that passes through an electrode into account. While moderate charges (charge density ≤ 90 µC/cm²) can be injected into electrode contacts made from PtIr without causing critical electrode corrosion, large charges (charge density ≤ 2 mC/cm²) require a high-performance electrode coating such as sputtered iridium oxide film (SIROF).

Based on the material properties provided above, one can calculate the minimal contact area for a given charge that shall safely pass through. When designing a stimulation/blocking cuff, one has to take into consideration which path of lowest resistance the injected current might take. Depending on the application, one must avoid currents leaving the cuff, causing side effects on adjacent tissue. In such a case, a tri-polar arrangement is recommended (see next paragraph).

In case of electrical recording contacts have to be designed in a way that they generate minimal electrical noise (the larger the contact area the better) and pick up the signal very locally (the smaller – in case of disk shaped contacts – or thinner – in case of ring shaped contacts – the better). A very popular design of a recording cuff consists of two ring-shaped contacts each close to one end of the cuf, a ring-shaped contact at the cuff center (might be divided into multiple disks) and a ground electrode contact at the outside of the cuff body.

The ground electrode is connected to the ground of the amplifier and reduces issues common mode signals of „real world" amplifiers. The other contacts are switched in a tri-polar recording arrangement, causing signals from outside the cuff being attenuated and signals generating from inside the cuff being amplified. The amplitude picked up by such a cuff scales with the length of the cuff: The longer the cuff, the larger the signal amplitude. This rule of thumb is valid up to the (impractical) cuff length of about 20 cm.



STERILIZING
& WETTING

2 Preparations

2.1 Cleaning | Disinfection | Sterilization

Cleaning and disinfection can be done by wiping off the cuffs with ethanol (60%-100%) or by ethanol dips (at least one minute). Sterilization is typically carried out in appropriate sterile packaging using autoclaving or ethylene oxide gassing. **CorTec** cuff electrodes can be sterilized using any of the two methods.

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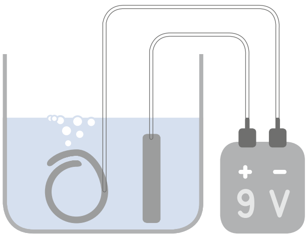
However, sterility of the cuff cannot be warranted by **CorTec** if sterilization is not done by **CorTec** itself. On request, cuffs are shipped sterile in appropriate packages, labelled accordingly.

BUBBLE TEST



2.2 Wetting

To avoid that air bubbles get trapped on the electrode contacts during implantation (leading to high electrode impedance and bad electrical coupling to the tissue), we recommend to implant the electrode while still moistened with saline according to the following protocol:

1. Wet surface with ethanol (60% – 100%)
Immersing the cuff in ethanol (at least one minute) will wet all surfaces, reducing the risk of having electrically insulating air bubbles sticking to the metal contacts.

2. Rinse in sterile saline solution
After having immersed the electrode in alcohol, submerge the electrode in sterile saline solution for at least 10 min to remove the alcohol (neurotoxin!) from the electrode and to provide proper hydration of the metallic surface. If bubbles on the contacts remain after this procedure, place the cuff in a small volume (≤ 2 L) low power (≤ 35 W) ultrasound bath filled with saline and sonicate it for not more than 90 seconds. Longer sonication might damage the cuffs. This procedure might only be practical in acute experiments because of sterility issues associated with the equipment used.

2.3 Functional Check | Impedance

Functional Check
If you have any doubts about the integrity of the electrical leads or their insulation, a simple test is a "bubble test" done *in vitro*. Place the cuff in a beaker filled with saline solution. Use a PP3 battery (9 volts), apply the positive pole to a large surface (some cm^2) metallic material, e.g. stainless steal. Then connect the negative pole of the battery consecutively to each wire of the cuff. When contact is made, you should see a stream of bubbles (hydrogen gas) coming from the connected electrode contact only and not from other contact or external point along electrode body or leads. After bubble testing, make sure all surfaces are wetted again.

Impedance
Electrochemical impedance is a measure for the electrical coupling between electrode and tissue. The lower the impedance the better. Some rules of thumb:

The LARGER the electrode contact surface, the lower the electrode impedance.

The LARGER the cuff diameter, the lower the electrode impedance.

The SMALLER the distance of two electrode contacts to each other, the lower the impedance measured across them.

The HIGHER the electrical conductivity of the medium inside the cuff (e.g. nerve), the lower the impedance.

Rough electrode contacts have a lower impedance at low frequencies (e.g. 10 or 100 Hz) compared to very smooth electrode contacts.

High performance coatings (e.g. SIROF) have a lower impedance at low frequencies (e.g. 10 or 100 Hz) compared to PtIr or stainless steel.

Low electrode impedance is associated with low electrochemical noise generated by the electrode.

Low electrode impedance is associated with low electrical losses during stimulation.

If impedance is measured *in vivo*, make sure to not electrically stimulate/block/harm the nerve. A good starting point is 100 mV amplitude of a 1 kHz sine wave for which the electrical current response is measured and the impedance is calculated.

›› Routing cables in meanders helps to avoid excessive forces being introduced on the cuff by the electrode cable.‹‹

3 Surgery

3.1 Nerve Handling & Fascia

The nerve segment should be freed from surrounding tissue attachments. Avoid cutting nerve branches, as these usually contain essential feeding blood vessels; rather include them in the electrode body if necessary.
Make sure there will be some slack in the nerve at either end. Make sure that the nerve will neither be kinked by an abrupt change of direction near the cuff end, nor stretched by attached connective tissue.

Do not touch the nerve directly with tweezers. Use surgical ligature to lift the nerve, if needed. Alternatively, handle the nerve by leaving a bit of fascia attached to it – grab the fascia with tweezers and handle the nerve indirectly. Stretching of the nerve must be avoided.

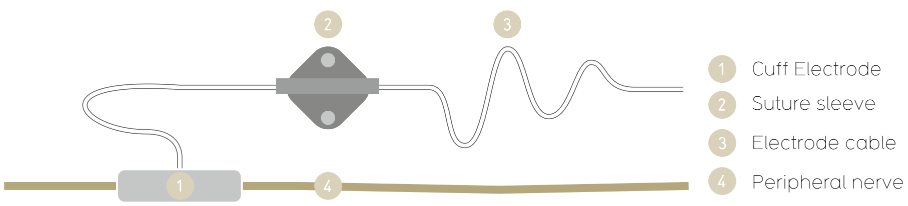
3.2 Cuff Handling

Choose wide and flat tweezers without any sharp or pointy edges. Tweezers coated with silicone rubber or epoxy allow for even safer handling. Any sharp tips might protrude through the cuff body, disrupting either the insulation properties of the silicone or breaking functional sections. Using sharp or toothed tools at the wires might damage the wire's insulation.
Make sure the cuff has been wetted before implantation. Inject sterile Ringer's solution or similar through one cuff end into the inside of the cuff once implanted in order to displace air bubbles potentially trapped inside the cuff.

3.3 Fitting

Wiring Acute vs Chronic

The cuff should sit on the nerve without the risk of coming off in the presence of small pull forces on its cable or activity of adjacent muscle tissue. However, one might argue that the result of pulling on the cable should rather be a cuff that slips off the nerve than severe nerve damage introduced by a cuff that clings to the nerve. As a consequence, it should be prevented that the cable introduces excessive forces on the cuff, e.g. by securing it to adjacent tissue using surgical suture. Using suture sleeves minimizes the risk of cable damage introduced by the suture. The cable should be routed away from the cuff location if possible in shape of a meander. Cable loops shall be avoided since the rubbing of the cable against itself is known to cause cable insulation failure.



4 Experiment

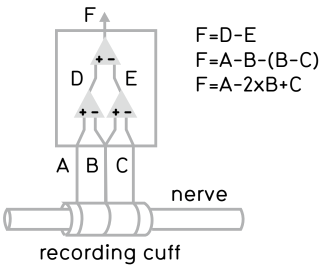
Other than **CorTec's** cuffs including the AirRay research Micro Cuffs not all cuff electrodes can be used equally well for recording and stimulation applications. Make sure that you use the right cuffs for the application that you are working on.

4.1 Impedance

Make sure you have no air bubbles trapped in your cuff. These can dramatically alter the electrical coupling and hence the impedance. Carry out the measurements as described above. Compared to 0.9% saline solution the *in vivo* impedance is expected to be higher since the nerve tissue has a lower electrical conductivity. In chronic experiments, the initial electrode impedance is expected to increase to about its 2- to 3-fold and slowly fall again before it stabilizes expectedly within the first three weeks.

4.2. Recording

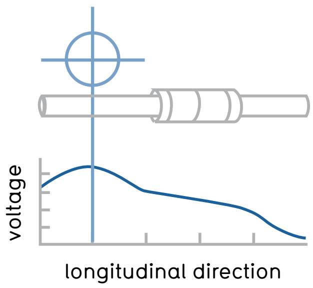
It is recommended to follow the scheme of the figure at the left for true-tripolar cuff recordings. In order to avoid problems associated with the pick-up of common-mode signals, the electronic ground of the amplifier circuit should be clamped to the body potential, e.g. by connecting it to a ground electrode contact very close to but outside the cuff.



i.

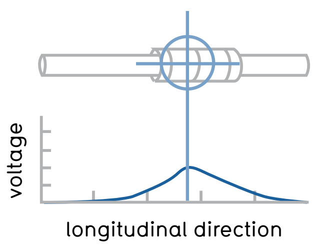
Tripolar nerve recording

Wiring of ring-shaped electrode sites to the true-tripolar amplifier:
Presuming a unity gain, the amplifier transfer function is F=A -2xB +C.
In the case of a linear relationship between voltages at electrode size A, B, and C (e.g. A=100 µV, B=80 µV, C=60 µV), the output voltage F is 0 µV.



ii.

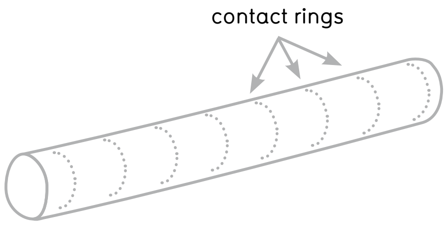
A signal generated outside the cuff (cross hair) results in a current flowing into the cuff. Since the cuff has a fixed diameter and is filled with a nerve tissue of a certain (constant) electrical conductivity, the voltage drop inside the cuff in longitudinal direction is linear and would be rejected by a true-tripolar amplifier.



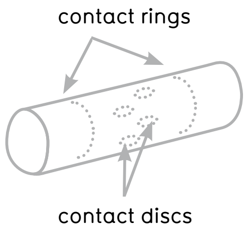
iii.

A signal generated inside the cuff (cross hair) causes a current to flow in both directions inside the cuff, causing a non-linear electrical voltage profile, which is electrically amplified by a true-tripolar amplifier.

Strongly dependent on your experiment, you will be able to record amplitudes from sub-microvolt level (e.g. natural nerve traffic) to over 100 µV (electrically evoked compound action potentials, CAP). The signals will have most of their power in the frequency band between 100 Hz and 3 kHz.
Nerve traffic can be recorded as whole nerve recordings (typical tripolar arrangement) or selectively from individual fiber types (multiple ring electrodes along a cuff) or individual fascicles (multiple disk-shaped electrodes distributed over the circumference of the nerve).



Multi-Contact Cuff for
Fiber-Selective Recording



Multi-Contact Cuff for
Fascicle-Selective
Recording and Stimulation

> **›› Inverse recruitment of fiber types is typical for** electrical stimulation: large fibers get electrically excited at lower stimulation levels than smaller ones.‹‹

4.3 Stimulation

Make sure you identified any possible way the stimulation current can flow. Please take into account that a ground electrode used by equipment different to your stimulator (e.g. an amplifier) still might provide the current return path of lowest impedance with the result that your stimulation result is very different from what you expect.

Ensure that the DC-decoupling of your stimulator is working properly, especially when using current-controlled pulses. Even very small DC currents can completely change the stimulation thresholds and might cause electrode corrosion followed by pH shifts and tissue irritation.

If you are unexperienced in electrical stimulation, it is advisable to begin your experiment with low stimulation intensity (such as 100 µA amplitude, 200 µs pulse width) charge balanced pulses and slowly increase the amplitude while observing the effect of the stimulus (muscle twitch, recorded CAP, etc.), but make sure to stay within the electrochemically safe limits (see above).

Electrical stimulation following the procedure described above will lead to inverse recruitment of fiber types: large diameter fibers will be electrically excited at lower stimulation intensities than smaller fibers. Applying AC blocking, DC-blocking (anodal blocking), or sub-threshold pre-pulses on tripolar cuff electrodes, you can reach orderly recruitment to some extent: stimulation of the small fibers without activation of the larger fibers (fiber selective stimulation).
If you want to selectively stimulate individual fascicles, you would select a cuff that has multiple disk-shaped electrode contacts located on the nerve circumference.

4.4 Blocking

If you are unexperienced in high frequency (kHz) blocking, it is recommended to begin your experiment with low amplitude (such as 100 µA) charge balanced sine waves or rectangular waveform at a frequency between 20 and 60 kHz and slowly increase the amplitude while observing the effect of the blocking (inhibited muscle twitch, recorded CAP, etc.), but make sure to stay well below the electrochemically safe limits since the charge injection limits might be somewhat lower than those for ordinary stimulation as described above. We recommend to use tripolar cuff electrodes for blocking.

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5 Explantation

5.1 Sterilisation/Cleaning

After an acute experiment, the cuff can easily be removed from the nerve and cleaned from liquids and tissue with swaps using ethanol/water.
After chronic experiments, the connective tissue that typically encapsulates the cuff has to be cut away with micro scissors or similar, the cuff is removed from the nerve and cleaned manually with tweezers. Organic residuals can be removed by applying an enzyme driven TrypsinEDTA solution for about 5 minutes followed by careful wiping with a microbrush, followed by an ethanol/water rinse.

5.2. Re-use

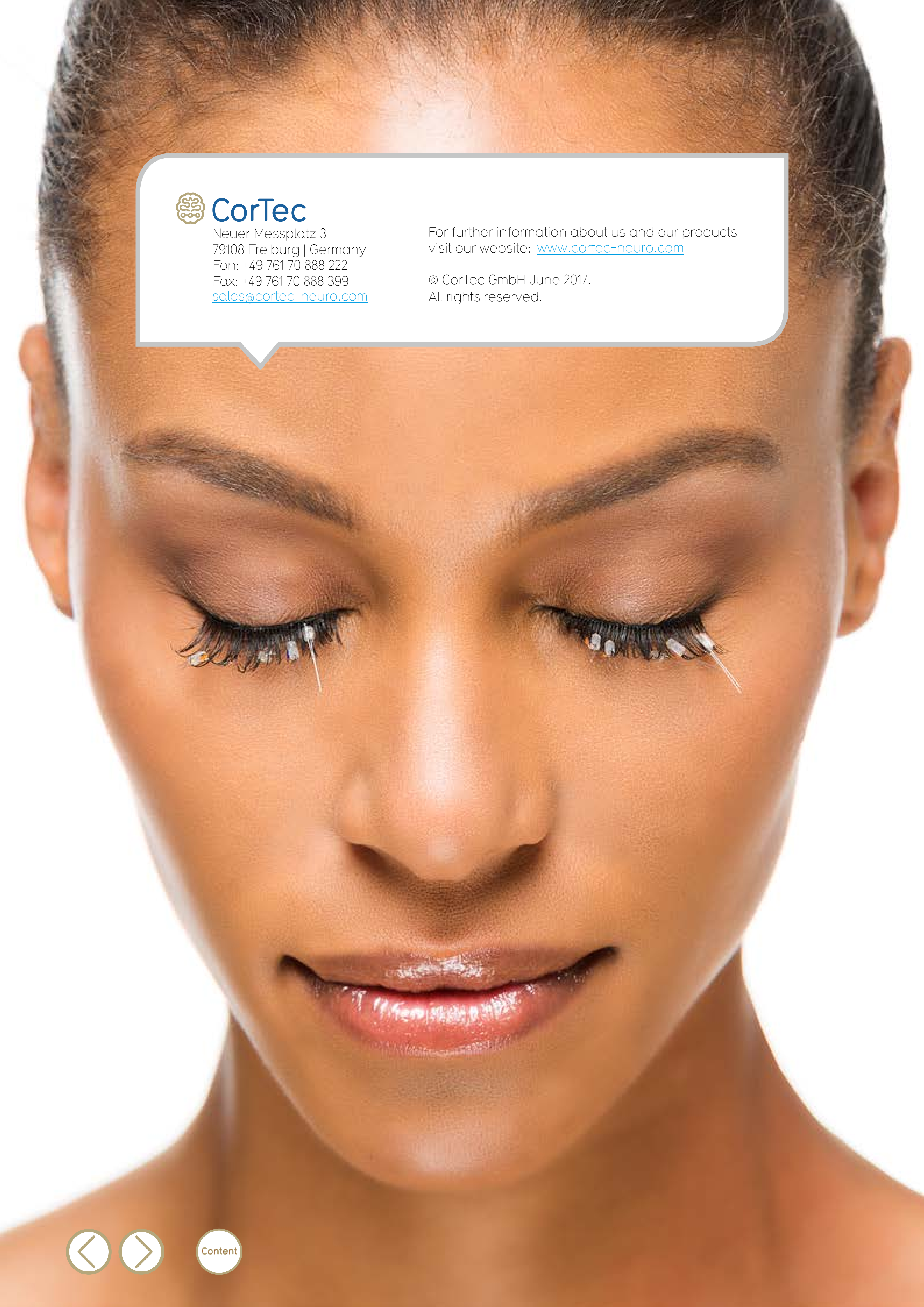
Electrodes can be re-used once the function has been proven not to be compromised. Before re-usage (especially for chronic experiments), make sure that all biologic contamination has been cleaned off and the cuff has been properly sterilized.

Contact us for further questions at
sales@cortec-neuro.com

Learn more about our products
AirRay research Micro Cuff Sling
AirRay research Micro Cuff Tunnel

Get to know **CorTec:**
www.cortec-neuro.com

These guidelines do not replace a dedicated product manual.



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