

## Computationally Designed Focal Deep Transcranial Magnetic Stimulation (fdTMS) Coils

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Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique used in neuroscience research and for treatment of psychiatric and neurological disorders. TMS involves the use of one or more current-carrying coils located near the scalp to induce electric fields (E-fields) inside the brain. These E-fields, in turn, modulate targeted neuronal networks. In TMS, the aim is often to excite specific regions of the brain while minimizing stimulation elsewhere. Unfortunately, electric fields generated by TMS coils diffuse and decay rapidly as they penetrate into the brain. As a result, TMS tends to stimulate relatively large regions of tissue near the brain surface.

To enhance TMS applications, it is desirable to have coils with more focal and/or deeper induced electric field. Many coil designs for improving the focality and depth of stimulation of TMS have been proposed. Of these, ‘figure-8’ coils, which consist of two circular windings arranged side-by-side, have been shown to be the most focal for each given penetration depth (Z. Deng, S. Lisanby and A. Peterchev, *Brain Stimul.*, 6 (1), 1-13, 2013). Recently, we developed an optimization framework for designing TMS coils that achieve optimal trade-offs between penetration depth and focality. Our framework finds optimum driving currents for an array of identical independently driven coil elements via a Genetic Algorithm (GA) construct. Then, the coils are replaced by concentric loops that achieve the same magnetic dipole moment when driven with an identical current source (L. Gomez, F. Cajko, L. Hernandez, A. Grbic and E. Michielssen, *IEEE Trans. Biomed. Eng.*, 60 (10), 2771-82, 2013). Though promising, our coils require high energy levels for stimulation making their implementation challenging.

To address the limitations of the previous algorithm, we have developed a new computational technique for designing TMS coils that achieve optimal trade-off between depth, focality, and energy of stimulation (fdTMS coils). We have shown that the algorithm designs coils that outperform figure-8 coils in terms of focality and depth, while maintaining tractable energy levels (L. Gomez, S. Goetz, A. Peterchev, *J. Neural Eng.*, 15 (4), 2018). Here we present extensions to our algorithm that enable the design of coils having an arbitrarily chosen coil support. We also present experimental validations confirming our numerical results. Briefly, the algorithm solves for optimum surface current distributions on a triangulated surface mesh of the coil support using a branch-and-bound optimization algorithm. Then, the surface current distributions are approximated by coil windings that closely match the magnetic dipole moment of the currents, thereby, producing virtually the same E-field as the surface current.

We used this framework to determine the fundamental limits of the focality vs. depth of stimulation trade-offs in a spherical head model when energy is not constrained. To reach target depths in the range of 1.0–3.4 cm from the cortical surface, the stimulated volume of fdTMS coils can be decreased by 42–55% relative to conventional coils. Furthermore, when fdTMS coil energy is constrained to practical levels, significant improvements in focality are still feasible. For example, the stimulated volume by a commercial Magstim figure-8 coil can be decreased by 36%, 43%, or 46%, for matched, doubled, or quadrupled energy. Finally, experimental results measuring the E-fields of a coil designed by this algorithm confirm these findings.

Computationally optimized fdTMS coils could enable more selective targeting of the induced E-field. The presented results appear to be the first significant advancement in the depth–focality trade-off of TMS coils since the introduction of the figure-8 coil three decades ago, and likely represent the fundamental physical limit.