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SPECIAL REPORT

The current status and future of using computational models to individually optimise cochlear implant stimulation

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ABSTRACT

Introduction: Computational modeling of cochlear implant stimulation has a long history, but its development has mostly been restricted to generic models, with patient-specific modeling being relatively rare, in spite of its potential applications in both research and clinical practice.

Areas covered: The present state of computational cochlear implant models is discussed in relation to patient-specific modeling. From three-dimensional geometries derived from clinical imaging to full end-to-end models of the electrically stimulated peripheral auditory system, computational cochlear implant models have progressed to the point where they can meaningfully simulate responses to complex (speech) stimuli.

Expert opinion: The development of patient-specific models that could be used to study the underlying mechanisms of cochlear implant functioning and ultimately be applied to make clinical diagnoses and recommendations, is within reach. However, there are still obstacles to overcome; the most immediate of these is the issue of auditory neural health, which is currently impossible to definitively assess in a living subject, yet has profound effects on electrical stimulation.

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Cochlear implants; computational modeling; patient-specific modeling; biophysical models; phenomenological models

1. Introduction

Computational models of the cochlea and cochlear implant (CI) stimulation have been in development since the 1970s [1,2]. They can be split up into phenomenological models and biophysical models, the latter of which are often built on computational models of electrically stimulated neurons which have an even longer history [3,4]. Thus far, the output of these models has mainly been compared to and validated by objective measures, such as electrically evoked compound action potentials (eCAP) or psychophysical measures, as for most of their development the models have not been advanced enough to meaningfully simulated responses to complex (speech) stimuli. However, these models, particularly the biophysical ones, have grown increasingly sophisticated over the years, taking advantage of advancements in the fields of histology, radiological imaging and electrophysiology to build more detailed models that can better describe and explain the workings of CI stimulation. Despite this, few studies have attempted to develop individualized computational models of/for CI subjects; instead, most have opted to use generic models that stand in for the 'typical' CI user, or specific sub-groups of CI users (e.g. subjects with certain forms of neural degeneration). This raises the question of whether patient-specific modeling represents an untapped potential in CI research and clinical practice, as individualized models might not only be helpful in making clinical predictions and evaluations, but also assist in further research into the underlying reasons for why CI performance varies between individuals. This review will discuss the present state of computational CI models in relation to the possible future role of patient-specific modeling in CI research and in the clinic.

2. Imaging and volume-conduction models

The increased availability and improvements of radiological imaging has been very beneficial for computational CI modeling, particularly for the construction of three-dimensional biophysical volume-conduction models. Where the geometries of early versions of generic, non-personalized models had to be extrapolated from single histological cross-sections of a cochlea [5–8], modern volume-conduction models have been derived from full micro-computed tomography (µCT) scans or similar imaging data, obtained postmortem [9–19].

This has led to researchers developing methods to derive subject-specific models from clinical imaging data; some of these methods were manual or semi-automated [13,16,18], but more fully automated methods using statistical shape models have appeared as well [10,20–25] (Figure 1). Although imaging data from clinical scans are less detailed than higher fidelity methods such as µCT or synchrotron imaging [26–29], the latter are only available for scanning temporal bones extracted from cadavers and cannot be used for living subjects. As such, geometries derived from clinical scans require some estimate of certain anatomical features, particularly the internal structures of the cochlear duct [30–33] and the trajectories of the auditory nerve fibers [13,15], the

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Article highlights

- The present state of computational cochlear implant models is discussed in relation to patient-specific modeling.
- Computational cochlear implant models have progressed to the point where they can meaningfully simulate responses to complex (speech) stimuli.
- Patient-specific models could be used to study the underlying mechanisms of cochlear implant functioning and ultimately be applied to make clinical diagnoses and recommendations.
- The development of patient-specific models that can meaningfully simulate CI performance is within reach.
- There are still obstacles to overcome; the most immediate of these is the issue of auditory neural health.

latter of which is generally accomplished with the aid of data from well-known histological studies of the human cochlea [27,34,35]. Despite the lack of anatomical details, models generated from clinical images are well-suited for simulating the spread of electrical fields inside the cochlea [9] and these models have little problem accurately simulating intracochlear potentials recorded by the cochlear implants themselves [9,10,13,18,36].

However, the electrical field distribution in the cochlea on its own has limited predictive or analytical value for CI performance; in order to meaningfully simulate aspects of electrically evoked perception, computational CI models couple their volume-conduction output to biophysical or phenomenological models of neural behavior that determine simulated excitation patterns in response to a given set of stimulus parameters. Following this approach, researchers have studied many factors relevant to CI functioning, such as electrode positioning [6,37,38], multipolar stimulation [15,39–41], cochlear tonotopy [13,42,43], facial nerve stimulation [44–46] and intracochlear electrocochleography (ECochG) [47]. Across these studies, multiple different biophysical nerve fiber models are used, stemming from the fact that many details regarding the morphology and kinetics of human auditory neurons are not (precisely) known, owing to the difficulty of obtaining human auditory neurons and performing experiments on them. As a consequence, for each model different assumptions or educated guesses are made for certain parameters, e.g. the diameters of the axons, or the number and lengths the of myelinated segments of the peripheral processes. As such, it should be noted, that the biophysical nerve fiber models are known to be imperfect, as none of these published non-linear cable models have managed to simulate all experimentally known aspects of auditory neurons accurately [48]; perceptual thresholds in particular are usually overestimated by these models, but in spite of this they produce overall plausible neural behavior.

3. Auditory neural health

CI computational modeling studies have frequently turned their attention to the matter of auditory neural health, unanimously finding that the nature and degree of neural degeneration affects many factors relevant to CI performance, such as perceptual threshold, pitch percepts, spread of excitation and polarity sensitivity [13–15,17,19,38,42,49–58]. Since adult CI-subjects can generally be assumed to have some degree of neural degeneration and even pediatric subjects may have neural abnormalities, accurately modeling the state of the auditory neurons is of considerable importance for achieving realistic results.

This poses a problem for patient-specific modeling, as state-of-the-art clinical imaging techniques are currently incapable of meaningfully determining the health or survival rate of a patient’s auditory neurons. In addition, there is still much uncertainty concerning the manner in which the auditory neurons are affected by hearing loss and (genetic) diseases. Various forms of damage or dysfunction of the neurons have been observed, such as axonal demyelination [59,60], reduced density or function of sodium channels [61–63] and gradual retrograde degeneration of the peripheral processes, resulting in complete loss of those processes or even the entire neuron [64–67]. Retrograde degeneration can also occur on a local level, rather than uniformly across all auditory neurons, which complicates matters even further. Some researchers have responded to this issue by including neural health/survival parameters in their models and trying to match patient-specific model output to objective and psychophysical measures [56,57,68]. Though this can lead to realistic looking model data, it does raise the question whether it uses currently unknowable neural health factors to force model output to behave like experimental data.

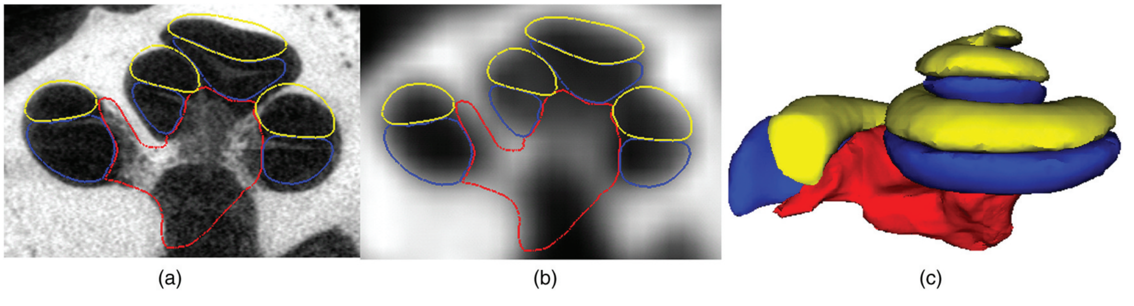

Figure 1. Example of a segmentation of the human cochlea from Cakir et al. [10], illustrating the current state-of-the-art of obtaining personalized cochlear geometries from clinical CT scans using active shape models. Panel a shows a μCT image of a human cochlea specimen, while panel b shows a corresponding conventional CT image of the same specimen. The red, blue and yellow lines in panel a and b indicate a segmentation obtained by applying an active shape model to the conventional CT data in panel b, which is compared to the higher resolution μCT image in panel a, showing that the active shape model is capable of fairly accurately predicting the cochlea’s internal structure from the conventional CT. Panel c shows the three-dimensional geometry resulting from the full segmentation.

Nevertheless, the idea that clinical and experimental measures are affected by neural degeneration has led researchers to speculate that it may be possible to infer neural health from objective measures such as the polarity sensitivity, the inter-phase gap effect, or neural synchrony measures derived from eCAP recordings [52,69–86]. While this would certainly be helpful in determining the state of an individual CI subject, modeling has also suggested that factors such as electrode positioning can confound results and that polarity sensitivity, in particular, is not a simple measure for aspects of neural health [14]. It should be noted, however, that these modeling results do not entirely align with psychophysical data, specifically when it comes to predicting polarity sensitivity at higher stimulus levels, so for the time being this matter requires more research.

4. End-to-end models

Despite their still present limitations, computational CI models have matured enough that researchers have recently started developing so-called end-to-end-models of CI stimulation, where the entire chain of information along the peripheral CI system is modeled, from speech coding complex sounds to electrode stimulation to the eventual spiking patterns along the auditory neurons (Figure 2). Though so far they have been restricted to generic, non-patient-specific simulations, they represent an important step in the development of computational CI modeling.

The first study to publish such a model was by Brochier et al. [58], which simulated responses to phonemes processed by a speech coding strategy based on CIS (Continuous Interleaved Sampling) [88], in a volume-conduction model of the human cochlea combined with a hybrid Hodgkin-Huxley /phenomenological neural model. The neural responses were used to train and use an automatic speech recognition neural network to simulate phoneme-recognition experiments. The study showed that the model was capable of recognizing phonemes comparably to CI-subjects. In particular, it showed a significant correlation between consonant recognition accuracy predicted by the model and the accuracy of actual CI-listeners, though this correlation was not found for vowel recognition simulations.

Next, researchers at the Hannover Medical School published a similar model, which simulated spectral modulation threshold (SMT) and speech reception threshold (SRT) experiments [55]. They used several configurations of the Fidelity120 sound coding strategy [89] and deployed the simulation framework for auditory discrimination experiments (FADE) [90] to perform simulated psychophysical discrimination tests with the neural responses generated in their hybrid biophysical/ phenomenological CI-model. Although the resulting model was able to show a loss in performance due to deteriorating neural health, the authors concluded that their model was not yet capable of plausibly simulating the performance of actual CI-users.

The most recently published end-to-end computational CI model was developed by researchers at the Leiden University Medical Center, who extended their existing biophysical CI-model with a phenomenological stochastic nerve model in order to efficiently process complex signals [51,91–96]. In one study, they used their end-to-end model to compare the way in which loudness is encoded at the neural level by the Fidelity120 processing strategy and the ACE (Advanced Combination Encoder) strategy [97], suggesting that although both strategies are proven to be clinically effective, they are fundamentally different in the way they achieve loudness perception and that their effects also depend on patient-specific factors, specifically electrode positioning [92]. In their next study [93], neural responses to spectral ripple and spectral-temporally modulated ripple stimuli were simulated in both the CI model as well as a phenomenological model of normal hearing published by Bruce et al. [98]. The results demonstrated a poorer spectral resolution for CI-listeners than for normal hearing; at low ripple density, spectral modulation was clearly visible in the simulated neurograms for both normal hearing and CI-hearing, but when increasing the ripple density, the modulated signal disappeared much more quickly for simulated CI-hearing than it did for normal hearing, which was in line with psychophysical studies (Figure 3). Finally, a novel vocoder framework was developed at Leiden University, which converted neurograms (maps of

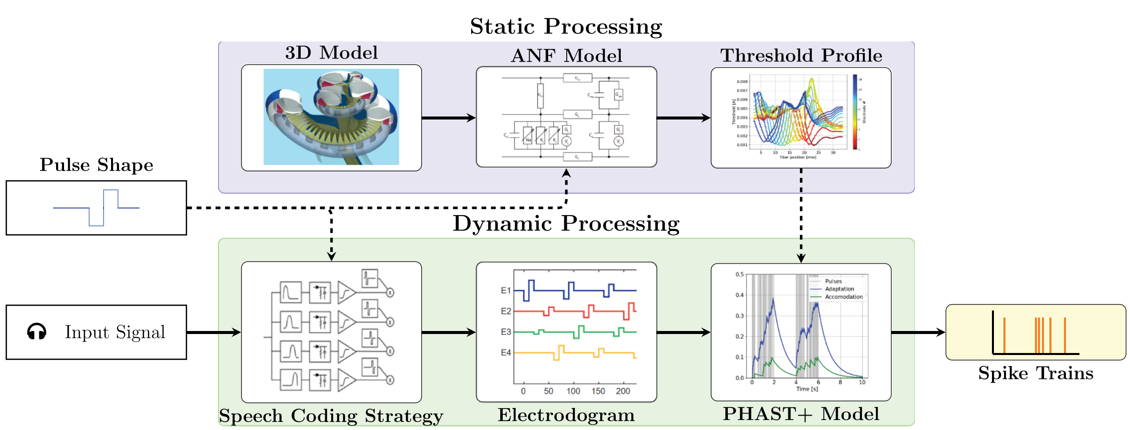

Figure 2. Structural overview of the end-to-end model used in De Nobel et al. [87]. An input signal is processed by a speech coding strategy, resulting in an electrodogram. This is fed to a phenomenological stochastic nerve fiber model ('PHAST+ Model'), which uses neural thresholds from a three-dimensional model of an implanted cochlea (i.e. the 'Static Processing' block) to determine simulated neural spike trains.

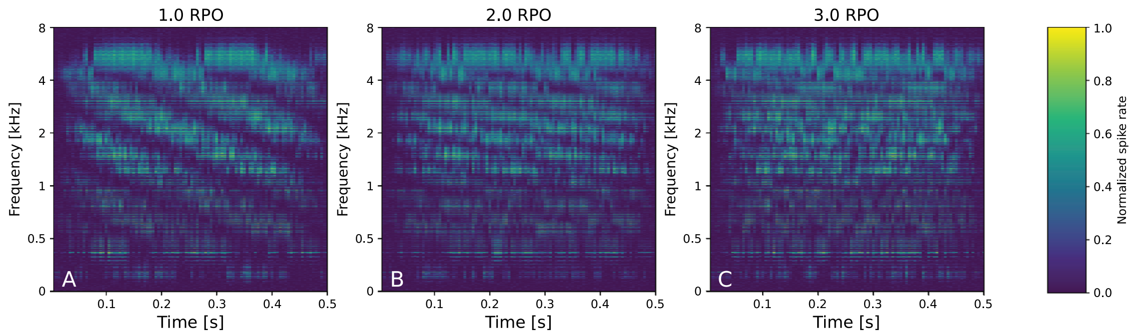

Figure 3. Neurograms from simulated responses to spectral ripple stimuli in CI hearing, from Martens et al. [93]. From left to right the number of ripples per octave (RPO) is increased 1 to 3; the spectral ripples (the diagonal 'bands' in the neurograms) are visible at 1 RPO, but are lost at higher RPO values, which is in line with CI subjects' performance.

neural spikes over a period of time, along a set of auditory neurons) into audio signals [87]. Although the vocoder framework itself was designed to be model-agnostic, the study used both the Leiden CI model as well as Bruce et al.'s normal hearing model to generate neurograms of the Digits-In-Noise (DIN) test stimuli [99] and converted those neurograms back into vocoded speech fragments, which were then used in an online version of the DIN test, intended for normal hearing listeners. Results showed that sound vocoded through Bruce et al.'s normal hearing model suffered some degradation but remained intelligible. In addition, participants of the online DIN-test performed comparably to CI-listeners when presented with speech that was vocoded from the CI-model's neurograms, suggesting that the modeling chain produced a plausible simulation of CI-hearing and that it may eventually be used to predict individual hearing performance from patient-specific simulated neurograms.

5. Conclusion

Computational models of CI stimulation have progressed to the point where they can meaningfully simulate neural responses to complex sounds. Though currently these are mostly generic models, meant to represent the typical or average CI-subject, there has also been development of patient-specific CI models from clinical radiological imaging. These subject-specific models have been used to analyze intra-cochlear potentials and make predictions on auditory neural health and facial nerve stimulation.

6. Expert opinion

Further development of patient-specific CI models is an enticing prospect, as it will hopefully lead to new ways to optimize individual CI users' performance. Ideally, this will take the form of so-called 'digital twins,' i.e. complete end-to-end models tailored to each individual patient, capable of accurately simulating and predicting their CI hearing performance. In the short term, however, patient-specific modeling will be useful as a research tool for gaining new insight into the underlying reasons for why there are considerable performance differences between CI-subjects, since there are still some significant hurdles to overcome before the models can confidently predict clinical outcomes of specific patients. The most pressing one is the question of auditory neural health in CI users. Modern radiological imaging is advanced enough to reliably determine the dimensions of a CI user's cochlea and the position of the CI electrode array, which makes developing individualized models based purely on geometrical measures determined from a CI user's clinical scans relatively straight-forward. Unfortunately, the survival and health of the auditory neurons cannot be meaningfully determined through clinical radiology and since it is apparent from experimental data and modeling studies that electrical neural stimulation is affected by neural health/survival, accurately modeling the state of the auditory neurons is crucial for developing patient-specific models. This makes it necessary to find ways to infer the state of the auditory neurons from objective and/or psychophysical measures. As an example, it might be possible to gain an understanding of the state of the auditory neurons by recording a comprehensive set of eCAP measures and analyzing amplitudes and temporal properties such as recovery time or the effect of the interphase gap.

As noted, auditory neural degeneration is presently understood to take on different forms which can occur in a localized fashion. By their nature, CIs have limited spatial resolution due to their small number of electrode contacts and large spread of excitation, so a detailed mapping of the state of a CI subject's auditory neurons under the present electrode design constraints will be challenging, if it is even possible. Computational models will be vital in this pursuit, since they allow for simulated experiments that would be impossible to perform in actual CI users or animal studies, as well as shedding light on the underlying mechanisms involved in clinical experiments. Obtaining large data sets of various objective measures in individual patients will be helpful in pinpointing what kind of simulated neural health conditions are best able to explain a subject's clinical data.

For this to have any chance of success it will be necessary to get biophysical models of the auditory neurons fully in line with experimental data, which involves improving our understanding of the properties of the auditory neurons and the extent and manner in which they are changed by neural degeneration. Ongoing histological and histopathological research will hopefully provide more insight; in the mean-time, researchers should take a critical look at their current models to determine if and where they are falling short.

However, even if researchers manage to bring the neural models fully in line with clinical and experimental data, there is an unresolved question of how much CI performance depends on central processing of the auditory information. There is a great deal of variability in CI performance between individuals; the causes of this variability are still not yet fully understood, but one can safely assume that to some degree it is caused by differences in the way different individuals process the auditory information presented by the CI. But the current computational models by and large focus on peripheral factors of the CI-auditory system (i.e. cochlear morphology, electrode position, state of the auditory neurons, etc.), implicitly treating human brains as interchangeable when it comes to processing auditory information. There is some evidence that this approach has its limitations, in particular regarding cochlear tonotopy and the modeling of pitch perception; psychophysical pitch-matching experiments show inconsistent and subject-dependent deviations from expected frequency maps in ways that are difficult to explain in terms of peripheral factors such as electrode position and the standard tonotopical arrangement of auditory neurons, suggesting that central processing plays a large role in pitch perception [43,100–104].

Therefore, it remains to be seen whether an individualized CI-model can be successful by using a one-size-fits-all approach to presenting auditory information (i.e. by assuming that all individuals process the information in the same way and that optimal performance depends entirely on peripheral factors), or if differences in central processing between subjects will mean that optimal stimulation/speech encoding strategies depend on how each individual CI subject processes information coming from the electrically stimulated peripheral auditory system.

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