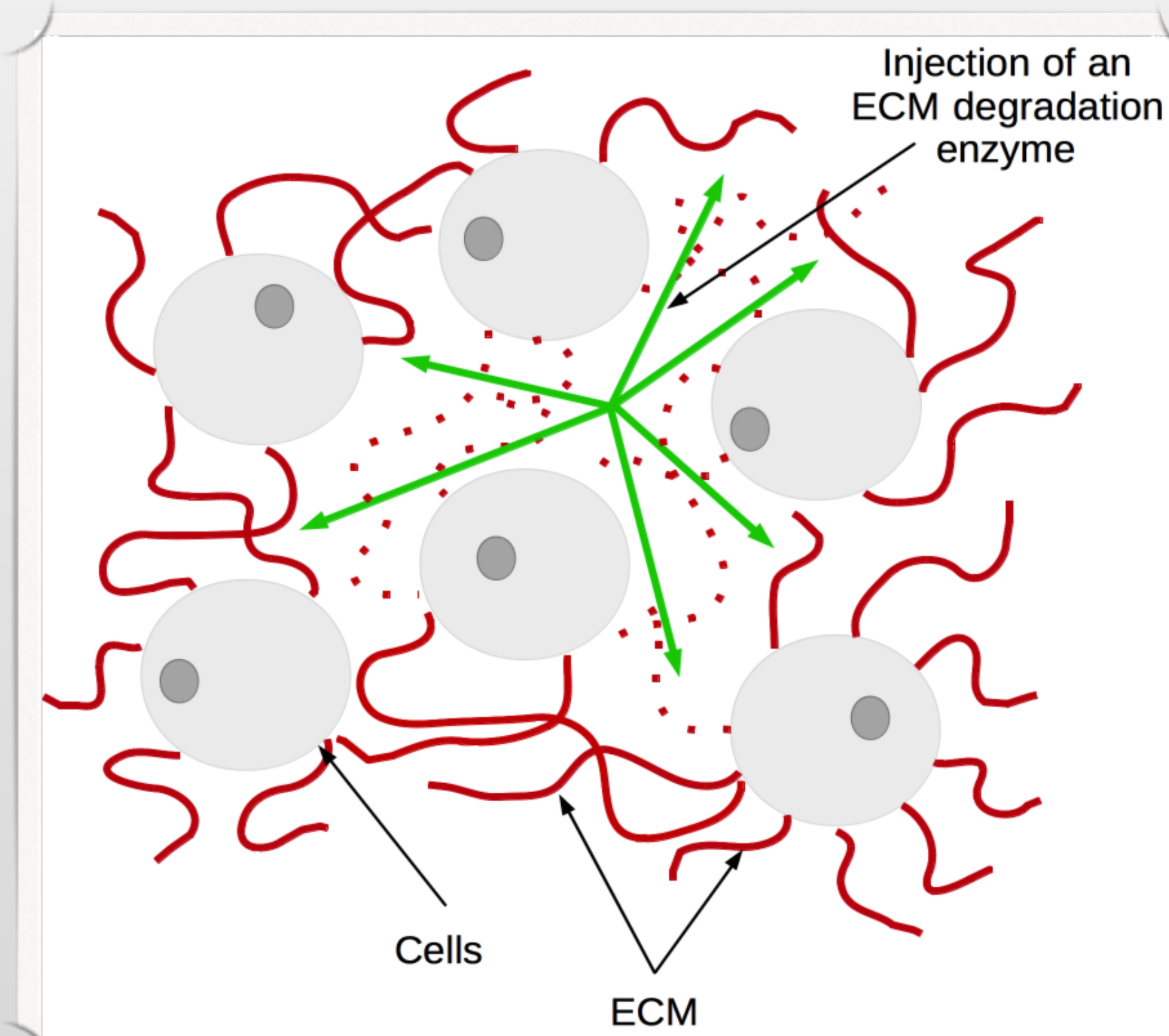


Abstract

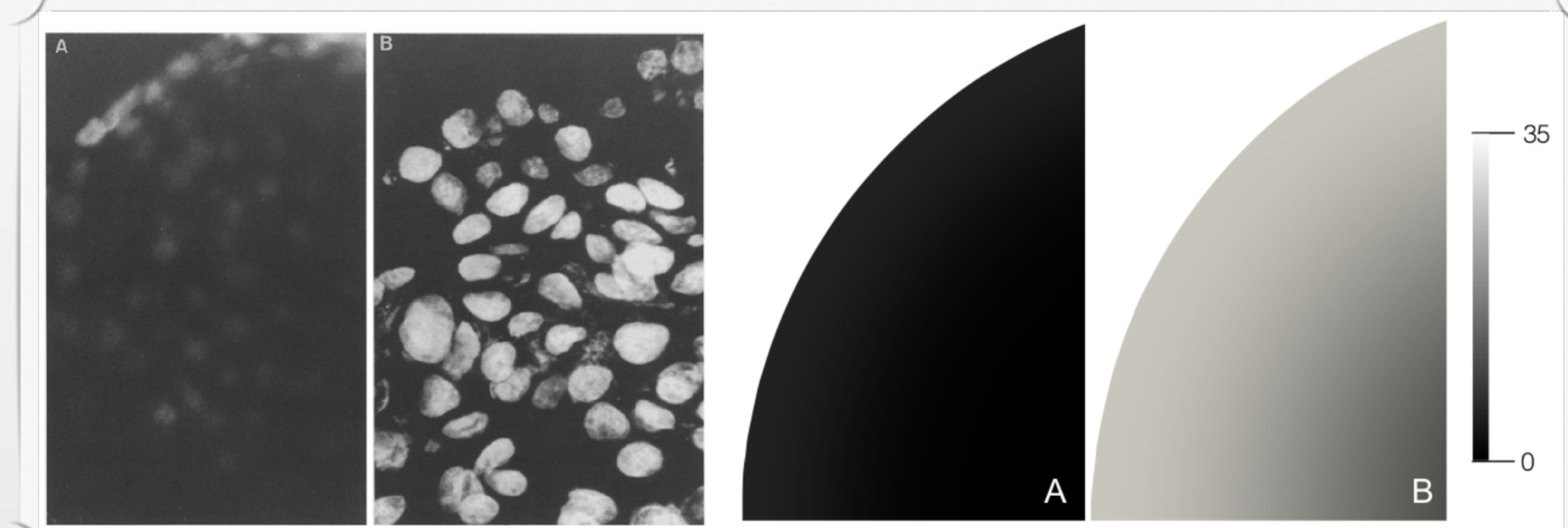
- ECM degrading enzymes can **degrade** some constituents of the **ECM**. They are used to enhance **gene transfection** or **penetration of drugs** into tumors. Our goal is to evaluate the **effect of an injection of ECM degrading enzymes on the porosity** of a biological tissue.
- We developed a **poroelastic macroscopic model** of biological tissue based on :
 - Balance laws
 - Constitutive relations
- We consider that the **changes of porosity** are due to :
 - the **elasticity** of the medium
 - the fact that cells are **slightly compressible**
 - the **effect of an ECM degrading enzyme**



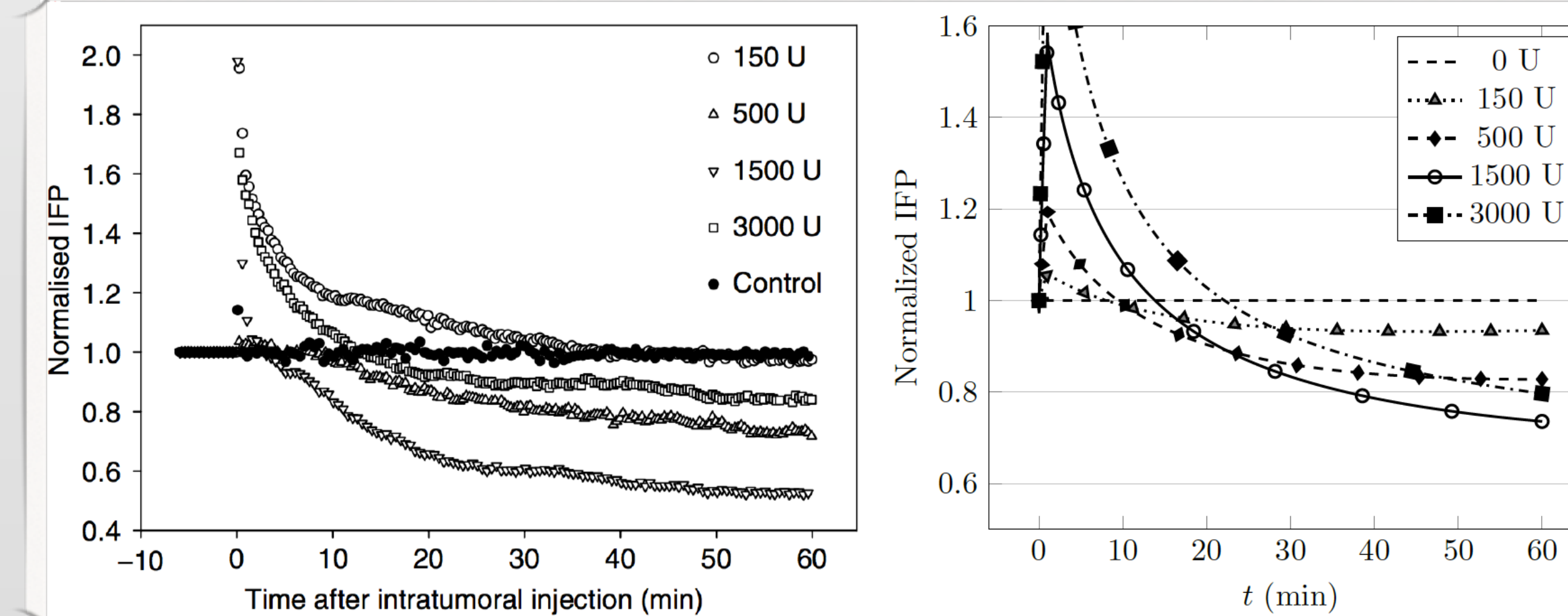
Drug penetration in tumors

An injection of matrix degrading enzymes **removes diffusive hindrance** to the penetration of therapeutic molecules

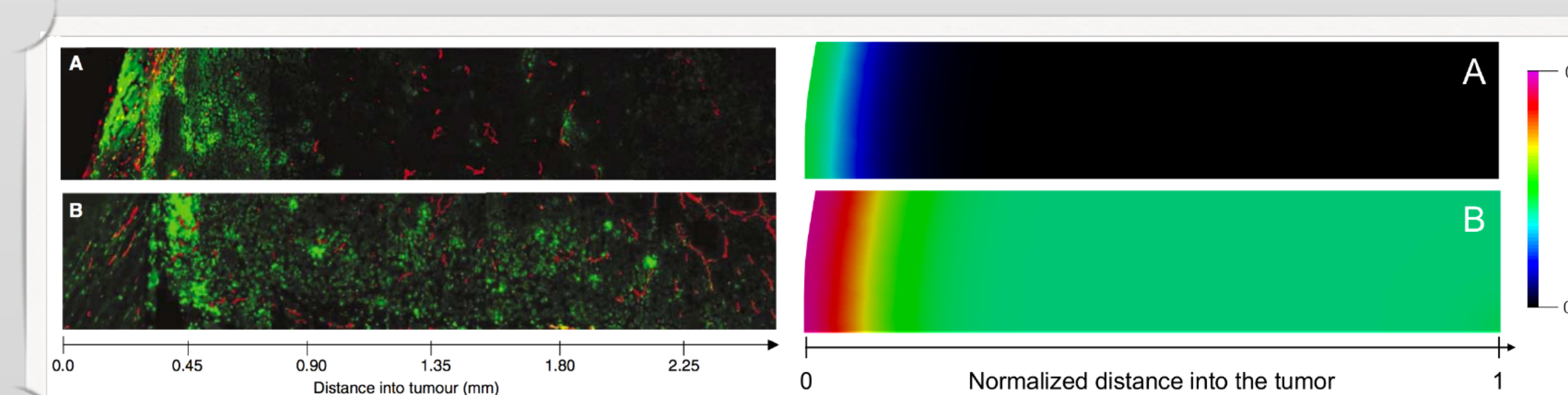
The **distribution** of therapeutic agents is **wider** when the spheroid was previously incubated into an ECM degrading enzyme, thereby **improving the diffusion process**.



Interstitial Fluid Pressure may be temporarily **reduced** by degrading the tumor ECM thus **improving the transcapillary transport** of therapeutic agents



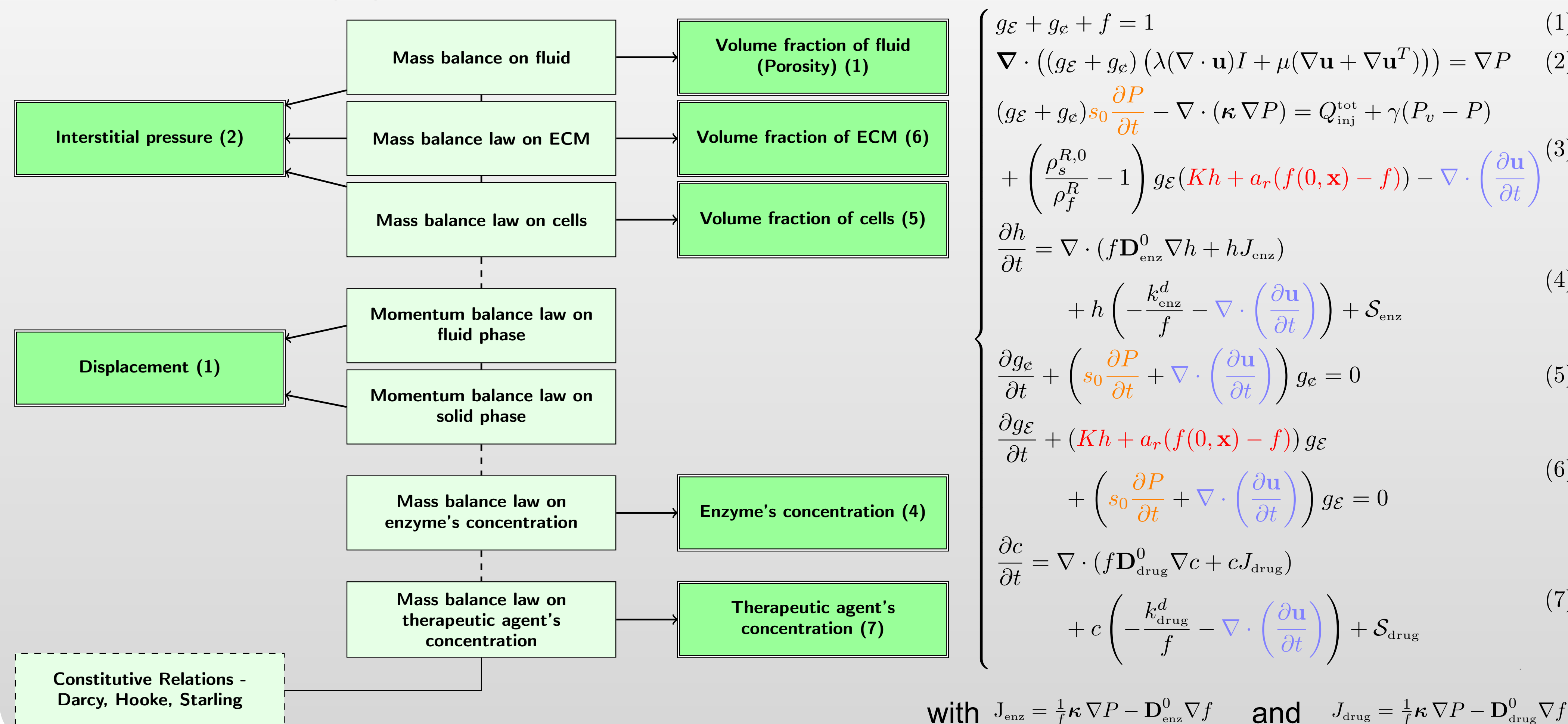
IFP is reduced in a dose-dependent manner up to a maximum reduction. Increasing the dose further, IFP is reduced to a lesser extent.



Without pretreatment, the drugs stay at the **periphery**. An enzyme pretreatment permits to obtain a **wider distribution**.

Mathematical Model

- Assumptions** : saturated medium, incompressible liquid phase, slightly compressible solid phase, negligible inertia



Conclusion

- An injection of ECM degrading enzyme enhances the distribution of drugs by improving both diffusion and convection
- Calibration with additional experimental data is needed

References

- Hyaluronidase induces a transcapillary pressure gradient and improves the distribution and uptake of liposomal doxorubicin (Caelyx) in human osteosarcoma xenografts, Eikenes, Tari, Tufto, Bruland and De Lange Davis (2010)
- Effects of hyaluronidase on doxorubicin penetration into squamous carcinoma multicellular tumor spheroids and its cell lethality, Kohno, Ohnuma, Truog (1994)
- Mathematical Modeling of a Solid-Liquid Mixture with Mass Exchange Between Constituents, L. Fusi, A. Farina, D. Ambrosi (2006)