Electronic Supplementary Material (ESI) for Lab on a Chip.

Supplementary Materials

1. Erythrocytes morphology under PBS solution and long squeeze condition, as shown in Fig.S1.

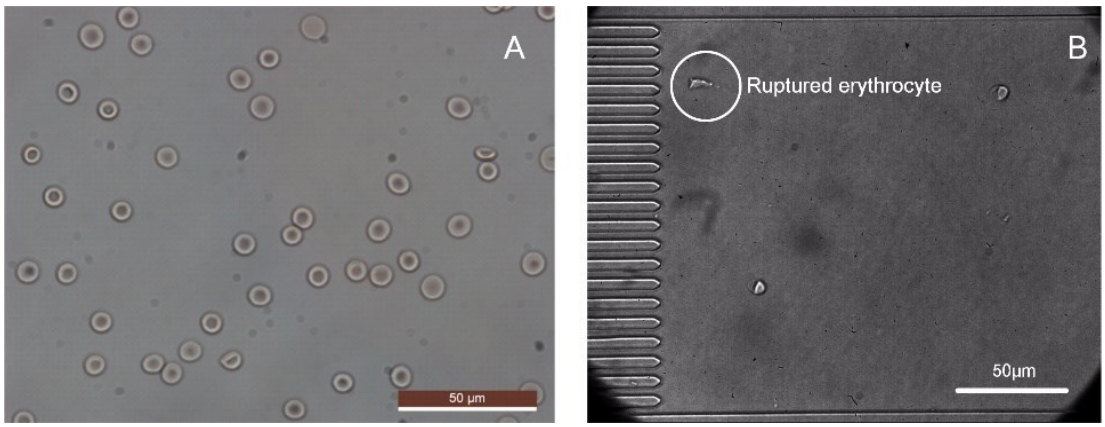

Figure S1. The morphology of erythrocytes. A. Erythrocytes in PBS solution before experiment. B. Observed ruptured erythrocytes in experiment with longer squeeze.

2. *In vivo* experiment on mice

In order to maintain the life of mice during the injection of insulin, pre-experiments were carried out. The results of pre-experiment on mice were shown in Figure S2. The other conditions have been described in manuscript, except for the injection interval. The arrows represented the injection time and dosage of insulin. And the erythrocytes morphology at 5 hours were presented. The images were obtained under optical microscope, few acanthocytes were observed. However, the resolution is not enough to distinguish erythrocytes from acanthocytes. In addition, the injection was not regular, resulting in the non-sustainable maintenance of low glucose concentration. Therefore, another three mice were arranged to carry out the experiments, as shown in manuscript.

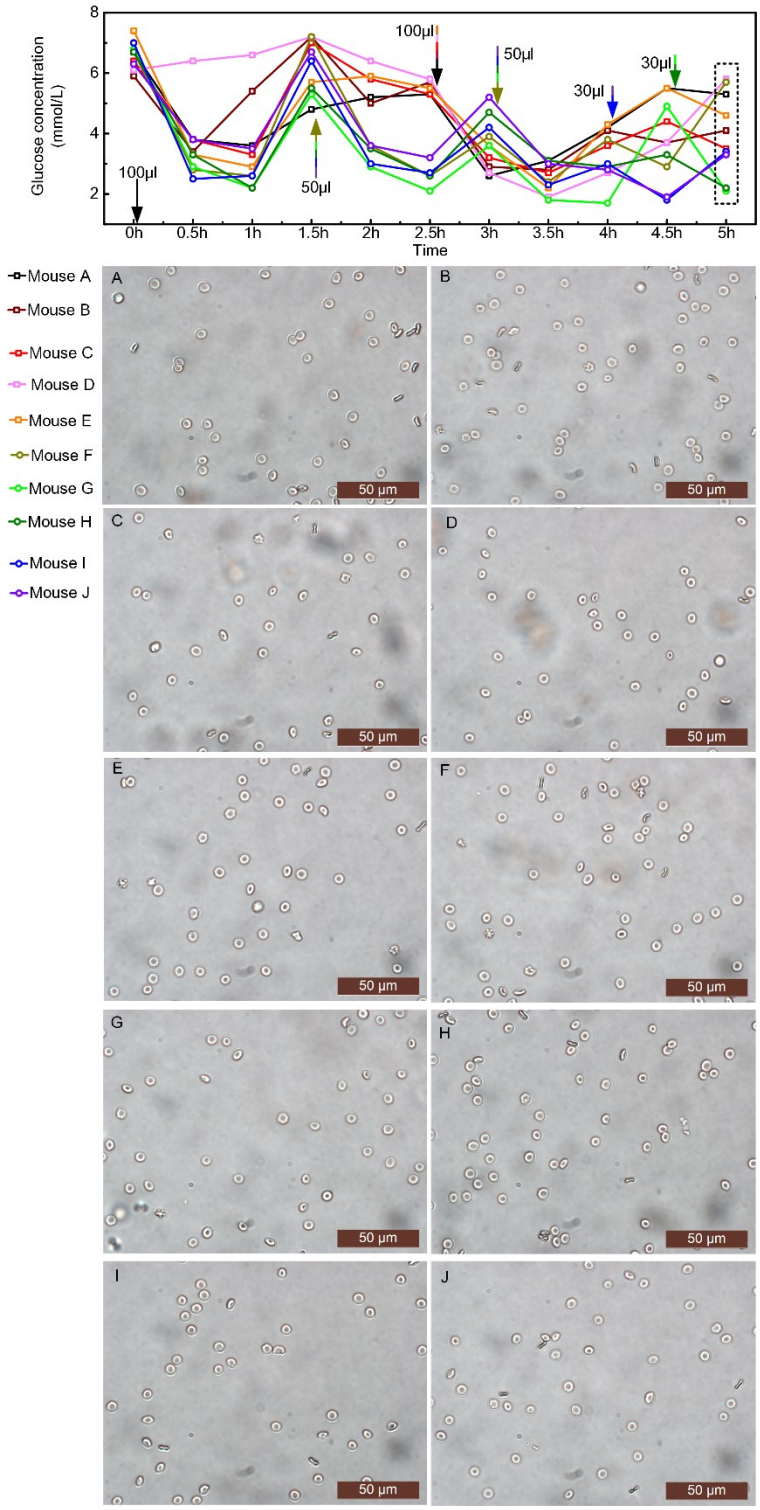

Figure S2. The pre-experiment on mice to detect the effect of low glucose concentration on erythrocytes morphology.

3. Control experiment on mice

Five mice were injected saline solution according to the experimental conditions, including the blood glucose testing condition and the injection time control. During the experiment, the mice were stopped from being fed. Despite fluctuations, the blood glucose overall became flat and decreased, as shown in Figure S3-A. Figure S3-C shows that the highest acanthocyte percent is

1.53% under saline injections, compared with nearly 20% when insulin is injected. That is, unlike insulin injections, saline injections have no effect on the state of erythrocytes.

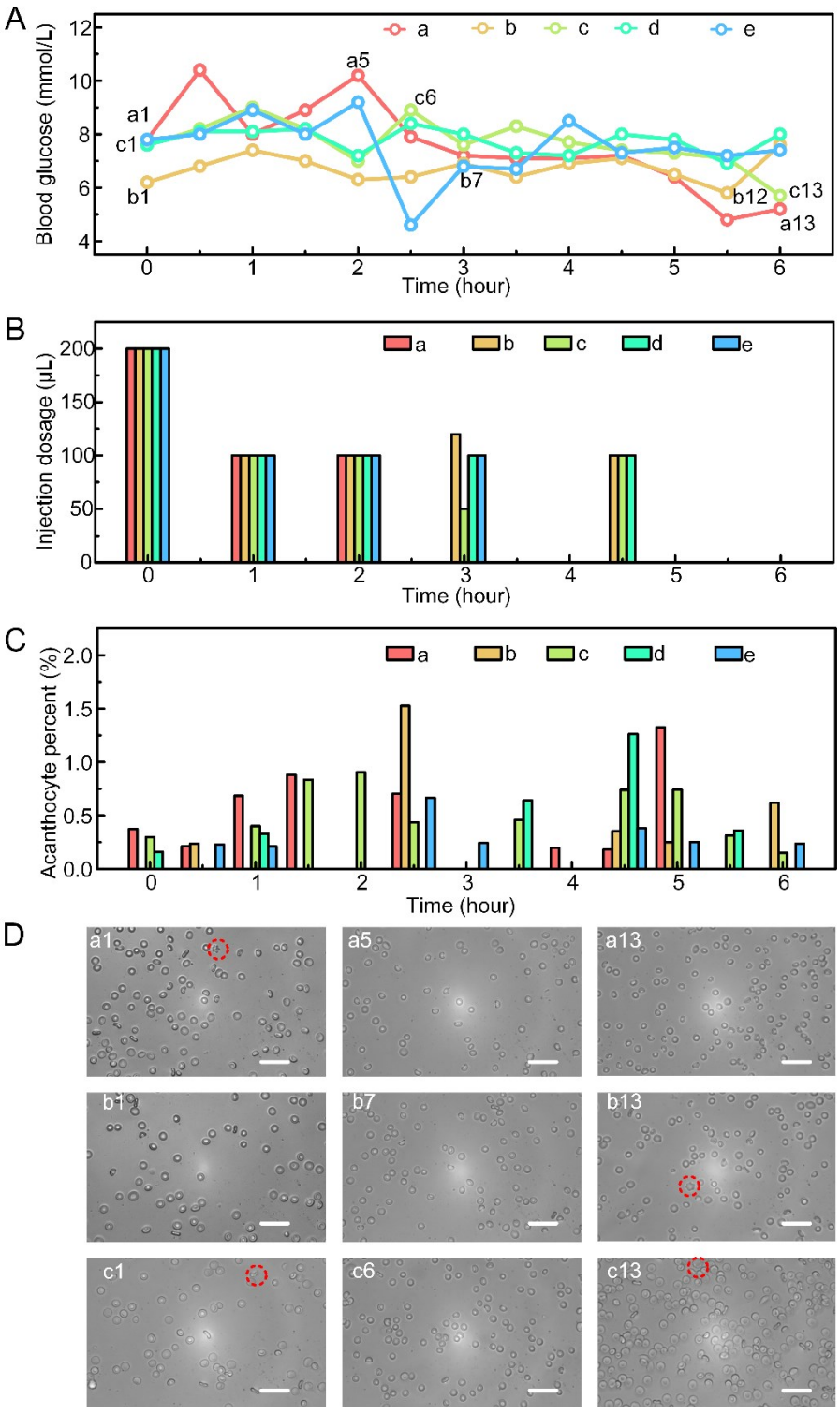

Figure S3. Control experiment of injection of saline into mice. (A) Time-course of mouse blood glucose. (B) Dosage of saline injected into mice. (C) Time dependence of acanthocyte composition. Each point includes 262-726 cells from 3-5 images, which were randomly taken from the view under an inverted microscope (Leica DMi8, X63 Lenz). (D) Morphology of the erythrocytes in the indicated mice (a#), (b#) and (c#) at different times. (Scale bar is 20μm)