Counting molecules, dodging blood cells: real-time molecular measurements directly in the living body

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The availability of technologies capable of tracking the levels of drugs, metabolites, and biomarkers in real time in the living body would revolutionize our understanding of health and our ability to detect and treat disease. Imagine, for example, a dosing regimen that, rather than relying on your watch ("take two pills twice a day"), is instead guided by second-to-second measurements of plasma drug levels wirelessly communicated to your smartphone. Such a technology would provide researchers and clinicians an unprecedented window into physiology and pharmacology, and could even support ultra-high-precision personalized medicine in which drug dosing is optimized minute-by-minute using closed-loop feedback control. Towards this goal, we have developed a biomimetic, electrochemical sensing platform that supports the high frequency, real-time measurement of specific molecules (irrespective of their chemical reactivity) in situ in the blood and solid tissues of awake, freely moving subjects.

Figures

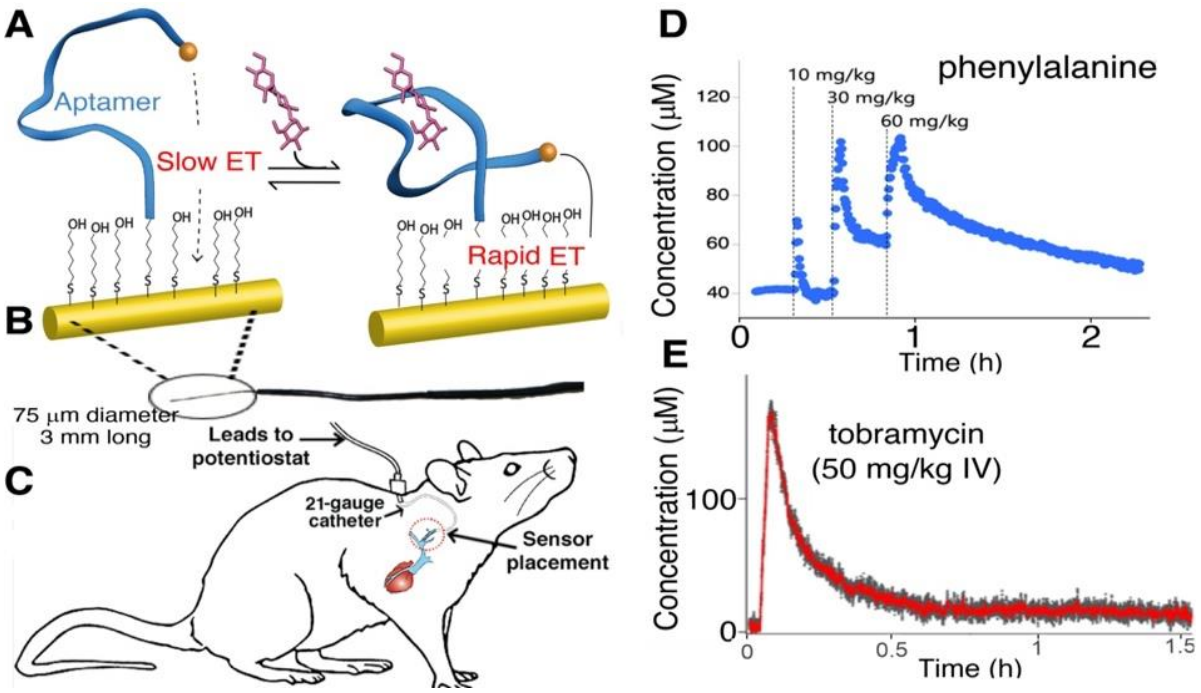

Figure 1: Electrochemical Aptamer-Based (EAB) sensors, a platform technology that relies on receptor binding, and not on the target's intrinsic chemical reactivity, to generate a signal, are (**A**) comprised of an aptamer re-engineered to undergo reversible binding-induced folding. This is modified with a redox reporter and attached (via a self-assembled monolayer) to a gold electrode. The binding-induced conformational change causes a corresponding change in electron transfer rate that is easily measured using electrochemistry. (**B**) Bundled with its counter and reference electrodes, current intravenous EAB sensors are small enough and flexible enough to (**C**) be emplaced via a 21-gauge guide catheter. (**D**) When interrogated using square-wave voltammetry, the resulting sensors achieve excellent precision and few-second resolution. Shown, for example, are 12-s resolved phenylalanine measurements performed in the jugular of a live rat. (**E**) Using chronoamperometry we can push the time resolution to milliseconds; shown, for example, are intravenous tobramycin levels measured every 300 ms (red line, a 3 s rolling average).