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In the third year of my Ph.D. program, I utilized previously fabricated graphene field-effect transistors at the 200 mm wafer scale to detect minute quantities of mutated synthetic DNA diluted in a large quantity of healthy DNA, mirroring the expected ratios in clinical samples (e.g., 0.1:100, 1:100, and 10:100). The sensors demonstrated sensitivity to mutated DNA, even when differing by only one base (SNP) from the unmutated sequence. Notably, the transistors could detect mutated DNA at femtomolar concentrations.

Moving toward the final goal of my work, I conducted experiments using a complex medium instead of a buffer. Various mediums, including synthetic phosphate buffer, spiked undiluted human plasma, and human plasma diluted in phosphate buffer, were used to detect synthetic DNA biomarkers. Results revealed that as the plasma dilution increased from 1× to 50×, there was a shift in the output signal slope from negative to positive. A plasma dilution of 25× yielded biosensing results comparable to those in an artificial buffer. These findings highlight the potential of graphene field-effect transistors for enhanced detection of circulating tumor DNA in complex matrixes. They also show the complexity of the sensor system, forcing us to understand in greater detail the graphene/biomolecule/electrolyte interface, which we are now addressing.

Additionally, control tests were carried out to validate the results. Negative controls, involving non-complementary DNA and blanks, were employed for all biomarkers, demonstrating higher sensitivity for complementary DNA and excluding the possibility of false negatives. To enhance sensitivity and reduce hybridization time, experiments were conducted at higher than RT temperatures. These experiments showed the ability to detect DNA with a sensitivity of 20 mV/decade, an improvement from 7 mV/decade at room temperature, while the necessary hybridization time was reduced from 1 hour to only 5 minutes. Similar experiments with noncomplementary DNA and blanks excluded the occurrence of false positives. These results are key to help and inform to design the operative mode of a clinical trial.