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Thought-controlled nanoscale robots in a living host

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Introduction: Until recently, no system could provide explicit temporal control of a drug, e.g. generating a sequence of alternating activation/inactivation of the drug for arbitrary periods of time. Recently, drug-loaded nanoscale robots were reported, which reversibly expose and conceal drugs to the environment while maintaining them physically linked to their chassis [1]. In this study we have established, for the first time, an interface between a human brain (mind) and a therapeutic molecule, by allowing electroencephalogram (EEG) patterns associated with cognitive states to remotely trigger, in real time, nanorobot activation in a living animal.

Material, Methods and Results: The nanoscale DNA robots used in this study were a modified version of the nanorobot we described previously [1]. The shell can be reversibly closed or opened by controlling gate strand hybridization, thus concealing or exposing molecular or nanoparticulate payloads from the environment. In order to control DNA remotely from outside the host's system, we re-designed the robots to enable the addition of functionalized metal nanoparticles, which could be heated by applying a radio frequency-induced electromagnetic field (RFMF) on the entire animal. As an animal model for this proof of concept we chose the insect *B. discoidalis* [2].

To induce cognitive load, we trained an algorithm for recognizing cognitive loads, operationalized as solving simple arithmetic problems. EEG was recorded using Ag/Cl active electrodes located at PZ, FZ, AF3 and AF4, As features we used EEG power in the 6 main frequency bands in the 4 electrodes, linear discriminant analysis (LDA) was used for feature reduction and support vector machine (SVM) for classification. DNA origami robots were designed according to a protocol described elsewhere [2].

The algorithm discriminated on-line between low and high cognitive load with average precision of 92.5% and sensitivity of 86.3%, over 6 subjects. The insects loaded with the nanorobots were placed inside an induction coil, and a 14.6 MHz RFMF was applied, only when the test subject's EEG pattern was classified as 'high' cognitive load. RFMF activation induced robot opening and subsequent cellular staining by the exposed fluorescent antibody fragments, which was tracked in real-time.

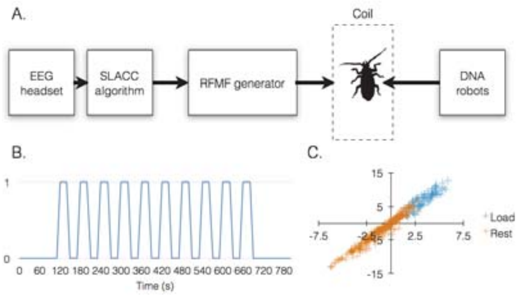

Figure 1. *System outline and performance. A. Basic system outline: signals recorded by the EEG headset on the subject were monitored by the algorithm, which controls the state of an RFMF generator connected to an induction coil. The test animal is placed inside the coil after being injected with DNA robots. B. Experimental protocol structure. 0 and 1 on the Y-axis denote states of cognitive rest and load, respectively, which are induced by displaying alternating screens showing either blank or a list of arithmetic problems. C. Classification of cognitive rest vs. cognitive load signals by LDA.*

The analysis showed that robots bearing metal nanoparticles opened and engaged the cells efficiently, while robots not bearing nanoparticles, or those that bear nanoparticles but were not loaded with fluorescent antibody, did not generate any visible signal.

Discussion: Albeit a very preliminary prototype, this system could inspire improved designs towards thought-mediated control over biochemical and physiological functions assisted by biocompatible molecular machines.

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References

[1] Douglas SM, Bachelet I, Church GM. A logic-gated nanorobot for targeted transport of molecular payloads. Science. 2012;335: 831–834.
[17] Amir Y, Ben-Ishay E, Levner D, Ittah S, Abu-Horowitz A, Bachelet I. Universal computing by DNA origami robots in a living animal. Nat Nanotechnol. 2014;9: 353–357.