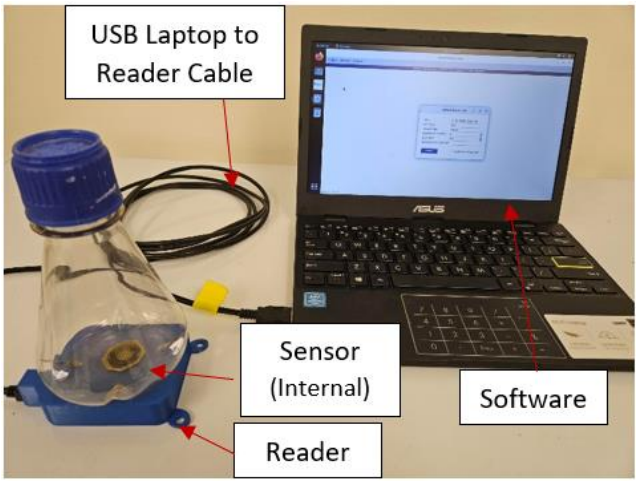
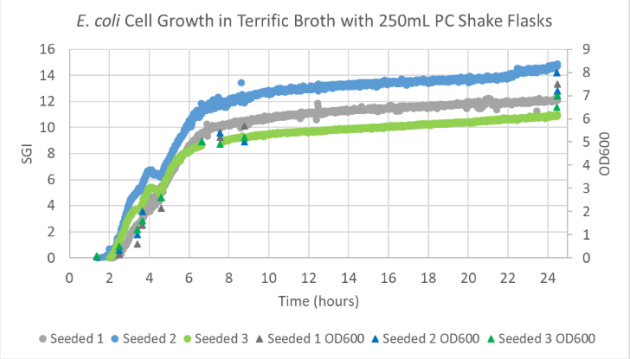
Skroot SMART Sensor: Continuous Tracking of Cell Growth Progression in Turbid Cell Cultures

Motivation: High-density cell culture is a common objective for bioproduction due to the increased biomass and higher levels of the desired product. However, such cultures can prove difficult to monitor. Optical-based methods that rely on light scattering (e.g. OD at 600 nm) saturate at a low growth level, and thus any measurement by this method requires dilution. Likewise, using an image based or cell counting method (hemocytometer) saturates and requires dilution. This increases the labor needed to provide a measurement and is another source of error. Continuous measurement of cell growth in turbid media is not possible with current solutions.

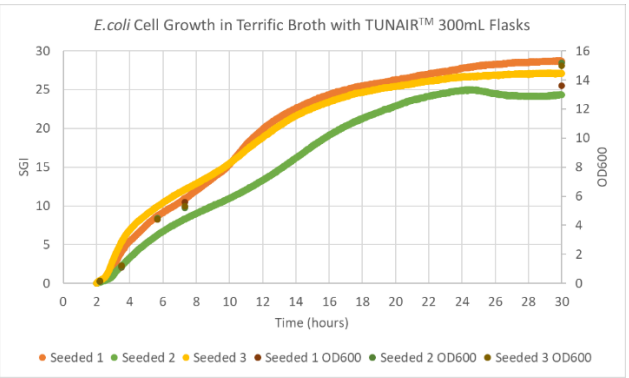
Solution: The Skroot Single-use, Metabolite Absorbing, Resonant Transducer (SMART) platform can be used to monitor cell growth in turbid conditions. The SMART platform is not optical based, but rather tracks secreted growth metabolites and information transmits through turbid solutions in the shortwave RF band. Passive (battery free) SMART sensors are placed inside shake flasks and the accompanying reader interrogates the resonant characteristics of the sensor which is communicated to the Skroot Labs software. The Skroot Labs software takes the sensor resonant characteristics and outputs a Skroot Growth Index (SGI) which tracks with cell growth.



Demonstration: To first demonstrate the use of Skroot SMART sensors in turbid bacterial cell growth, sensors were placed in unbaffled 250 mL polycarbonate shake flasks with 80 mL of Terrific broth. *E.coli* 5α was cultured in the flasks at a temperature of 37°C. For correlation with the Skroot SMART sensor output, SGI, 1 mL media samples were manually sampled and evaluated with a spectrophotometer (OD600). Below is the cell growth plot as indicated by the data from the spectrophotometer and the Skroot SMART sensor system, demonstrating the Skroot SMART system's effectiveness in monitoring bacterial cell growth above OD 1 (where dilution is commonly suggested).



Second Demonstration: To further explore the utility of Skroot SMART sensors in turbid media, the previous demonstration was repeated in three baffled TUNAIR™ 300 mL shake flasks (half baffle) with a working volume of 100 mL. TUNAIR™ flasks were selected due to their demonstrated capacity for higher cell density growth, in particular their ability to yield >2X *E.coli* as compared to traditional shake flasks. Indeed, the culture extent exceeded the previous growth, slowing at OD 14-15. The Skroot SMART platform proved capable of monitoring these more turbid cultures without sampling or dilution.



Intellectual Property:

1. Wireless Sensor (US Patent #11105761)
2. Transduction Cell Membrane (Application at USPTO)
3. Resonant Sensor Reader (WO Patent #236534)

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