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A Fast Response Mechanism for Insulin Storage in Crystals May Involve a Novel Mode of Kink Generation

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Crystals, likely rhombohedral, of Zn-insulin hexamers form in the islets of Langerhans in the pancreases of many mammals. The suggested function of crystal formation is to protect the insulin from proteases and increase the degree of conversion of soluble proinsulin. To accomplish this, crystal growth should be fast and adaptable to rate fluctuations in the conversion reaction. Zn-insulin crystals grow layer-by-layer. Each layer spreads by the attachment of molecules to kinks located at the layers' edges, also called steps. The kinks are thought to be generated either by thermal fluctuations, as postulated by Gibbs, or by one-dimensional nucleation of new crystalline rows. The kink density determines the rate at which steps advance, and these two kink-generation mechanisms lead to weak near-linear responses of the growth rate to concentration variations. We demonstrate for the crystallization of Zn-insulin a novel mechanism of kink generation, whereby 2D clusters of several insulin molecules pre-formed on the terraces between steps associate to the steps. This mechanism results in several-fold higher kink density, faster rate of crystallization, and a high sensitivity of the kinetics to small increases of the solute concentration. If the found mechanism operates during insulin crystallization *in vivo*, it could be a part of the biological regulation of insulin production and function. For other crystallizing materials in biological and non-biological systems, this mechanism provides an understanding of the often seen non-linear acceleration of the kinetics.