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The evaluation of a continuous blood glucose monitoring sensor system in harbour seals

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Introduction

A commercially available continuous blood glucose (CBG) monitor was trialled with a view to developing a remote glucose sensor for short term deployments on animals in the field (hours) and for eventual integration into a telemetry tag for longer deployments (days to months). There are a number of different research questions that would benefit from this technology, for example investigating how fasting weaned grey seal pups manage their glucose levels during this prolonged period of aphagia before they go to sea for the first time. This method could also provide invaluable data on the feeding behaviour of seals. Whilst movement and dive data collected by telemetry tags can indicate where an animal may be feeding, it does not verify that the animal has actually consumed prey during a putative foraging bout. Monitoring changes in blood glucose will allow us to confirm behavioural inferences and to estimate the consumption of prey by seals in a given area or during a particular foraging trip.

Method

A Dexcom™ Continuous Glucose Monitor was used to investigate the utility of this method for determining changes in blood glucose in phocid seals. The device uses a microneedle sensor to detect changes in glucose in the interstitial fluid of the skin which is highly correlated with circulating blood glucose. The sensor needle was inserted into the skin of the seals using the sterile insertion pack provided for use with humans and the transmitter clipped to the sensor head which was held in place by a purpose built carriage plate and guide glued to the fur of the animal. The sensor was deployed and calibrated according to the manufacturer's instructions, using the standard blood stick glucometer method (GlucoRx™ HCT meter, which incorporates haematocrit correction). This particular glucometer has been validated for seals (Bennett et al. in press), and although there is some degree of variation compared with the 'gold' standard laboratory colourimetric method for the determination of glucose in plasma (Randox™ glucose kits, Bennett et al. in press), the bias is systematic and can be accounted for using a linear correction. This correction was therefore applied before the calibration values were entered into the CBG device. The receiver was then placed in the enclosure with this seal and allowed to equilibrate for ~20 hours (as recommended by the manufacturer). In addition to this initial calibration and equilibration period, the CBG method requires re-calibration every 12 hours and this was carried out again using the results instantaneously obtained using the GlucoRx sticks. Trials with three captive harbour seals were carried out on three consecutive days and blood samples collected for the laboratory method analysis to compare with the GlucoRx and CBG results recorded every 5 mins. GlucoRx and laboratory results were analysed in duplicate and the mean concentration was reported.

Results

In general there was good correspondence between the CBG method and the colourimetric (lab) method (Fig. 1.) with an average of 12.5% difference in the concentrations. This is well within acceptable limits. There was clearly some drift of the sensor during the 21 h equilibration period

and if the values prior to recalibration are excluded the difference was only 6.9% (Fig. 2.), with some individuals showing better correspondence than others. The mean concentrations and standard errors for all three animals by time are shown in Fig. 3. Whilst the pre-calibration concentrations, particularly for seal Ulf, were much lower than the concentrations recorded using the two other methods, in general the patterns of change in blood glucose were well captured using the CBG. There was a general underestimation of the true glucose levels but this bias was consistent with time and if necessary could be accounted for in the analysis.

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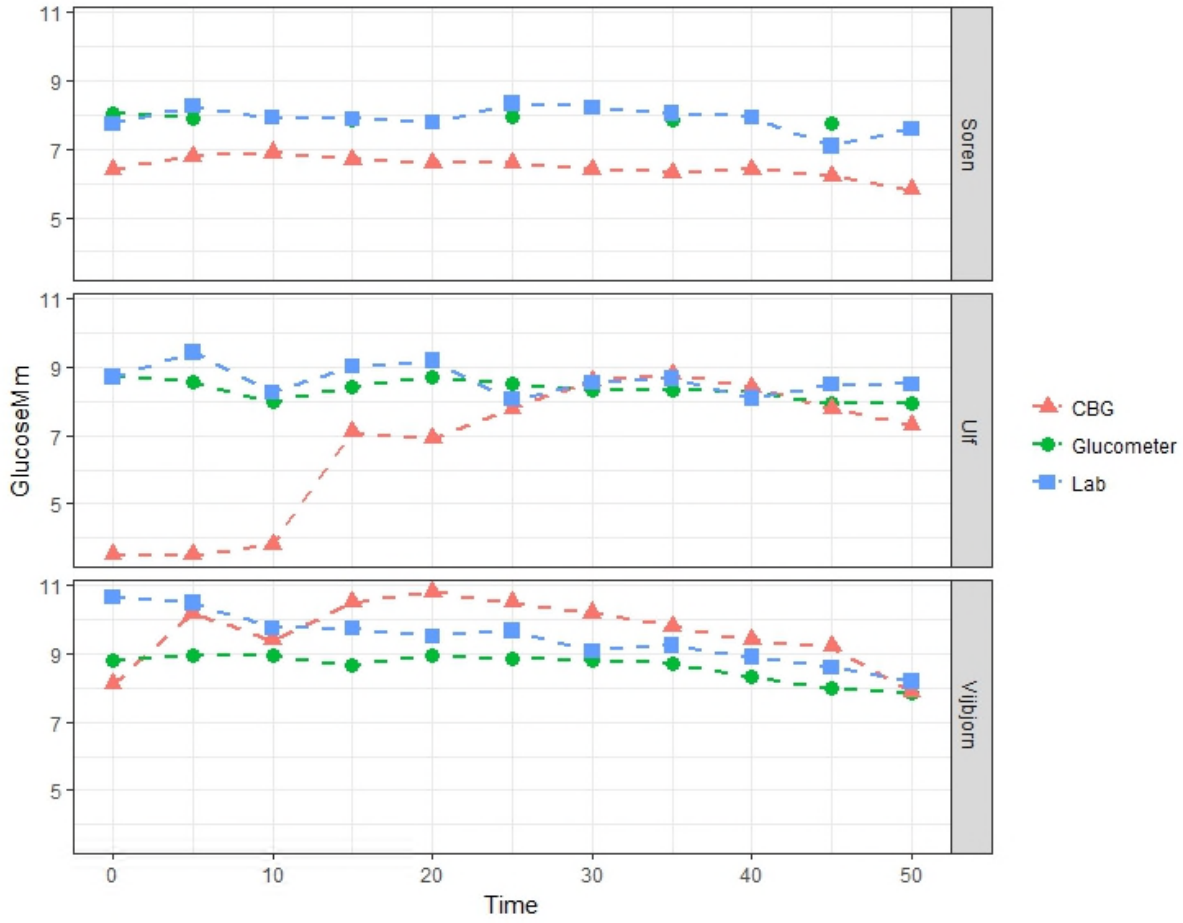


Figure 1. Blood glucose in three captive seals measured using three methods (CBG = Continuous Blood Glucose, Glucometer = GlucoRx stick method, Lab = Laboratory Colourimetric method).

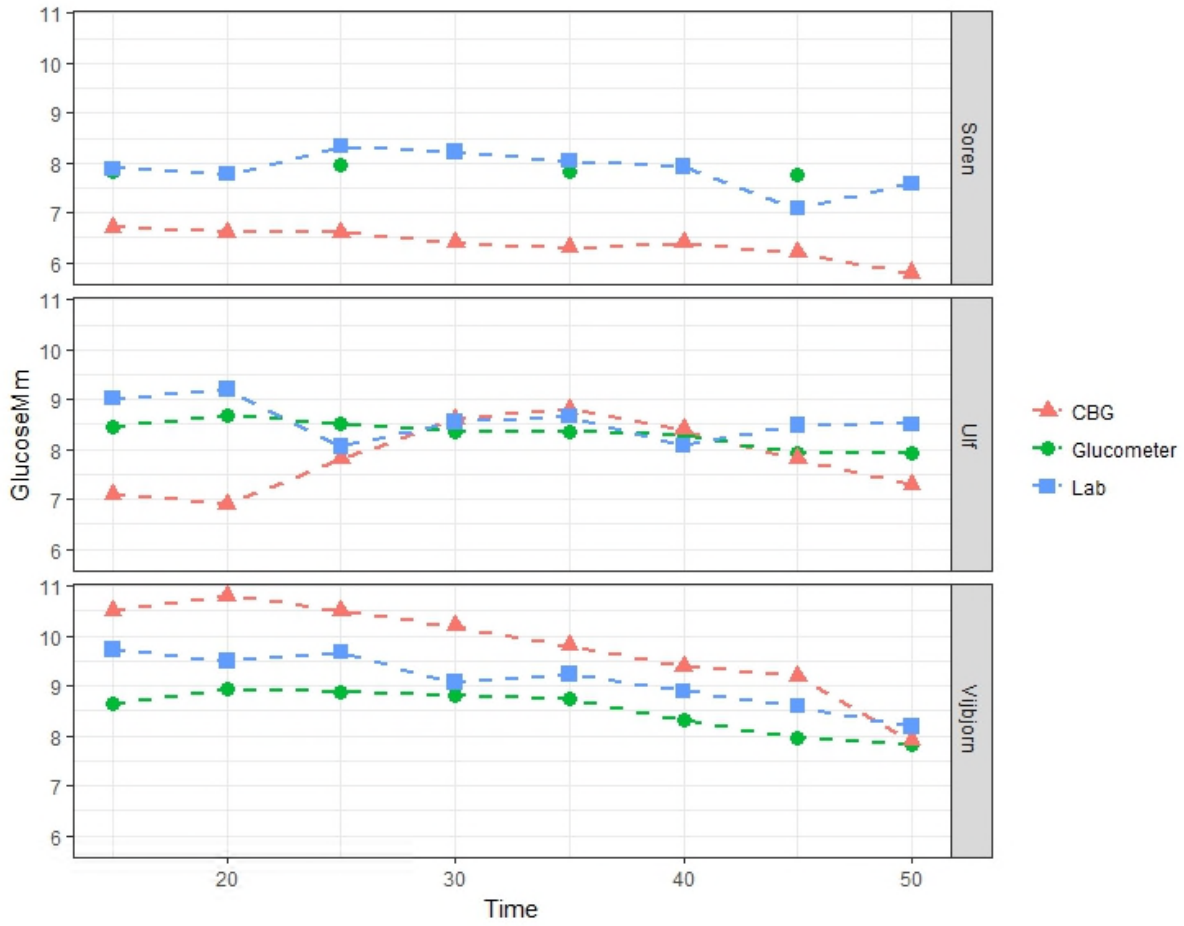


Figure 2. Blood glucose in three captive seals measured using three methods (CBG = Continuous Blood Glucose, Glucometer = GlucoRx stick method, Lab = Laboratory Colourimetric method) excluding the pre-recalibration samples. Some Glucometer results were missed for seal Soren due to the number of sticks available.

All the data collected while the CBG was deployed on the animals is stored in the receiver and can be viewed and analysed using the Dexcom STUDIO software which is available to download from their website. An example of the plots generated by this software are shown in Fig. 4. Additional CGM data for some of the animals was collected during the equilibration times, particularly for Ulf and Soren. The trace is not complete due to the behaviour of the animals and the range of the receiver (6m) which meant the signal was not always captured. However, there are a number of very interesting periods of data acquisition when 2-3 hours of continuous readings were recorded.

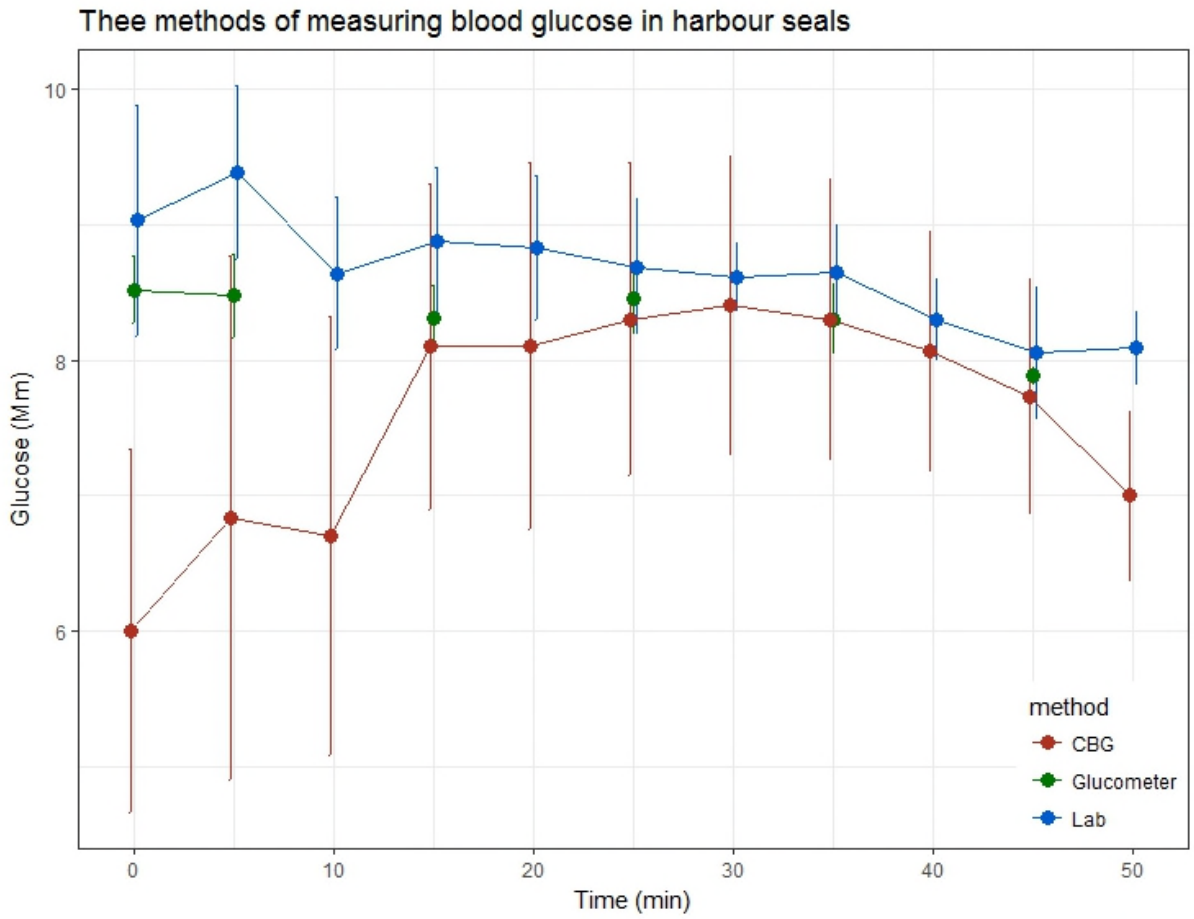
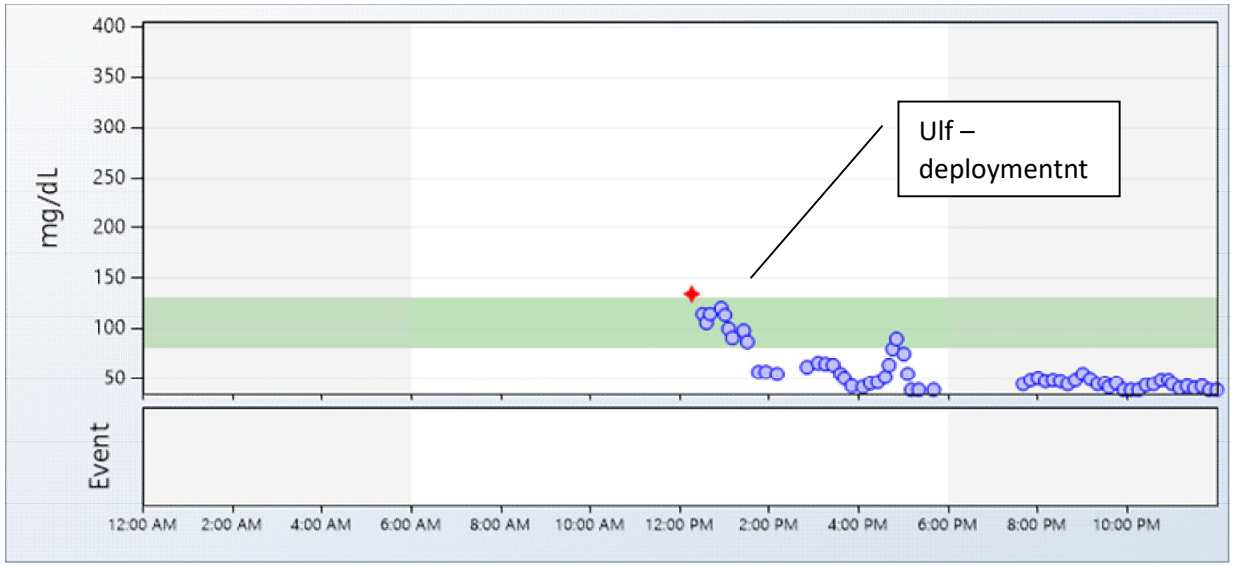


Figure 3. Mean glucose concentrations and standard errors by time and method of measurement.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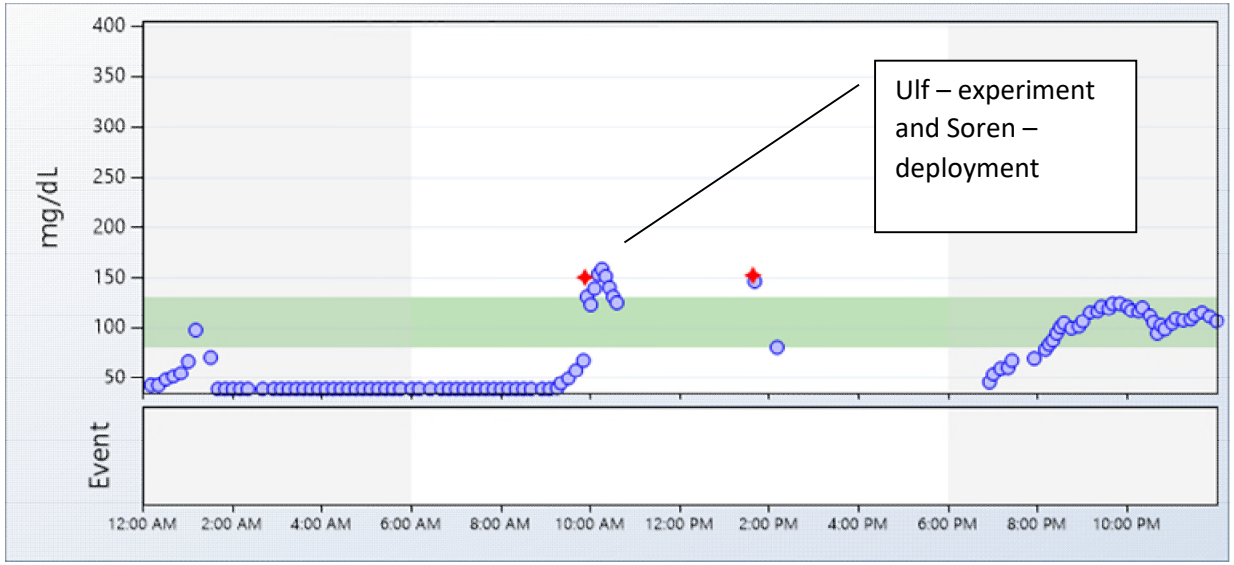
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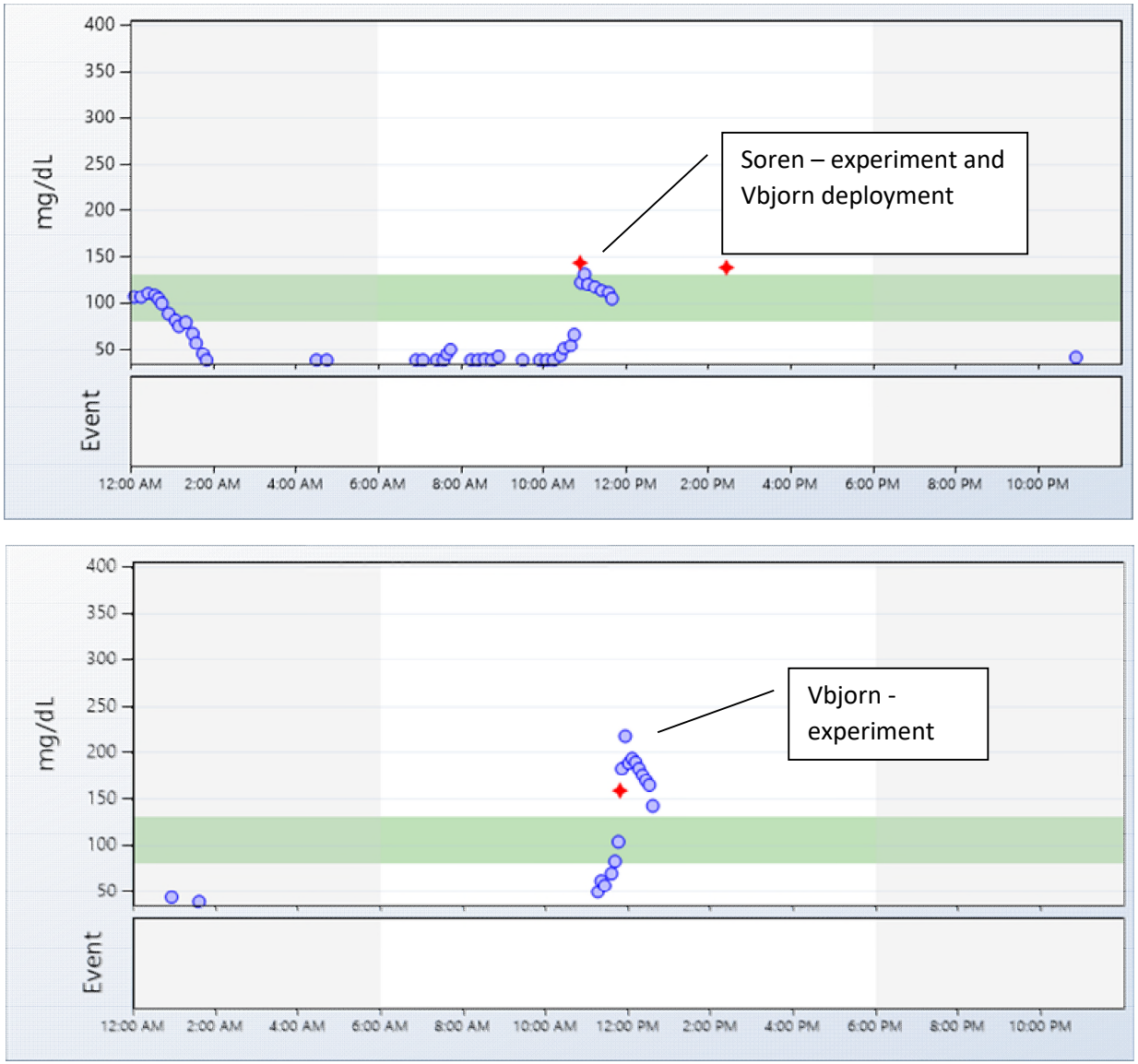

Figure 4. All data collected by CBG monitor

Conclusions

These initial results show that the CBG method for determining glucose over time in phocid seals is very promising. However, there are challenges to overcome, particularly because of the drift in the sensor overnight and the need for recalibration after 12 h of deployment. In addition there was quite a degree of individual variation in the correspondence between the CBG results and the other methods which could be due to the placement of the sensor and possibly other aspects of deployment that need to be further investigated.

All the continuous data collected by the receiver will be analysed in more detail in the near future. In particular the manufacturers have indicated that they will be able to assist in retrieving the raw signal data from the device which means we will be able to investigate the drift in more detail and to find out if there are ways to internally recalibrate the device so that it can measure glucose for longer than 12 h. However, even with this constraint, we feel this method is highly adaptable for the field and that being able to remotely monitor blood glucose in seals over relevant time periods will certainly allow us to address some of the physiological questions posed.

Reference

Bennett K., Turner, L., Millward, S., Moss S. and Hall A.J. (in press). Obtaining accurate glucose measurements from wild animals under field conditions: comparing a hand held glucometer with a standard laboratory technique in grey seals. Conservation Physiology.