Modelling gastric bypass-induced improvement of glycaemic control following a meal

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Gastric bypass surgery has been shown consistently to result in improved glycaemic control in obese, Type II Diabetic subjects. The mechanisms causing this marked effect include profound changes of gastro-intestinal physiology, gut hormone secretion, and bodyweight. As the surgery affects the gastro-intestinal system directly, the physiology of -and response to- the ingestion of a meal are particularly perturbed. Although it is clear that postprandial glucose and insulin levels are better controlled post-surgery than in pre-surgery subjects, this effect is not well understood as it is a result of a dynamic interplay of multiple mechanisms. Quantifying the contributions of each of these components to the improvement in glycemic control thus remains a challenge. In order to untangle this response, to characterise the improved glucose tolerance of the post-surgery subject and to provide an integrated view of gastric bypass improvement mechanisms we propose a mathematical model-based method. We applied a dynamic model to describe the meal response of morbidly obese subjects undergoing Roux-en-Y gastric bypass. Measurements of the meal response of obese controls, non-diabetic subjects undergoing bypass surgery and diabetic subjects undergoing bypass surgery (both before and after surgery) were obtained. The data included glucose meal rate of appearance, in addition to gut hormones kinetics. We report preliminary results of the model analysis, in which we examine whether the model is able to incorporate the observed changes of GLP-1 kinetics and glucose rate of appearance, as both are known to change markedly following gastric bypass. The model is then used to analyse the transition of glucose control from the pre- to post-gastric bypass surgery situation.

Smith, Robert

Decoupling activity from activation: shifting phytochrome signals away from red light

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Synthetic biologists aim to engineer tools that can be used uniformly across biological systems to achieve desired responses. Out of this research, the field of optogenetics has emerged using light-regulated synthetic networks to control biological systems. Recent constructs have used plant photoreceptors to control cellular mechanisms, such as transcription, protein localization and hormone concentrations. The system we use in this study consists of the red/far-red photoreceptor phytochrome B (phyB) and its interaction partner PHYTOCHROME INTERACTING FACTOR 6 (PIF6). Under red light, a chromophore attached to phyB forms the active Pfr state allowing phyB to interact with PIF6 and regulate transcription. Under far-red light illumination, the chromophore reverts back to the inactive Pr state preventing phyB-PIF6 interactions and downstream processes. Thus, both in synthetic systems – that use the phyB (1-650) protein fragment – and in planta, phyB activity occurs specifically when exposed to red light. In this study, we decouple absorption of light by phyB and wavelength-dependent activity of phyB. Experimentally, we measured absorption spectra of phyB (1-650) and a transcriptional readout (SEAP) across the light spectrum. Using this information, we constructed a mathematical model of the system. From this, sensitivity analysis determines which model parameters can be manipulated to produce shifts in phyB