Glucose-Lactate: A biomarker that accounts for glycolysis after blood draw
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Glucose is a key biomarker for assessing current health status and predicting future disease risk. In unprocessed whole blood samples, glucose levels decrease over time due to glycolysis. In clinical practice, this is mitigated by using fluoride tubes, but the issue is common in plasma and serum collected in tubes used for research studies. Nightingale Health measures both glucose and lactate simultaneously using NMR, allowing for estimation of the physiological glucose level, even with extended delays in serum/plasma preparation.

Glucose gets converted into lactate in whole blood by anaerobic glycolysis. This process continues until blood cells are removed during serum or plasma preparation. Figure 1A illustrates how glucose levels decrease at an approximately constant rate after blood draw until centrifugation in nine samples. The corresponding increase in lactate in the same samples is shown in Figure 1B.

Each glucose molecule is converted into two lactate molecules during anaerobic glycolysis. Assuming this is the only reaction occurring in the sample, the sum of glucose and ½*lactate remains constant. We refer to this sum as the "glucose-lactate" biomarker. Figure 1C demonstrates that the concentration of glucose-lactate remains constant regardless of the time elapsed from sample draw to centrifugation.

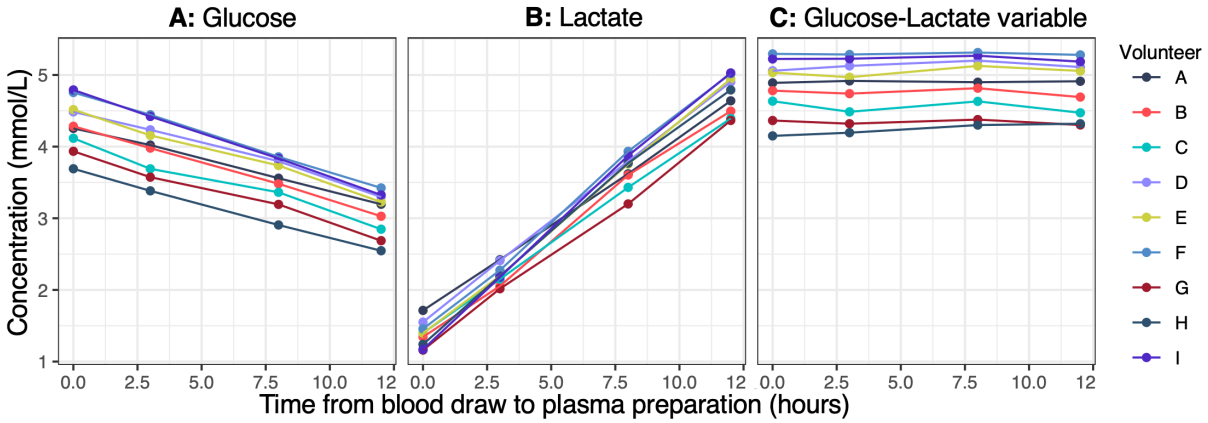

Figure 1. A) Concentration of glucose in 9 samples as a function of time from blood draw until centrifugation. B) Concentration of lactate in the same samples. C) Concentration of the glucose-lactate biomarker in these samples is essentially constant regardless of time to centrifugation.

A concrete example: If the concentration of glucose right after blood draw is 5 mmol/L and lactate is 1 mmol/L, then glucose-lactate is 5.5 mmol/L. After 12 hours, the concentration of glucose is 3 mmol/L, lactate is 1 + 2*2 = 5 mmol/L, and glucose-lactate is still 5.5 mmol/L.

The glucose-lactate biomarker is highly correlated with plasma glucose in cohort studies with optimal sample collection settings. For example, the correlation is R > 0.9 in the FinHealth 2017 cohort. Despite the high correlation, glucose-lactate is more strongly associated with the incidence of type 2 diabetes in the UK Biobank than serum glucose alone (hazard ratios 2.0 and 1.9, respectively, per 1-SD).

Experiments demonstrate that glucose-lactate levels are stable for at least 48 hours at room temperature, and even longer if the blood samples are kept refrigerated prior to serum/plasma preparation.

The optimal scaling factor may differ from ½ since other reactions are ongoing. The scaling factor may also differ for serum and EDTA plasma, as the conversion rate from pyruvate to lactate depends on the type of sample tubes used.

We note that lipids and other metabolites, aside from glucose, lactate, and pyruvate, are not affected by glycolysis after the sample draw. These biomarkers are therefore generally stable with long durations to serum/plasma preparation.