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# The effect of ultrasound irradiation in nanoparticle diffusion in hydrogels

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A major challenge in cancer chemotherapy is the targeted delivery of drugs to tumor cells. Enhanced delivery to tumor tissue can be achieved by loading drugs into nanoparticles (NPs), leveraging the enhanced permeability and retention effect, which promotes NP extravasation into the tumor. However, NPs often accumulate near blood vessels instead of spreading throughout the tissue due to diffusion limitations imposed by the extracellular matrix. Focused ultrasound, especially in combination with microbubbles, has been shown to improve drug and NP delivery to tumors [1]. Despite promising clinical results, molecular-level insights into how ultrasound affects NP transport through the extracellular matrix remain limited.
Recent in-vitro experiments tracking NP transport in agarose hydrogels showed that ultrasound irradiation moderately increases the diffusion coefficient of the NPs [2]. To bridge these experimental observations with molecular mechanisms, we designed a coarse-grained model of NP diffusing in an agarose hydrogel, mimicking the in-vitro setup. The model incorporates excluded volume, NP-hydrogel attractive interactions and an effective US-like oscillatory external force, simulating the hindered diffusion of NPs through the hydrogel. Using this model, we investigate under which conditions US can lead to an enhancement of the NP transport through the hydrogel, thereby explaining the macroscopic experimental measurements.
[1] Snipstad, S. et al. Adv. Drug Deliv. Rev. (2021), 177, 113846.
[2] Ma, D. et al. JASA (2018), 144(6), 3496-3502.

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