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Modeling of crown de- and remineralization to repair teeth using nanomedicine approaches

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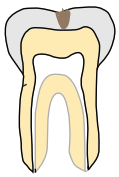
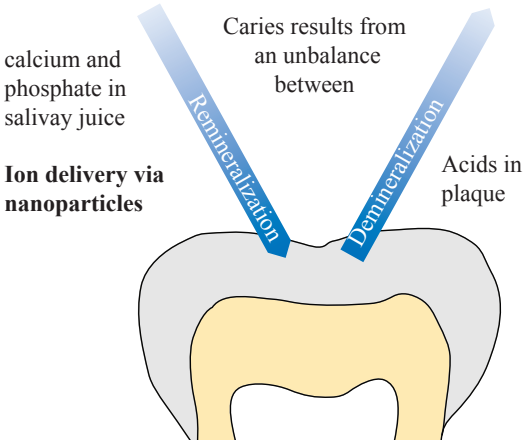
INTRODUCTION



In teeth, early carious lesions can be reversed by ion delivery to the demineralized tissue [1, 2]. The remineralization process is limited by the severe reduction of the guiding enamel matrix and the ionic diffusion that mainly mineralizes the surface and prevents further mineralization inside the lesion. Delivery systems based on nanoparticles are promised to overcome these limitations because of their reaction potential resulting from the large surface-to-bulk ratio [3]. Recent studies have shown that even after severe demineralization due to caries the overall nanostructural framework of the crown tissue remains intact [4, 5]. As a result, the remineralization of moderate carious lesions can become feasible.

MOTIVATION

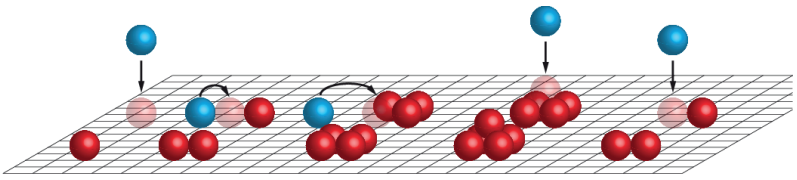


FRAMEWORK

Since mineral grains grow from nucleation and dissociate from dissolution processes [6, 7], the simulation of these phenomena will provide a deep insight into the interplay of de- and remineralization taking place in the human oral cavity every day.
The release of ions from intentionally delivered nanoparticles increase the concentration of calcium. The growth of the calcium phosphate crystallites mediated by nucleation and aggregation of available calcium ions decreases their concentration. The solution of ions and the growth of crystallites are rather complex biomineralization processes but can generally be described by dissolution theory [8], mean-field nucleation theory, scaling theory, and rate equation analysis [9]. Based on these first principles, mathematical models were derived to cover the entire process chain ranging from the delivery via nucleation to mineralization. The underlying kinetics were partly understood and published [10]. Quantities such as the size of the critical nucleus and the activation barriers for monomer migration and binding have to be derived from the spare literature data and later be deduced from experiments.

RATE EQUATION

The rate-equation approach involves a set of deterministic coupled reaction-diffusion equations describing the time dependence of the average island density while conserving mass. Here one of the simplest situations is illustrated, namely the two-dimensional growth of one-atom-high islands on a square lattice assuming that the dimer is the smallest stable island. The individual parts are explained using key words and schematic drawings. The time-dependent monomer density is increased by the incoming monomers and decreased by migration-limited nucleation and aggregation processes. The island density is increasing by the island formation and decreasing by coalescence of islands. Further processes including dissociation phenomena can be easily included and the extension towards the third dimension is available [11].



$$\frac{dn_1}{dt} = R - 2D\sigma_1 n_1^2 - D\sigma_x n_1 n_x - R(Rt - n_1) - 10Rn_1$$

$$\frac{dn_x}{dt} = D\sigma_1 n_1^2 + 5Rn_1 - 2n_x\left(-\frac{dn_1}{dt} + R\right)$$

Island formation — Island merging

SUMMARY

The in silico experiments will not only provide a detailed understanding of the fundamental processes in vitro and in vivo but also promote the optimization of the nanoparticle efficacy. The input arguments of the optimization will include the size of the nanoparticle core and its surface or coating including composition, which determines the kinetics of the dominating physico-chemical processes involved. Both the amount of materials and their kinetics affect the final outcome of the mineralization profile. The challenge consists of maximizing the homogeneity of the profile while minimizing the transport loss of the delivery. The results will not only be restricted to teeth, but also applied to bone and later to soft tissue nanocomponents.

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