Supplementary information

Progressive glucose stimulation of islet beta cells reveals a transition from segregated to integrated modular functional connectivity patterns

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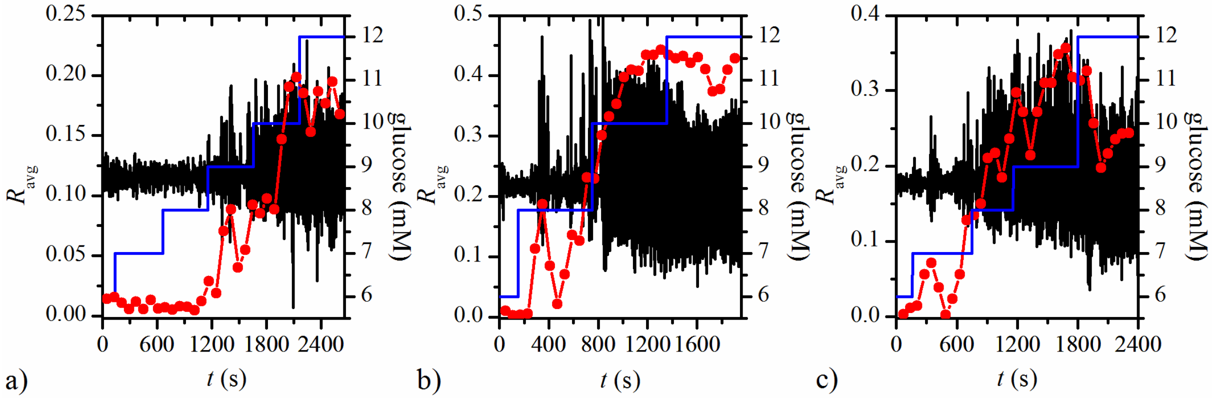

Figure S1. The temporal evolution of the average correlation coefficient (red line with symbols) and the mean-field signal of EEMD processed $[Ca^{2+}]_i$ activity of beta cells (black line) under progressive stepwise stimulation with glucose (blue line). The calculation was performed for three different islets with 270 (a), 152 (b) and 100 (c) cells.

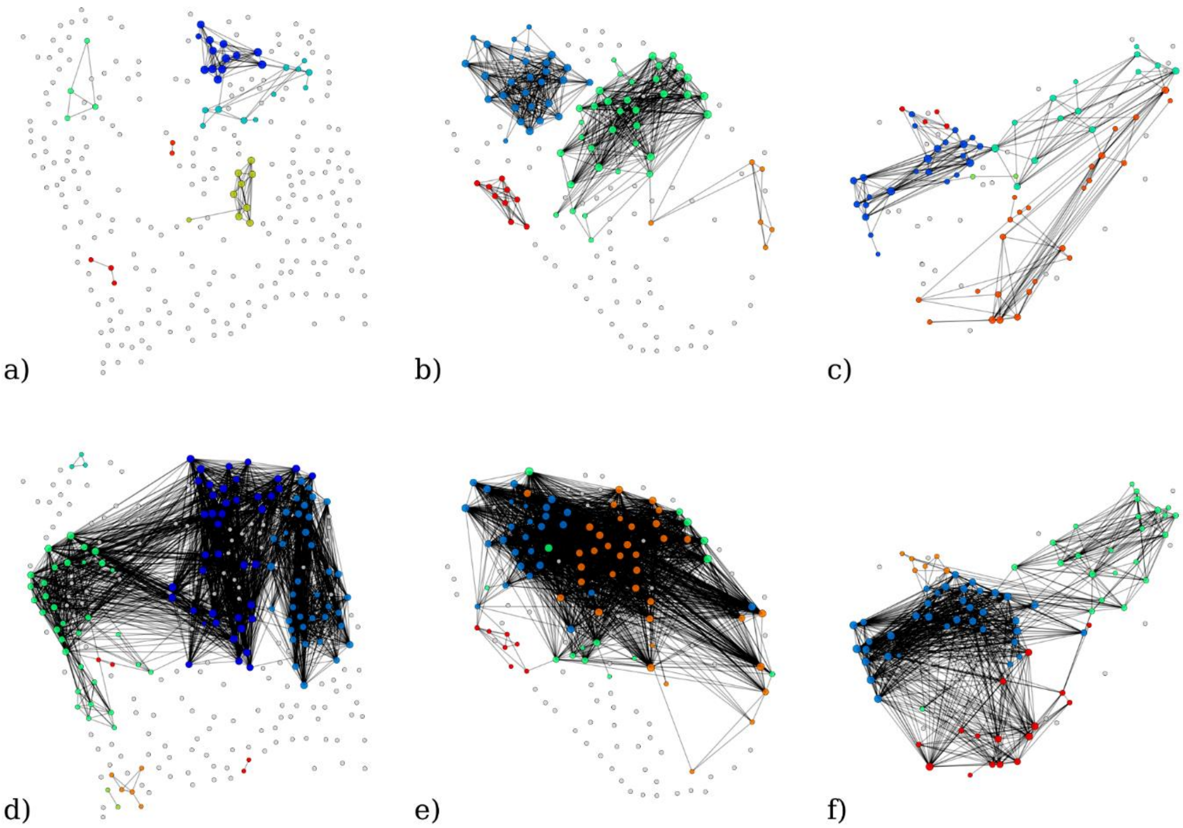

Figure S2. Functional networks of beta cells at 8 mM (a-c) and 12 mM (d-f) concentrations of glucose for three different islets with 270 (a,d), 152 (b,e) and 100 (c,f) cells (the same islets as in Fig. S1). Colors of circles denote the modularity classes (communities). Grey circles signify unconnected cells. The threshold for functional connectivity R_{th} was set to 0.7. The positions of nodes correspond to physical positions of cells within the examined islet of Langerhans. It can be observed that well pronounced localized communities exist in the beta cell syncytium, which become more interconnected at higher glucose concentrations.

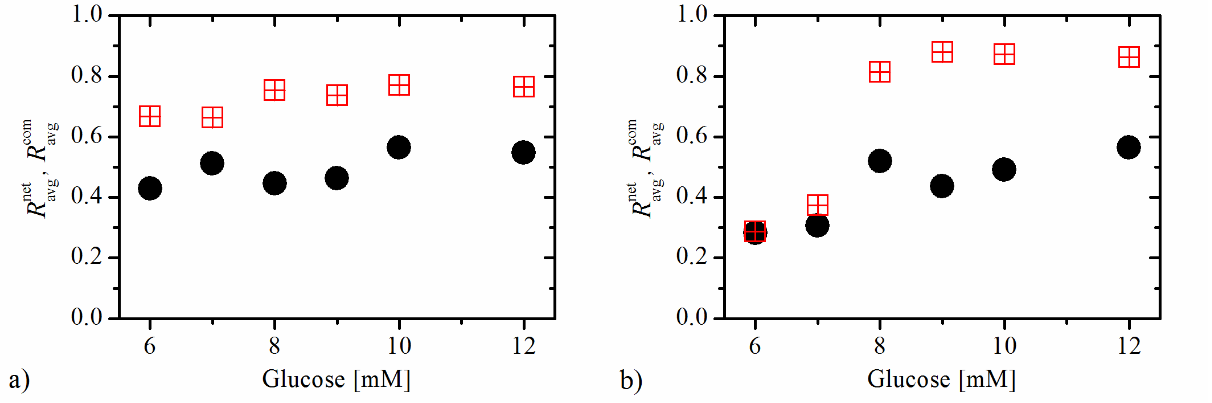

Figure S3. Average correlation between cell pairs in individual communities R_{avg}^{com} (red squares) and between all connected cells in the network R_{avg}^{net} (black circles) at different concentrations of glucose. In the panel (a) the connectivity threshold R_{th} was set to 0.6 and in panel (b) to 0.8. The results are based on the average of four different functional networks (slices presented in Figs. 3 and S2). The average correlations between cell pairs in individual communities are much higher than the correlation at the level of the whole slice, irrespective of the connectivity threshold value.

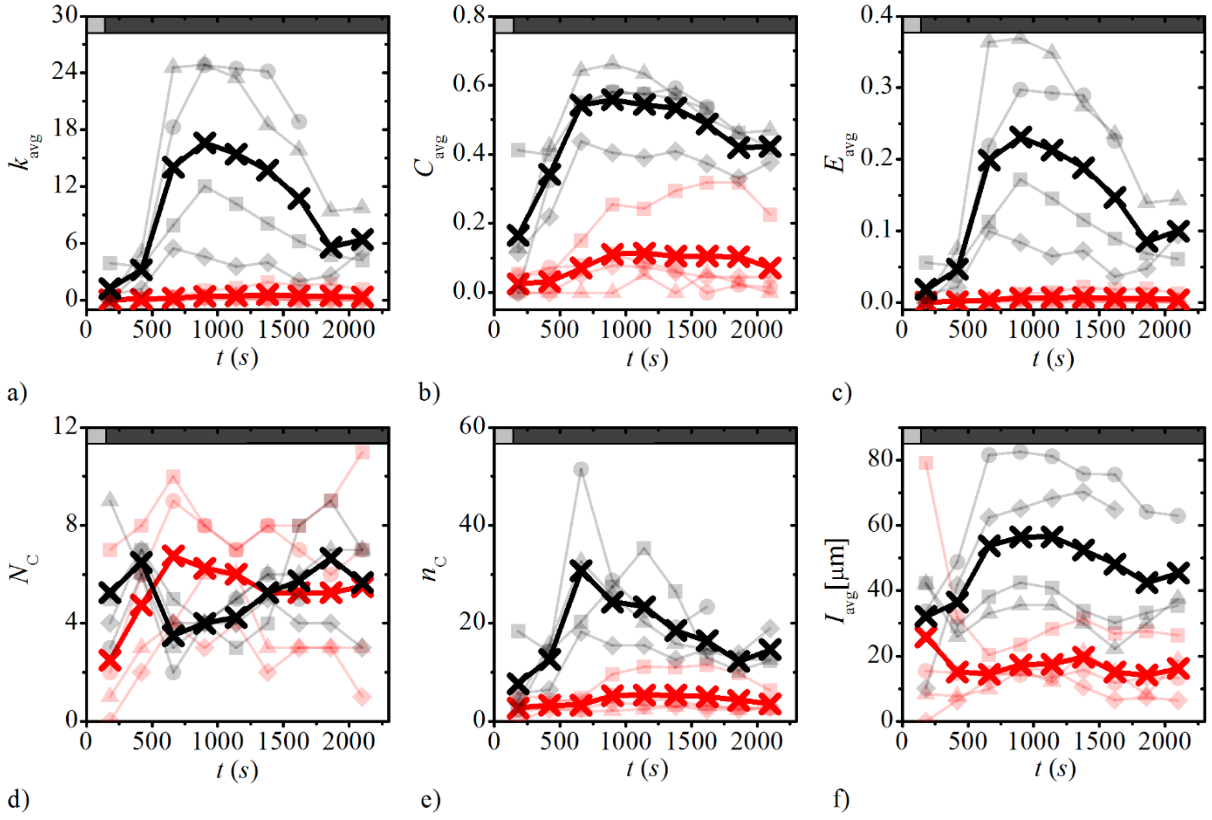

Figure S4. The temporal evolution of different network measures under constant stimulation with 8 mM (red lines with symbols) and 12 mM (black lines with symbols) glucose: a) average degree, b) average clustering coefficient, c) global efficiency, d) average number of communities, e) average size of communities, f) average length of functional connections. In all calculations the connectivity threshold R_{th} was set to 0.7. The light grey box in the top of the panels indicates 6 mM glucose and the dark grey box signifies 8 mM or 12 mM glucose. Thick lines with crosses signify the average for a given glucose concentration, whereas individual transparent lines with symbols represent the network metrics for individual slices. Altogether 4 islets (556 cells) stimulated with 8 mM glucose and 4 islets (540 cells) stimulated with 12 mM glucose were used in the analysis.