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具高輸出擺幅之非侵入式時頻差擾動刺激器電路設計與應用

Circuit Design and Application of a Non-Invasive Temporal Interference Stimulator with High Output Swing

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摘　　要

隨著科技的進步與社會穩定，人類的平均壽命越來越長，可以說是人類一大福祉。然而，生命延長所伴隨的一些神經退化疾病也慢慢浮現且逐漸被重視。

本篇論文是基於 Nir. Grossman *et al.*. [1] 在 2017 年發布的 Noninvasive Deep Brain Stimulation via Temporally Interfering Electric Fields 做爲發想，內容提到可以以非侵入式的方式對人類深腦進行有效刺激。我們期望設計一個可以協助醫療體系的晶片來救治飽受失智症所苦的病人。而此種刺激方式於 2023 年 Nature Neuroscience 中得到人體實驗的初步證實可以有效治療失智症 [2]。

本非侵入式時頻差擾動刺激器是以 TSMC 0.18um CMOS High Voltage Mixed Signal Based Generation II BCD 製程來設計，是一個可以產生 20 V_{pp} 且可調式弦波振幅的時頻差擾動刺激器 (Temporal Interference Stimulator,TIS)。透過一個外灌的方波給到輸入端，由低通濾波器將高頻訊號濾除後送到反向放大器進行放大。之後訊號會透過共源放大器做第二次放大，以輸出一個高輸出擺幅的弦波信號。我們的晶片在理想的環境進行成功測試。接著我們成功在模擬人類大腦組織的 agar[3] 量測到振幅調變訊號（Amplitude Modulation，AM）。並驗證透過改變電壓大小達到控制左右移動來追蹤最大刺激目標點的移動軌跡。最後，成功在活體豬腦上進行有效刺激，且成功誘發豬腦產生低頻訊號 (Beat Frequency)。

本篇論文將探討如何透過電路設計方式協助生醫應用，以非侵入式的交流訊號電壓刺激 (TACS)[4] 爲發想進行電路設計。論文將呈現從生醫理論和數學理論的推導爲基礎，並以此理論來實現電路設計。最後，成功於 agar [3] 和動物實驗觀測波形的以驗證電路的可行性。未來本刺激機器將整合直接數位合成技術 (Direct Digital synthesis，DDS)[5] 於單晶片上來達到可攜式的目的，讓病人的治療不再受限於醫療院所進行治療

可以舒緩醫療量能並改善人口結構高齡化所遇到的神經退化疾病 [6]。

關鍵字：時頻差擾動刺激器、非侵入式、失智症

Circuit Design and Application of a Non-Invasive Temporal Interference Stimulator with High Output Swing

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Abstract

With the advancement of technology and societal stability, human life expectancy is increasing, which can be considered a significant welfare for humanity. However, the extension of life has brought to light and increased the importance of several neurodegenerative diseases.

This paper is predicated on the concept of Noninvasive Deep Brain Stimulation via Temporally Interfering Electric Fields, published by Grossman *et al.*. [1] in 2017. The content suggests that effective stimulation can be applied to the human deep brain in a non-invasive method. We hope to design a chip that can assist the medical system in treating patients suffering from dementia. This stimulation method was preliminarily confirmed in human trials in Nature Neuroscience in 2023 to effectively treat dementia [2].

This Non-Invasive Temporal Interference Stimulator is designed using the TSMC 0.18um CMOS High Voltage Mixed Signal Based Generation II BCD process. It is a Temporal Interference Stimulator (TIS) capable of generating a 20 V_{pp} sine wave with adjustable voltage magnitude. Through an externally supplied square wave to the input end, the high-frequency signal is filtered out by the low-pass filter and then sent to the inverting amplifier for amplification. The signal is then amplified for the second time through the common source amplifier to output a high output amplitude sine wave signal. Our chip was successfully tested in an ideal environment. We then successfully measured the amplitude modulation (AM) signal on agar [3] simulating human brain tissue. We also verified that by changing the voltage magnitude, we can control the left and right movement to track the movement trajectory of the maximum stimulation target point. Finally, we successfully administered effective stimulation to the in vivo porcine brain and recorded the low-frequency signal (Beat Frequency).

This paper will discuss how to assist biomedical applications through circuit design, with the idea of non-invasive high-frequency alternating current signal voltage stimulation (TACS)[4] as the inspiration for circuit design. The paper will present the derivation of biomedical theory and mathematical theory as the basis, and use this theory to implement circuit design. Finally, the feasibility of the circuit was verified by observing waveforms in agar [3] and animal experiments. In the future, this stimulator will integrate direct digital synthesis technology (DDS)[5] on a single chip to achieve portability, so that patients' treatment is no longer limited to treatment in medical institutions, which can alleviate medical capacity and improve the neurodegenerative diseases encountered by the aging population structure[6].

Keyword: Temporal Interference Stimulation, TIS, Non-Invasive, Dementia