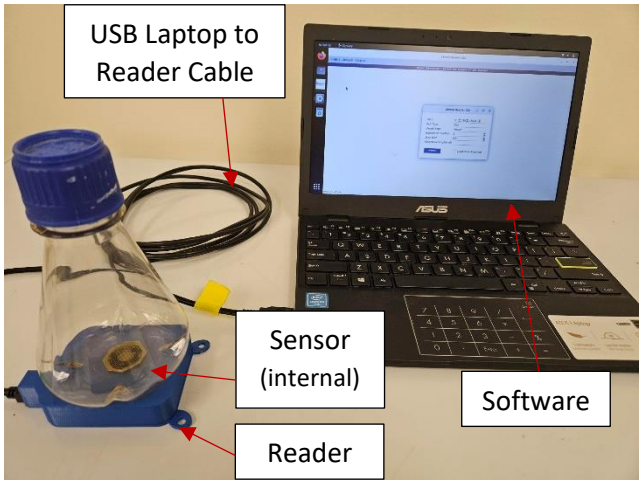
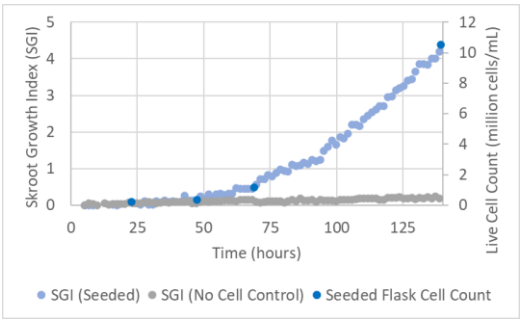
Skroot SMART Platform: Monitoring Suspended CHO-S Cell Growth Profiles in Shake Flasks

Motivation: Suspended CHO cell cultures are a commonly used chassis for biomanufacturing within mammalian cell lines. Due to their adaptability to withstand the shear forces in shake flasks, suspended CHO cells can grow to higher cell densities than other traditional mammalian cell chassis. During the cell culture run, it is important to recognize the growth phase (lag, log, and stationary) of the culture and to identify the optimal harvest time. Constructing an accurate cell growth phase plot requires considerable effort and frequent media sampling. The more frequent the sampling, the more effort is needed from the operator and the risk of contamination increases.

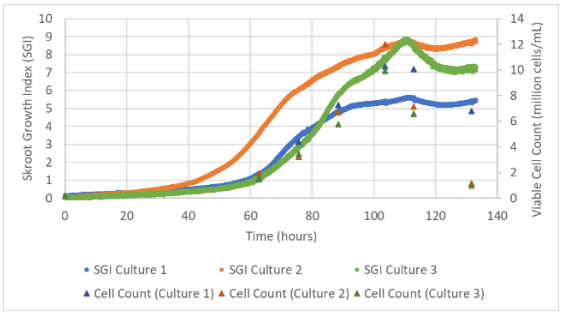
Solution: The Skroot Single-use, Metabolite Absorbing, Resonant Transducer (SMART) sensor can be used to continuously monitor the growth of cell cultures. By placing the sterile Skroot SMART sensor inside of a shake flask, the sensor can provide a minute-to-minute response to how a cell culture is growing, without the need for sampling the culture. With the application of a Skroot SMART sensor, accompanied by a reader and appropriate software, the platform reports real-time responses to cell growth. The Skroot SMART sensor absorbs naturally secreted secondary metabolites via a cell transduction layer which in turn changes the sensor's radiofrequency (RF) resonant characteristics. This is done wirelessly and passively (no onboard power needed for the sensor sticker). Additionally, due to the non-optical based sensing mechanism, Skroot SMART sensors can be used in a variety of different media, including turbid media or at high cell densities.



Demonstration: To showcase the utility of Skroot SMART sensors in tracking suspended mammalian cell growth, SMART sensors were placed inside 250 mL shake flasks to track the growth of FreeStyle CHO cells. Cells were grown at 37°C with 5% CO_2 and shaken at 120 RPM. 80 mL of FreeStyle CHO media was used to grow the cell culture with Glutamax supplementation (8mM). CHO cells were seeded at a density of 0.2 million cells/mL whereas the control vessel was not seeded. Live cell densities were taken with the Countess 3 (Thermo Fisher) with a 1:1 addition of Trypan Blue. Sensor readings were taken every hour and a half and reported in Skroot Growth Index values (SGI). As shown in the plot below, the sensor tracked CHO cell growth, even at high densities (no dilution), with clear differentiation from the no growth control.



In comparative growths, The SGI can be used as an approximate cell count, but end point measures are still strongly encouraged to get the most accurate measure of cells. The SMART platform is best used to track growth phases. To demonstrate this, three independent CHO cultures were run following the same protocol as above (results shown below). In each case the rates of change captured by the sensor correlate to the stationary and death phases of the cells.



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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