REVOLUTIONARY DIAGNOSTICS – NONTRADITIONAL APPROACHES FOR DEVELOPING BREAKTHROUGH CAPABILITIES AGAINST EMERGING THREATS

Rapid, Agile, And Portable Diagnostics Based On Breath Biomarkers Using Highly-selective Sorbents

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There are numerous volatile organic compounds (VOCs) present in exhaled human breath including, for example, alcohols, ketones, and aldehydes. The biological response to pathogens and diseases produces unique profiles of VOCs, providing a chemical fingerprint that can be used as a diagnostic targeting, for example, COVID-19, influenza, tuberculosis, malaria, lung cancer, or kidney disease.

Detecting these specific signatures in a complex mixture of air, water, CO2, and other non-marker VOCs is a significant challenge. Target molecules must be selectively isolated and accurately measured for a reliable diagnosis, and this is a fundamentally challenging chemical separations problem. We present the results of ongoing work to solve this problem using nanoporous materials (metal-organic frameworks, or MOFs) with high selectivity for specific VOCs. MOFs represent an ideal platform for this application owing to their varied pore sizes, pore shapes, and chemical properties, that can be tailored to specific adsorption applications. We are using a highly iterative feedback loop between predictive molecular modeling, materials synthesis and characterization, and testing. Specifically, we implement high-throughput molecular simulations to identify the most promising candidates, tailored to adsorb specific target VOCs with high selectivity over competing molecules (e.g. water, CO2). Using inexpensive atomistic simulations, we are screening tens of thousands of materials quickly and find the best candidates for specific VOC targets. Further, we use detailed simulations (e.g.. molecular dynamics) to study the top candidates which are then downselected for synthesis and testing in the lab.

We have identified and synthesized several promising MOFs with high selectivity for VOCs known to be indicators for COVID-19 and validated their adsorption capacity with portable chemical sensors, such as miniature ion mobility spectrometry (IMS). As more than one VOC is generally needed for an accurate diagnosis, we will also discuss how arrays of MOFs – each tuned to a specific VOC –can be used to detect specific VOC profiles. This technology has advantages over methods like exhaled breath condensate (EBC) that require substantial refrigeration (for condensation of the sample to a liquid state), severely limiting portability and range of use.

While to date we have focused on COVID-19, our technique is agile and can be easily adapted for both known and emerging diseases with relative rapidity, by choosing a different set of MOFs appropriate for new targets. If VOC biomarker targets were identified for another infection or disease state, we would use high-throughput molecular simulations to identify existing or novel MOF structure to adsorb those molecules, and then synthesize and test them against the target VOCs. These new MOFs could easily be incorporated into the portable detector assembly and deployed. This design pipeline would enable rapid adaptation of this approach to emerging diseases of interest. The final assay would be rapid (providing results within minutes), non-invasive (requiring only exhaled breath or headspace from biological samples), and portable (battery-operated with few consumables), making it ideal for use in remote locations with little medical infrastructure.
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