

ARTICLE TYPE

Characterization and Evaluation of Interferential Current Stimulation for Functional Electrical Stimulation

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Abstract

Background

Interferential Current Stimulation (ICS) has long been employed in neuromodulation and physical therapy, yet its mechanisms and potential applications in Functional Electrical Stimulation (FES) remain under-explored. We present new data, including neural activation reported by muscle force measurement, to evaluate the potential advantages of ICS, such as selective targeting and reduced discomfort.

Methods

Experiments were conducted on human participants, focusing on ulnar and median nerve activation with stainless steel and commercial conductive hydrogel electrodes. Key parameters, including electrode configuration, frequency, current amplitude, and skin preparation, were investigated to test their effects on activation thresholds, force generation, and user comfort.

Results

Our results revealed that ICS can achieve proportional muscle force control, although its efficiency was lower than rectangular biphasic pulse stimulation. The application of moisturising cream and gel significantly improved comfort and reduced activation thresholds, underscoring their importance in optimising ICS protocols. However, ICS required higher electrical power and caused discomfort during burst initiation with all electrodes, presenting challenges for its practical use in FES. Furthermore, our findings indicated that ICS did not exclusively activate neural regions at the difference or “beat” frequency but also by the carrier frequency, challenging some prior assumptions in the literature.

Conclusion

These results highlight the need for further research and practical measurements of neural recruitment and muscle fatigue and into the mechanisms of nerve activation and neuromuscular junction transmission with stimulation via the skin surface. Innovations in electrode design, stimulation waveforms, and protocols are also needed to enhance the efficacy and comfort of ICS.

KEYWORDS

Interferential Current Stimulation, Functional Electrical Stimulation, Neuromodulation.

1 | INTRODUCTION

The precise application of transcutaneous electrical current to generate useful muscular contractions is a substantial challenge. Several groups have used matrices of electrodes over the forearm, for example, with

an algorithmic approach to choose the best combination of electrodes, current amplitude, and pulse parameters to allow functional activation with an acceptable level of sensation^{1–6}. There has been a resurgence of interest in activating neural tissue through the skin through two interfering current fields⁽⁷⁾. Interferential Current Stimulation (ICS) is based on delivering these fields at slightly different kHz frequencies, for example, 4000 Hz and 4010 Hz, with the intention that excitable tissue below the skin might be activated at the difference or beat frequency (10 Hz in

this example) generated by the alternating voltage caused by successive constructive and destructive interference of the two waves.

The method has been used and described since the 1950s, but experienced physical therapy practitioners are still undecided on its application or superiority over any other method of transcutaneous stimulation. ICS is suggested for deep tissue stimulation due to reduced tissue impedance at higher frequencies, allowing for deeper penetration and predominant nerve stimulation via the beat effect (^{8,9}).

Earlier studies proposed various hypotheses on the biophysics of neural activation by ICS.¹⁰ suggested that the neural membrane demodulates the interferential currents, acting as a low-pass filter.¹¹ argued that the axon membrane rectifies and filters modulated currents, as neurons' filtering properties alone cannot explain the effect. Mirzakhilili et al. proposed the existence of interference regions where kilohertz frequencies interact and non-interference zones dominated by one input current, which may exhibit no activation or kilohertz conduction block, typically occurring at 20–40 kHz (¹²).

While various studies have explored ICS for Pain Relief (¹³) and Deep Brain Stimulation (^{10,14}), there is a lack of research on the neural activation mechanism triggered by ICS, particularly in the context of Functional Electrical Stimulation (FES). Very few empirical studies have compared the transcutaneous current input with the excitatory output in terms of interstitial voltage, induced neural activation or muscle force. We wished to test the potential advantages of lower skin sensation, deeper and more selective activation, and the ability to steer the area of activation by adjusting high-frequency current between two or more pairs of electrodes depending on the positioning and type of electrode and the absolute currents applied.

Using carefully controlled positioning and delivery of current, we collected data in rats and humans. We will use numerical models to test any potential benefit of intermittent stimulation over pulse stimulation and optimise the electrode and currents chosen for a specific goal. We present early experiments in two human models activating nerves in the wrist.

⁷ summarise several testable hypotheses which provide a useful framework for our experiments so that we can decide in what context these are true and in what context they might fail.

- Interferential stimulation relies on multiple high-frequency electric fields that only cause neuronal activation where they constructively overlap.
- By controlling field orientation and frequency offset, the hot spot of constructive interference can be precisely targeted.
- Frequencies above 1 kHz can be considered as non-stimulating.
- Using the same electrodes and applying traditional TENS does not evoke a peripheral nerve stimulation response for the same amplitude of stimulation used with transcutaneous interferential stimulation.

Our practical experiments demonstrate that these statements are not generally applicable.

There have been a few recent experiments in which a demonstration of low-frequency neural response has been made in a setting of interferential activation.¹⁰ showed recordings from patch-clamped neurons in the somatosensory cortex and hippocampus of the anaesthetised mouse in which sinusoidal stimulation at 2000 Hz in one pair of 1mm diameter scalp electrodes and 2010 Hz in another pair caused repetitive firing of action potentials at 10Hz. The response was similar to 10 Hz stimulation at a slightly higher amplitude, but no firing occurred with 2000 Hz applied through one set or both pairs of electrodes. Additionally, neural activation was stronger in deeper brain tissue and could be redirected toward electrodes delivering less current.

In FES using peripheral nerve stimulation, there are scenarios in which it would be useful to relocate an activation function beneath the skin, possibly to avoid activation of sensory receptors in the skin while recruiting deep nerves such as the femoral nerve, and to capture different nerves such as median or ulnar nerves in the wrist or tibial and peroneal nerves in the lower limb. If current could be usefully controlled in this manner, the requirement for large numbers of skin contacts in a matrix of electrodes might be reduced.

Using a spatially distributed electrode matrix requires smaller contact patches as spatial resolution increases. Previous work, primarily using adhesive gel electrodes with contact areas over 2.5 cm², has focused on selecting motor points in the forearm to activate hand muscles rather than targeting specific nerves¹⁵. Complex spatial and temporal activation patterns have also been explored to distribute current and reduce discomfort and fatigue.

We conducted experiments with stainless steel electrode matrices and off-the-shelf surface electrodes to examine the effects of electrode positioning, frequency, and current amplitude during interferential current stimulation. The forearm serves as an ideal testbed for analysing hand flexor and extensor contractions via stimulation of the closely located median and ulnar nerves, enabling evaluation of stimulation specificity.

2 | METHODS

2.1 | Ulnar Nerve activation using stainless steel electrode matrix

The data presented in this section came from a single participant who provided informed consent (LJMU 23/SSPS/076).

The stainless steel electrodes were made of 6mm diameter stainless steel (Austenitic stainless steel, RS Components) with approximately hemispherical contact surfaces so that the skin contact area was about 0.5 cm² with 1 cm spacing between electrodes. The electrode pins were connected to single wires using phosphoric acid flux (85 wt.% in H₂O. Sigma Aldrich, Glasgow, Scotland) and tin-lead rosin-core solder (RS Components, Corby, UK), and the wires were to a female gold-plated pin adapter. The output from the stimulators could thus be directed by

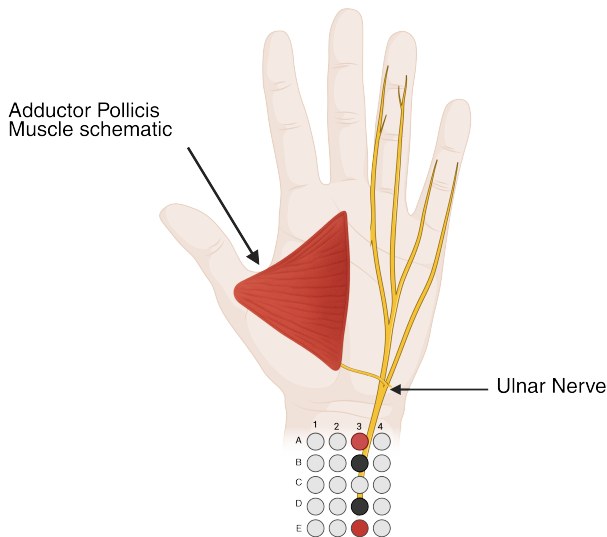


FIGURE 1 Schematic representation of the experimental setup using a 5×4 stainless steel pin electrode matrix with two electrode configurations targeting ulnar nerve activation. The two configurations implemented were "Axial", used for pulse stimulation and "Axial cross" used for ICS. In the "Axial" configuration, electrodes on rows C2 and C4 are active (indicated in black [cathode] and red [anode]), while in the "Axial cross" configuration, electrodes on columns A3 and D3 form channel 1, whilst B3 and E3 form channel 2. The electrode matrix is positioned on the skin over the ulnar nerve, alongside the tendon of the flexor carpi ulnaris and above the ulnar artery specifically to stimulate the AP. The adductor pollicis illustrated in its position under the skin of the palmar surface of the hand, originating mainly from the third metacarpal bone and inserting onto the proximal phalanx of the thumb.

the choice of the wires to be connected to their output. A force transducer (Statham Gould UC3, Radwell, Newcastle Under Lyme, UK) was calibrated with a 500 g weight and connected to a copper ring encircling the proximal phalanx of the left thumb to measure the adduction force generated by the adductor pollicis muscle (AP). The AP is the only muscle acting on the thumb that derives innervation from the ulnar nerve. To maintain stability, the participant sat alongside a bench on which the forearm was secured with a custom foam cast with webbing straps and a loose clamp on the palm, which gently pressed the back of the hand into the foam cast. The wrist was maintained in the neutral position (neither flexed nor extended).

Biphasic voltage pulses, delivered either singly or in brief bursts, were generated in LabChart Version 8 (AD Instruments, Oxford, UK) and applied through one of the DS5 stimulators (Digitimer, Welwyn Garden City, UK). Two Digitimer DS5 stimulators, controlled by a 2-channel KeySight function generator (Keysight Technologies UK, Wokingham, UK.), were used to deliver interferential stimulation at two slightly different kilohertz frequencies. In some trials, to enhance current flow into

the skin, CeraVe moisturizer (CeraVe, L'Oréal, USA) was applied to the skin before electrode placement and gently massaged into the skin for 1 minute. We measured the recruitment curve for single pulse stimulation before and after this skin treatment in one case. Each stimulation protocol was recorded within a 2-second sampling period. Stimulation onset was delayed by 0.2 seconds so that passive (resting) force could be recorded and subtracted from each active contraction to give the developed force which we have reported here.

Various electrode configurations with respect to the ulnar nerve were tried, including an axial, and axial cross (Figure 1) to compare activation thresholds and maximal activation levels. For the crossed patterns, one of the electrodes in the first channel was placed between the electrodes delivering the second channel. Stimulation protocols were evaluated across frequencies (or beat frequencies for interferential stimulation) of 2, 5, 10, and 20 Hz, with carrier frequencies for interferential stimulation ranging from 2 to 5 kHz. Test-retest reliability was evaluated in the axial configuration with a pulse width of 0.5 ms and current intensities from 2.5 to 25 mA. Additionally, the effect of CeraVe moisturiser on activation efficiency was tested using 0.5, 1, and 2 ms pulse widths with the same current range. Recruitment curves were constructed to analyse the relationship between stimulation amplitude and force output.

The measurements reported were made during 2 sessions over a period of 7 days with an assessment of the stability of the preparation with and between sessions. Both sessions took place at Liverpool John Moores University. The participant gave informed consent (23/SPS/076). The participant looked away from the display of recorded data. We made preliminary trials with pre-set parameters to find the approximate thresholds for activation. For the trials presented here, the activation was progressively increased until the participant asked not to continue. Thus, the data is generally shown up to the threshold for significant discomfort and past the level that would be considered as appropriate for routine use in therapy or research in naive participants.

Data was exported from LabChart as .txt files in both 20 ks/s and downsampled formats (factor of 10), then imported into Python version 3.13.0, (Python Software Foundation, Wilmington, USA) for analysis. Stimulation bouts were labelled by identifying sections starting at Time (s) = 0. Passive tension was calculated as the mean Force (g) between 0.1 and 0.2 seconds before stimulation, and developed force was computed by subtracting passive tension from each Force (g) value. The first 0.05 seconds were excluded to reduce onset artefacts.

For each bout, peak developed force (after 0.2 seconds), and peak voltage values were measured. ICS charge was calculated from Channel 1 and 2 ICS (V_{pp}) RMS values, and pulse charge from Pulse Channel (V) using a 1 ms pulse width (0.5 ms each phase). Processed data were saved in labelled text files, including values for developed force, voltage peaks, and calculated charges per activation.

The data output from Python was imported into R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria) for visualisation. Peak force and amplitude plots were generated using *ggplot2* (Hadley Wickham / RStudio, Boston, USA) to explore the relationships between stimulation parameters and developed force. Stimulation bouts were

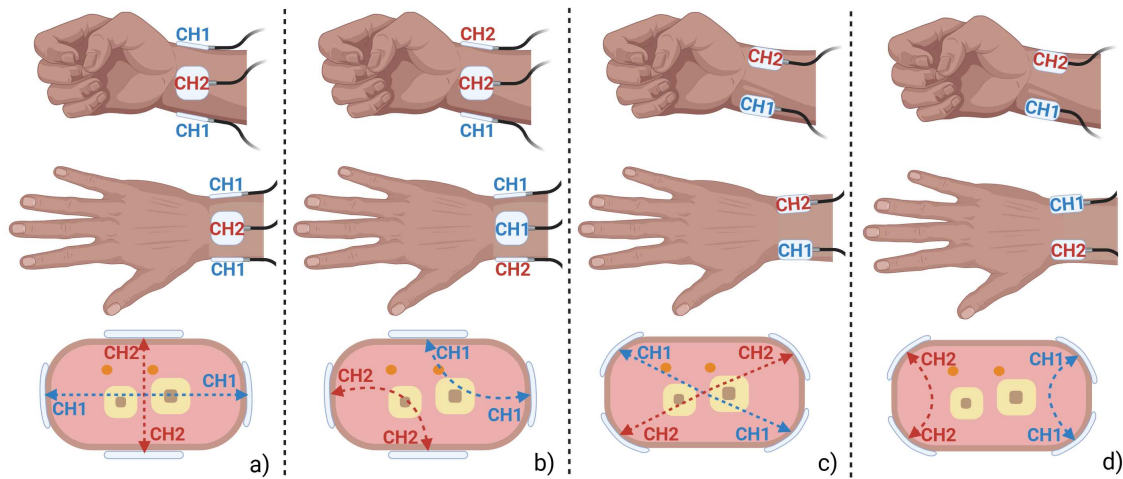


FIGURE 2 Representation of the electrode placement around the wrist using 4x4 cm squared electrodes. From top to bottom: Frontal view of the hand, back view of the hand, and transverse section of the wrist viewed from the forearm (The orange dots represent the median and ulnar nerve, the yellow squares represent the ulna and radius). CH1 and CH2 represent the stimulator channels. **a)** Lateral and anteroposterior placement - crossed channels configuration. **b)** Lateral and anteroposterior placement - separated channels configuration. **c)** Diagonal configuration - crossed channels. **d)** Diagonal configuration - separated channels.

categorised into specific frequency groups for both pulse and ICS simulations (e.g., 5 Hz, 10 Hz, and 20 Hz for a pulse; 2 kHz, 4 kHz, and 6 kHz for ICS). The stimulation test-retest protocol was performed with moisturiser applied at the beginning of the experiment, again at the end of the same experiment (+1h), and after an additional experiment conducted 7 days later. An approximate volume of 1 mL of the cream was applied to the skin on the wrist, specifically over an area measuring 5x5 cm that corresponds with the electrode matrix. The cream was meticulously massaged into the skin for a duration of approximately 10 minutes until complete absorption was achieved.

To quantify the charge delivered during each stimulation bout, both ICS and pulse charges were calculated in μC . ICS charge was derived from ICS channel 1 using the root mean square (RMS) formula: $V_{rms} = V_{p-p} / (2 * \sqrt{2})$, with a scaling factor of 2.5, because the DS5 stimulator was set to $IV = 2.5\text{mA}$. Pulse charge was calculated from the pulse Channel, with a pulse width of 1 ms, and was converted to μC . For Pulse stimulations, the pulse charge was further scaled by multiplying by the stimulation frequency (e.g., 5 Hz, 10 Hz, or 20 Hz) to account for the cumulative charge delivered per number of repeats. For ICS simulations, the calculated charge was doubled to account for using two channels, which in this study provided identical currents.

2.2 | Median Nerve activation using hydrogel interface electrode experiments

2.2.1 | Placed around the wrist

Six healthy volunteers (three males and three females, 22-43 years) participated in the study. The experiment followed the guidelines in the Declaration of Helsinki and was approved by the Vice-Rectorate for Research and Development of the Universidad de Concepción, Chile (CEBB 1605-2024).

The subjects were asked to remain seated with their right forearm resting on a table. The subjects' wrist circumferences were measured using a measuring tape ($17.35\text{ cm} \pm 1.90$). After an alcohol wipe cleaning, four 5x5 cm Valutrode® Axelgaard (Axelgaard Manufacturing Co., California, USA) electrodes were positioned around the wrist as illustrated in Figure 2. Two different electrode positions were used: lateral and anteroposterior of the wrist (L/AP configuration) and diagonal to the wrist (Diagonal configuration). The stimulation channels were shifted to obtain a crossed or separated pairing, as shown in Figure 2.

An Ultima Neo Pro (Pain Management Technologies, Ohio, USA) stimulator generated sinusoidal waves at 4000 Hz and 4020 Hz, obtaining an interferential current with a beat frequency of 20 Hz. Each subject's current intensity was slowly increased by 1 mA until a visual finger motor response was achieved, determining the activation threshold with a maximum of 30 mA per channel. At the threshold current, the stimulation remained active for 4 seconds.

This experiment aimed to determine which configuration performs better for eliciting a flexion and abduction of the thumb by stimulating

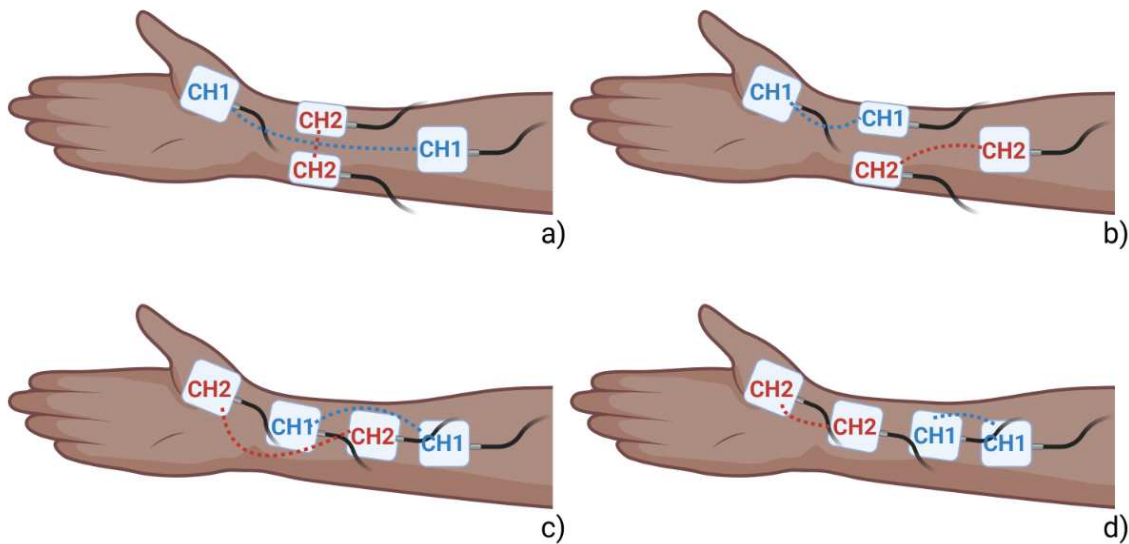


FIGURE 3 Representation of the electrode configurations along the forearm using 4x4 cm squared electrodes. The electrodes are placed with the median nerve as a reference. **a)** Perpendicular placement - crossed channels. **b)** Perpendicular placement - separated channels. **c)** In-line placement - crossed channels. **d)** In-line placement - separated channels. The distal and proximal electrodes are separated by 11 cm. In **a)** and **b)**, the central electrodes are placed midline between the proximal and distal electrodes, separated by 4 cm. In **c)** and **d)**, the electrodes are separated by 1 cm.

the median nerve and avoiding motor responses of fingers innervated by the ulnar nerve. The participant's sensory appreciation of the level of discomfort at the threshold currents was assessed by applying a Visual Analogue Scale (VAS) for pain (¹⁶). To test the presence of conduction block effects by the presence of high-frequency stimuli (as presented in 1), an external mechanical stimulus was made by gently touching the subject with a non-conductive plastic probe in the area between the electrodes while the stimulation was delivered. The participants were asked not to look at the plastic probe to avoid sensory bias.

2.2.2 | Placed along the forearm

Five volunteers (three females and two males, 27-32 years old) participated in the study. The experiment followed the guidelines in the Declaration of Helsinki and was approved by the Vice-Rectorate for Research and Development of the Universidad de Concepción, Chile (CEBB 1605-2024).

The subjects were asked to remain seated with their right forearm resting on a table, relaxing their hands and fingers. The subjects' wrist circumferences were measured using a measuring tape ($16.3 \text{ cm} \pm 1.79$). After an alcohol wipe cleaning, four 5x5 cm electrodes were positioned over the anterior forearm in two different position configurations, as shown in Figure 3. For each position, the channels were shifted to modify the interaction of the current path and evaluate its influence on the resultant interferential current.

The methodology was identical to that presented in Section 2.2.1. An Ultima Neo Pro stimulator produced interferential sinusoidal currents at 4000 Hz and 4020 Hz, generating an interferential current of 20 Hz. Each subject's current intensity was slowly increased by 1 mA until a visual finger contraction was achieved, reporting the current intensity as the threshold. During a 4-second stimulation at the threshold current intensity, the activation of skin afferent nerves was tested with a plastic probe passing over the skin between the electrodes. At the same time, the volunteers did not make visual contact with their forearms.

These electrode configurations were intended to stimulate the median nerve to achieve specific thumb flexion and abduction, evaluating the effect of promoting the current paths crossing for controlling the directions of interference zones. In the case of generating accessory activation of other fingers, the stimulation is considered non-specific. To identify the presence of a conduction block produced by either of the kHz input currents, the plastic probe method was implemented as presented in 2.2.1.

3 | RESULTS

3.1 | Ulnar Nerve activation using stainless steel electrode matrix

Figures 4, 5, and 6 were generated from data collected during the initial experiment, while Figure 7 was based on data from the +7-day experiment. Results are shown from the axial configuration in which the anode

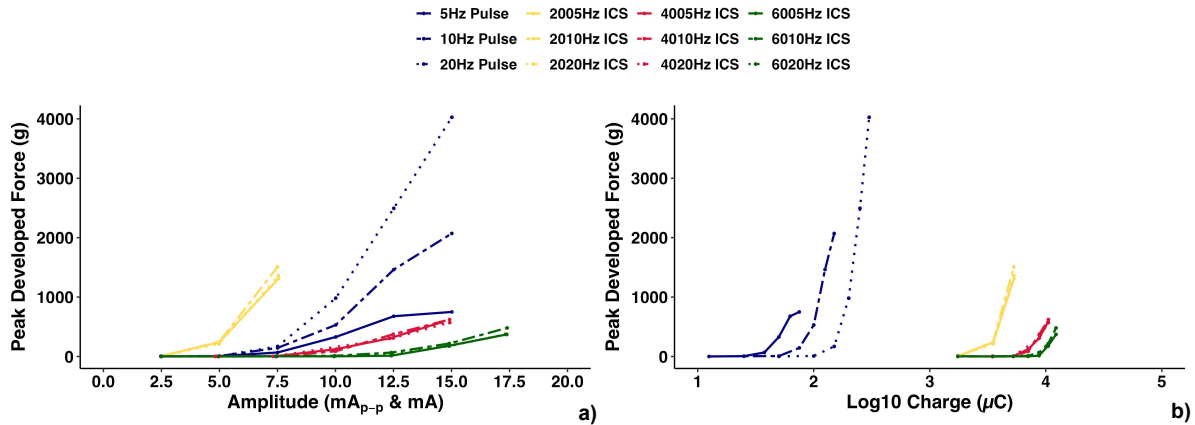


FIGURE 4 a) Peak developed force in response to axial configuration stimulation plotted against amplitude. This figure illustrates pulse and ICS stimulation responses, with amplitude in mA for pulse stimulation and mA_{p-p} for ICS. Different colours represent distinct carrier frequencies, while different line types indicate various beat frequencies, as shown in the legend. b) Peak developed force in response to axial configuration stimulation plotted against total charge ($\log_{10}$ scale). Charge is calculated for 1-second stimulation periods, using RMS values based on the following formulas: $RMS = mA_p \times \text{pulse width} \times \text{number of pulses in the burst}$ for pulse stimulation and $RMS = mA_{p-p} / (2\sqrt{2})$ for ICS. The $\log_{10}$ scale is applied to facilitate comparison across simulations. Colours represent different carrier frequencies, as indicated in the legend, while different line types indicate various beat frequencies. The charge required for ICS activation is two orders of magnitude higher than for pulse activation.

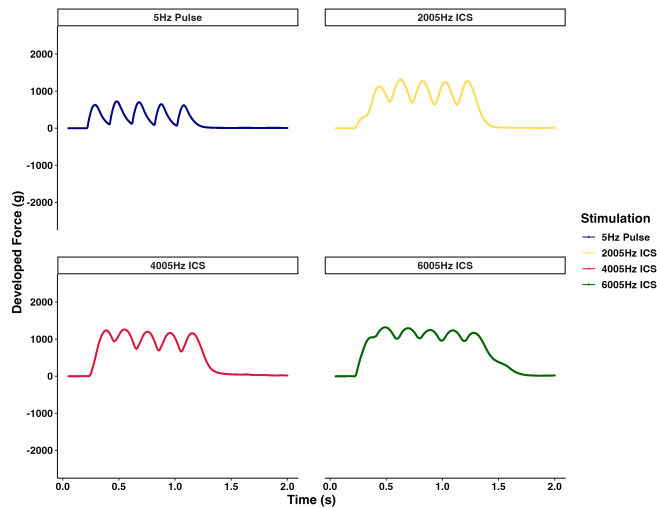


FIGURE 5 Developed force traces over time in response to different stimulation frequencies near to maximal recruitment in the axial configuration. Each subplot shows a specific stimulation frequency: Pulse 5 Hz, and ICS frequencies of 2005 Hz, 4005 Hz, and 6005 Hz, all set with a 5 Hz beat frequency on channel 2. Developed force (g) is displayed on the y-axis, while time (s) is shown on the x-axis, with each trace covering a duration of 2 seconds.

and cathode, or both anodes and cathodes for ICS, were arranged along the anatomical course of the ulnar nerve. Choosing electrode positions

placed transversely from the nerve resulted in much higher thresholds for activation.

Figure 4a shows that the current threshold for nerve activation with pulse stimulation lies between ICS at 2 kHz and 4 or 6 kHz. The developed force with ICS at 2 kHz is greater than that achieved with 4 or 6 kHz, but less than that achievable with pulse stimulation. In each trace, the gradation of the force with amplitude is clear and we confirmed the stability of these responses with several test/retest exercises (Figure 7).

If the recruitment force is considered in terms of electrical charge delivered rather than the maximum current (Figure 4b) then the efficiency of pulse stimulation is shown to be two orders of magnitude higher than ICS.

Figure 5 shows the force traces with the pulse stimulation at 5 Hz and with ICS at a difference frequency of 5 Hz, with a carrier frequency of 2, 4 or 6 kHz. In a mixed nerve such as the ulnar nerve, we find that activation of the neural structures exclusively at the difference frequency is not achievable. The force traces for ICS show that force oscillation modulates the recruitment rather than synchronous activation and relaxation as with pulse stimulation. We have tried to illustrate exclusive interferential activation by recording near the threshold for activation, but our data do not support the claim that ICS causes neuronal activation only where the current fields constructively overlap.

Figure 6a demonstrates the substantial reduction of the activation threshold achieved by using CeraVe cream. Panel a) shows that very little force is developed using stainless steel electrodes applied to clean skin with constant current pulses up to 30 mA if the pulse width is below 2 ms. By contrast, with the cream, a 0.5 ms pulse produces almost full recruitment of adductor pollicis at about 15 mA, with a 1 ms pulse at

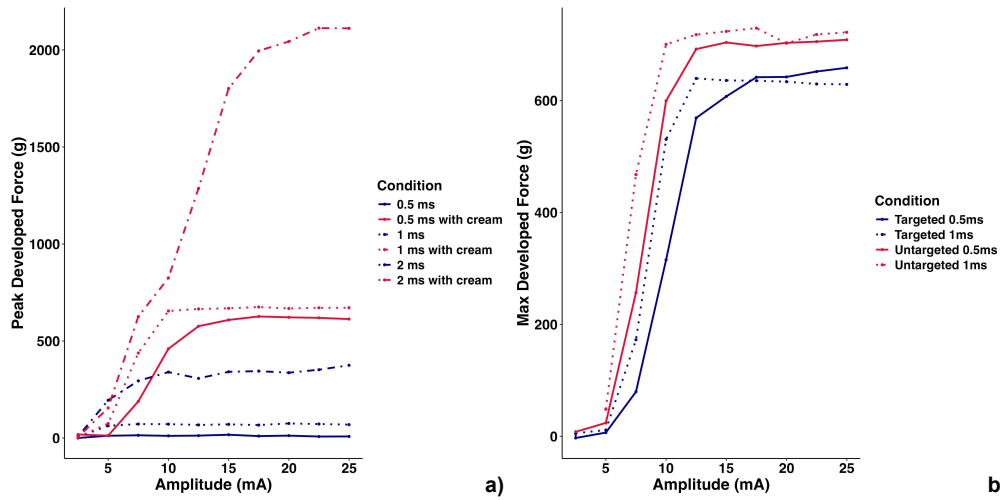


FIGURE 6 a) Effect of moisturiser cream on ulnar nerve activation across a range of amplitudes from 2.5 to 25 mA, using Pulse stimulation in the axial configuration. Different pulse widths are represented by line types: solid for 0.5 ms, dotted for 1 ms, and dash-dot for 2 ms. Colour indicates moisturiser condition: red lines represent stimulation with cream, and blue lines represent stimulation without cream. Peak developed force (g) is shown on the y-axis, and amplitude (mA) on the x-axis. This figure illustrates the impact of moisturiser on force generation at various pulse durations. b) Comparison of developed force across stimulation conditions. Maximum developed force (g) is plotted against amplitude (mA) for four conditions: “Targeted 0.5 ms” (blue solid), “Targeted 1 ms” (blue dotted), “Untargeted 0.5 ms” (red solid), and “Untargeted 1 ms” (red dotted). “Targeted” only applies moisturising cream to the area of the skin in contact with the active electrode, while “Untargeted” covers the entire skin area under the electrode configuration with moisturising cream.

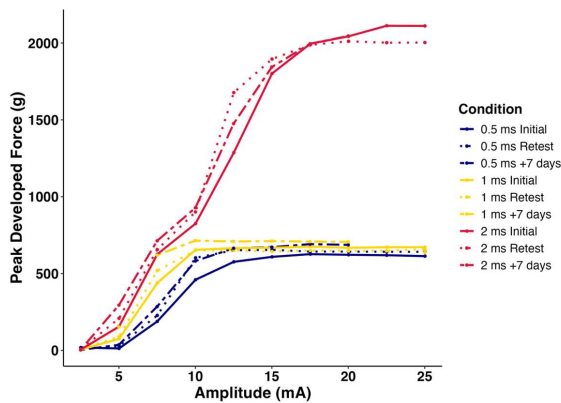


FIGURE 7 Displays the peak developed force (g) as a function of amplitude (mA) for nine conditions, representing three different pulse widths (0.5 ms, 1 ms, and 2 ms), each tested three times (initial, retest and +7 and days). Each condition is distinguished by unique colours and line types: solid lines represent initial tests, dashed lines represent +7-day tests, and dotted lines represent retests. The 0.5 ms condition is shown in blue, 1 ms in yellow, and 2 ms in red.

about 10 mA, and with a 2 ms pulse produces full recruitment at about 7 mA, then recruitment of a much larger force, probably as a result of recruitment of the thenar muscles via the median nerve.

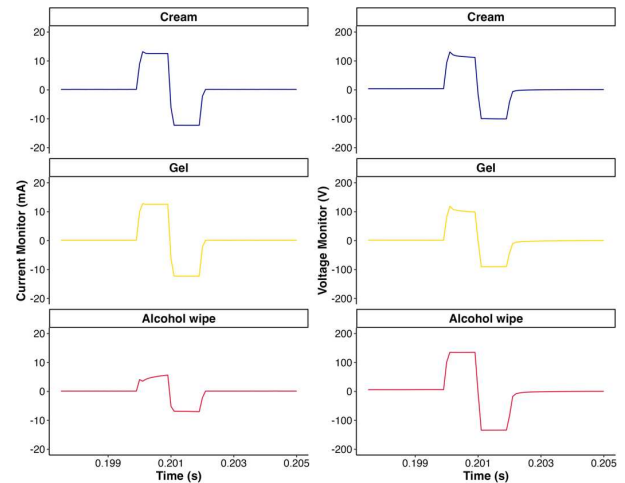


FIGURE 8 Comparison of current and voltage monitor outputs for different conductive media: cream, gel, and alcohol wipe (dry skin). The left column shows the current monitor (mA) for each medium, while the right column displays the corresponding voltage monitor (V).

Figure 6b shows that the advantage of lowering the activation threshold with cream under each electrode contact is preserved when the skin surface under and between the electrode contact is moisturised.

Figure 7 demonstrates that the electrode matrix can be re-positioned with an interval of a week between testing sessions to achieve very similar recruitment curves from one participant in a test-retest trial.

Figure 8 shows current and voltage traces when a 12.5 mA constant current biphasic pulse (0.5 ms per phase) is required from the DS5 stimulator. The current monitor is derived from the voltage across a 1 Ω resistor connected in series with one of the electrodes. In the case of alcohol wipe clean dry skin, the voltage is limited by the compliance voltage of the stimulator, and the current fails to reach the required value. With conductive gel under the electrodes or with moisturising cream applied, the required current is supplied with similar driving voltages, showing that the electrode impedance is similar in both cases.

3.2 | Median Nerve activation using hydrogel interface electrode experiments

3.2.1 | Placed around the wrist

All participants exhibited motor responses during the experimental protocol. The configuration involving crossed stimulation channels elicited motor responses in the fingers at lower current amplitudes than other configurations with a mean current threshold between 16-17 mA, as shown in 9. Conversely, the separated channel configurations were observed to be the least effective in producing motor responses. None of the tested configurations resulted in specific thumb adduction without also inducing flexion in other fingers, demonstrating a lack of selectivity. The registered current thresholds and VAS scores were plotted using bioRender Graph (BioRender, Toronto, Canada). The statistical significance of the studied groups was performed using a Kruskal-Wallis non-parametric test. The test showed no statistically significant differences between the groups.

The sensory evaluation using the Visual Analogue Scale (VAS) revealed a uniform distribution of discomfort perception across participants for all tested configurations, indicating a consistent subjective stimulation experience evaluated in a mean VAS score of 3. Figure 9 illustrates the distribution of current thresholds obtained alongside the VAS evaluation for each electrode configuration, providing a comparative visual representation of the results.

3.2.2 | Placed along the forearm

All participants exhibited motor responses across all four stages of the experimental protocol. Among the tested configurations, the In-Line configuration elicited finger flexion responses at the lowest current thresholds, demonstrating its relative efficiency. In contrast, no statistically significant differences were observed between the perpendicular crossed and separated configurations, while the In-Line separated configuration was associated with slightly higher current thresholds, as presented in 10. The registered current thresholds and VAS scores were plotted using bioRender Graph. The statistical significance of the studied groups was performed using a Kruskal-Wallis non-parametric test. The test showed no statistically significant differences between the groups.

The In-Line configurations were particularly effective in generating specific thumb flexion in most cases. This was in contrast to the perpendicular configurations, which consistently induced accessory motor responses in the middle and little fingers, highlighting a distinct activation pattern.

The Visual Analogue Scale (VAS) application to assess discomfort did not reveal notable differences in the participants' perception of discomfort across configurations. However, the In-Line crossed configuration was reported to provide a comparatively more comfortable sensation among the volunteers. Figure 10 presents the distribution of the current

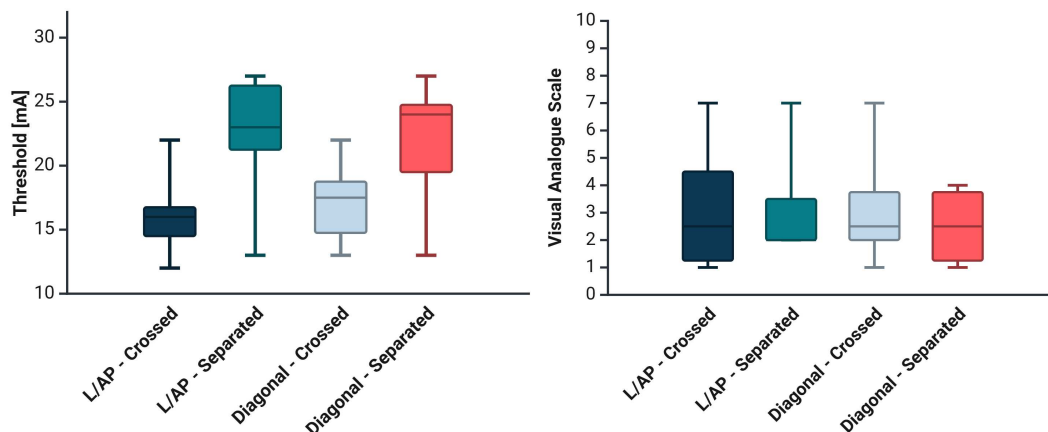


FIGURE 9 Comparison of the distribution of current activation threshold (left) and VAS evaluation from the subject perception (right) for the electrodes placed around the wrist experiment. A Kruskal-Wallis statistical test showed no significant differences between groups.

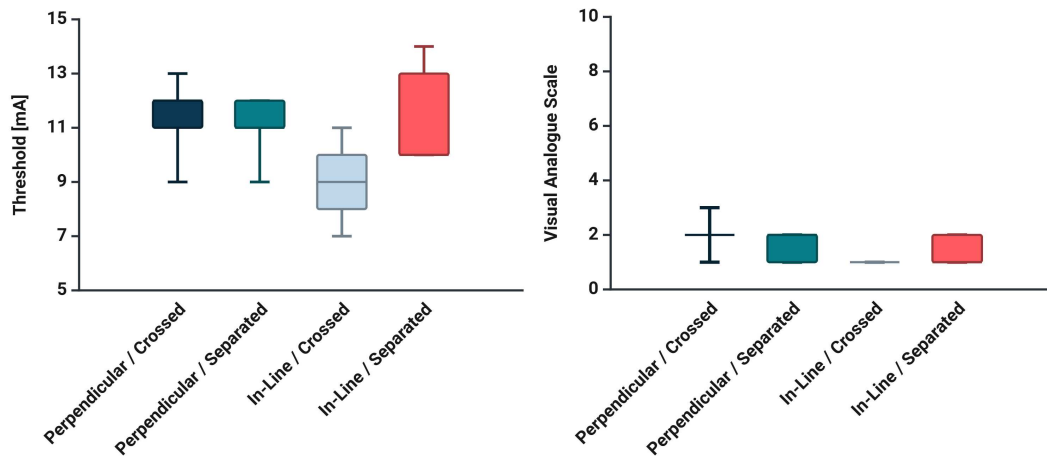


FIGURE 10 Comparison of the distribution of current activation threshold (left) and VAS evaluation from the subject perception (right) for the electrodes placed along the forearm experiment. A Kruskal-Wallis statistical test showed no significant differences between groups.

thresholds and the corresponding VAS evaluations, offering a detailed comparison of the results for each electrode configuration.

All participants reported reduced skin afferent sensation when the ICS was activated and a plastic probe was moved across the skin between the electrodes. This effect was particularly pronounced in the crossed-channel configurations, where volunteers experienced difficulty in blindly identifying whether the probe was in contact with their skin.

4 | DISCUSSION

The forearm testbed provides a convenient way to examine the motor and sensory response to rectangular and ICS stimulation. Figure 7 illustrates that the matrix electrode system provides a repeatable and precise way to don the array on different occasions and test different electrode pairs.

The force amplitude results shown in Figure 4 demonstrate that the recruitment curve does increase with increased current (a key requirement for FES control), although not as sharply as with rectangular pulses. ICS using carrier frequencies 2000 - 2020 were more efficient with a steeper recruitment characteristic than higher carrier frequencies studied. This effect may depend on the specific anatomical impedance distribution presented to the carrier currents immediately beneath the matrix, so it may not hold for other anatomical sites.

The forces produced by bursts of stimulation, shown in Figure 5, indicate ICS to have similar rise and fall times compared to rectangular pulse stimulation. Also, single activations (twitches) per beat were not observed. These results do not support the view that stimulated forces are purely pulsatile at the beat frequency.

Figure 5 shows a plateau-like contraction with smaller mini contractions superimposed during each ON/OFF cycle. The response is

consistent with desynchronized action potentials causing fused contraction in lower-threshold axons. Kilohertz-frequency ICS applied to a peripheral nerve likely activates multiple sites, leading to desynchronized firing, collision blocking, and ACh depletion at the neuromuscular junction. These high-frequency activations may rapidly reduce muscle force, inducing fatigue. However, reducing the average frequency by switching ON and OFF may increase discomfort due to heightened pricking sensations at each onset.

Desynchronized nerve activation from kilohertz frequency stimulation has been reported^(17,18) and may affect FES control by activating low-threshold motor units at abnormally high rates compared to typical FES frequencies (<50 Hz), potentially causing rapid fatigue in larger, more fatigable motor units. Further research is needed to understand these fatigue dynamics. Superimposed mini contractions occurred in sync with the ICS beat frequency, linked to short bursts of increased recruitment near the beat's peak amplitude. These bursts cause small fused contractions, likely mediated by smaller, fatigue-resistant motor units. While these motor units may experience faster fatigue due to activation at multiple beat frequencies, the impact on FES control is likely less significant than the high-frequency activation of larger motor units.

Uncomfortable prickly sensations were reported at the onset of a burst of ICS. This was observed to occur on each burst in the matrix tests. These sensations were less than with rectangular stimuli, which is in general agreement with cutaneous sensation being reduced with increased stimulus frequency⁽¹⁹⁾.

Figure 4 shows that ICS activation requires two orders of magnitude more charge than rectangular pulse stimulation, consistent with reports that sine waves demand higher power than rectangular pulses in FES⁽²⁰⁾. This impacts battery size in wearable FES devices. The higher power requirement and lower skin impedance at high frequencies necessitate caution to avoid excessive current density at electrodes. The introduction of modern digital synthesis devices and microcontrollers has significantly simplified the accurate generation of sinusoidal and

other waveforms, now achievable with low-cost microcontrollers such as the Raspberry Pi Pico.

The applied ICS currents are assumed to be purely sinusoidal near the electrodes, thus reducing discomfort due to skin afferent activation. Within the tissue, amplitude modulation occurs due to the summation of the carrier currents producing regions from minimal modulation to full (equal amplitudes) modulation carrier. At these ICS kilohertz frequencies, there may also be regions of nerve blockade (²¹).

In the tests with Axelgaard surface electrodes, the target region for nerve activation can be obtained by at least two different sets of electrodes. Configurations placed along the nerve, rather than circumferentially, had the advantage of a reduction in intensity threshold and discomfort from the stimulus. This has implications for FES, particularly when sensation is preserved or where this may elicit undesirable reflex activity.

In trials involving the matrix electrode, Figure 6 indicates that moisturising cream had the advantage of reducing the threshold for both rectangular stimuli and ICS. In Figure 6, the use of cream produced an increase in force. occurs mainly because when the long pulse width is used with the cream, the activation spreads to the median nerve, thereby activating other muscles that affect the force applied to the transducer. In Figure 8, the effect on skin impedance can be seen to be similar to using an electrode gel.

We propose the forearm as a testbed to study the effects of electrical stimulation under various conditions, parameters, and electrode placements while recognising its limitation in demonstrating ICS's potential to reach deeper neural targets. Complementary in-silico validation using FEM models will enhance understanding of ICS effects on neural and muscular tissue. Thigh muscles offer a more suitable alternative for testing deeper neural activation.

5 | CONCLUSION

The study focuses on addressing the challenges and exploring the potential of ICS as an effective alternative method for FES. While ICS has been used in physical therapy and neuromodulation, its mechanisms, effectiveness, and practical applications in FES remain underexplored. The key aspects we evaluated were:

- **Selectivity and Comfort:** Determining whether ICS can provide selective activation of neural targets with reduced discomfort compared to conventional rectangular pulse stimulation.
- **Efficiency:** Assessing the power requirements of ICS and its implications for practicality in wearable or clinical devices.
- **Biophysical Influence:** Investigating whether ICS activates nerves exclusively at the beat frequency or through more complex patterns, challenging prior assumptions in the literature.
- **Optimization Needs:** Identifying how electrode materials, configurations, skin preparation, and stimulation parameters impact neural

activation, muscle force generation, and user comfort when applying ICS.

This study highlights the potential of ICS in FES therapy. ICS offers proportional control of muscle force and greater comfort than traditional rectangular pulse stimulation. However, the discomfort caused by the onset of stimulation bursts may limit its application in short-duration contractions. Experiments showed that moisturising agents can significantly reduce activation thresholds and improve comfort for ICS and rectangular stimuli. Despite this, moisturisers compromise electrode adhesion, requiring additional fixation methods that complicate clinical or home use.

ICS also demands higher electrical power than rectangular pulses for comparable neural activation, raising concerns about power consumption and unsafe current densities in wearable FES devices. Additionally, the results challenge the assumption that ICS selectively activates nerves at the beat frequency, suggesting a more complex interplay of nerve and muscle recruitment mechanisms. The study emphasises the need for further research to optimise stimulation parameters, electrode designs, and waveforms to fully leverage ICS's benefits while addressing its limitations, paving the way for more effective and comfortable FES therapies.

AUTHOR CONTRIBUTIONS

RO and JE contributed equally. RO, JE, PA, BA, and JJ designed the studies. RO, JE, and JJ collected experimental data. RO, JE, JJ, and BA performed data analysis and interpretation. SH, JA, AP, JF, and PA made critical revisions and proofread the article. All authors reviewed, approved and provided input into the manuscript.

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None reported.

CONFLICT OF INTEREST

The authors declare no potential conflict of interests.

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