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Anatomy of transducing interfaces: the core of large-area label-free ultrasensitive electronic biosensors

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Biosensors operating via large-area transducing interfaces have demonstrated single molecule detection capability, selectivity, compactness and robustness of the electronic transduction.1–3 The electrical signal arises from the integrated response triggered by selective binding events and is amplified by complex collective phenomena generated at the biolayer interface. Understanding the detailed chain of collective physical and chemical processes responsible for the huge amplification of the transduction signals is now essential and can no longer be postponed to rationally guide the further development of single molecule electronic biosensors.

We will review our recent experimental results, providing direct demonstration that a few antigen-antibody binding events generate extended and irreversible work function changes on large-area biofunctionalized Au surfaces. We have used a combination of atomic force and Kelvin probe force microscopies, attenuated total reflection infrared spectroscopy, surface plasmon resonance and cyclic voltammetry. Our results compare well with the electrical characteristics of single-molecule electrolyte-gated transistor sensors, our statistical modeling based on Einstein's diffusion-theory of ligands, Poisson's distribution of binding events, and the molecular modelling of self-assembled monolayers. Our findings have profound implications for understanding the chain of irreversible and cooperative surface state transitions induced by a ligand/receptor interaction under the application of an external electric field.

1. Macchia, E. et al. Single-molecule detection with a millimetre-sized transistor. Nat. Commun. 9, (2018).
2. A sensor detects the light touch of a single molecule. Nature 560, 413–413 (2018).
3. Macchia, E. et al. Large-Area Interfaces for Single-Molecule Label-free Bioelectronic Detection. Chem. Rev. (2022) doi:10.1021/acs.chemrev.1c00290.