In Silico Model for Tumor Diagnosis Based on Bloodstream Penetrating Extracellular Vesicles

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Introduction

Extracellular Vesicles (EVs) are a common biomarker to detect tumors. EVs are tiny lipid-bound particles, 30 nm to 5 µm in size, released by cells. By modeling the flow of EVs in tissue and bloodstream in silico, we are now able to derive the progress of a tumors size, even for very small tumors with a size of 50 µm []. In comparison – human hair is up to 100 µm.

- Lack of research in EV transportation through barriers of tissue.
- The use of in silico models as cost-effective alternatives to in vivo or in vitro experiments is mentioned in both.

System Model

- Realistic biological scenario with distinct zones: the artery, vein, capillary network (Ω_c), tumor area (Ω_t), and healthy tissue (Ω_h)
- EV Transport: Governed by advection-diffusion with region-specific degradation, flow, and diffusion. Blood velocity from Navier-Stokes drives EV drift in capillaries.
- Exchange Dynamics: EVs cross interfaces via:

$$\hat{n} \cdot \mathsf{J}_{t(h)} = k_p(c_{t(h)} - c_c), \quad c_h = k_t c_t,$$

where k_p and k_t define permeability and partitioning.

- Output: EV flux into the bloodstream is quantified by:

$$R_s = \iint_{\mathrm{VCS}} c(\mathsf{r}, t)\, u_n(\mathsf{r}, t)\, ds$$

indicating tumor presence and size via bloodstream EV concentration.

Results

- For the modeling computational modeling, COSMOL Multiphysics was used.
- Strong buildup of EVs in tumor regions due to dense tissue structure and lower diffusion rates, leading to significant barriers for capillary access.
- Inverse relationship between tumor size and the rate at which tumor-derived EVs enter the bloodstream. Shown in Figure 3.
- Small tumors (200 µm) release EVs rapidly, peaking at approximately 18 hours
- Larger tumors (600 µm) produce weaker signals, with peak amplitudes reduced by 60% and slower rise times.

Conclusion

- In silico framework offers a promising avenue for non-invasive cancer detection using circulating EV profiles, with potential sensitivity down to 50 µm, which is below the threshold of conventional imaging modalities.
- The temporal evolution of EV release is presented as a new diagnostic dimension beyond static imaging, enabling early detection.
- In future work, different EV sizes should be considered
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Figure 1

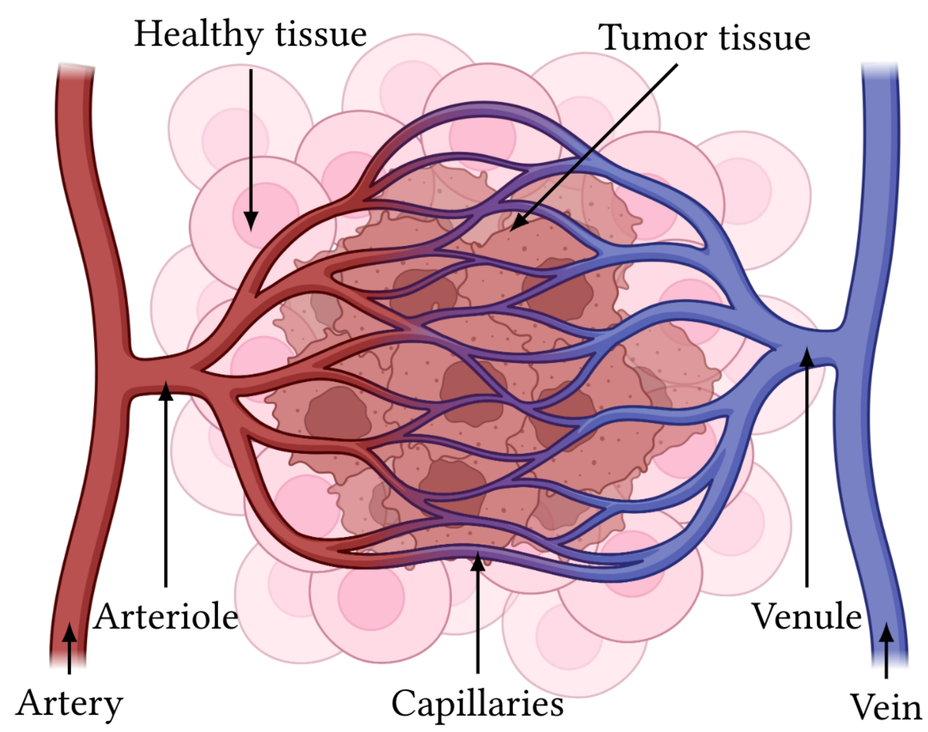


Figure 2

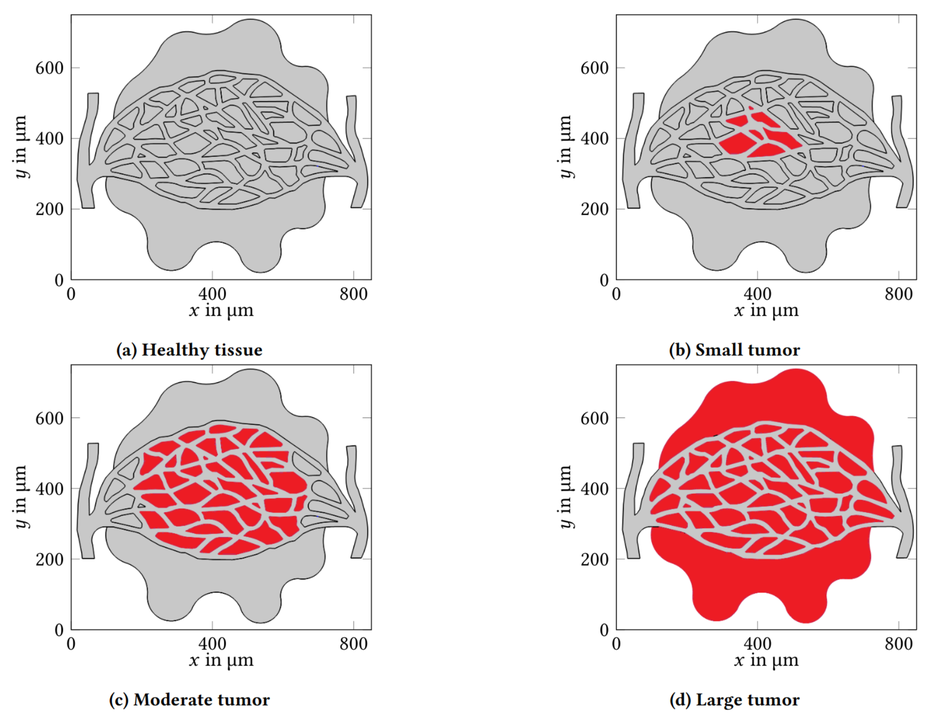
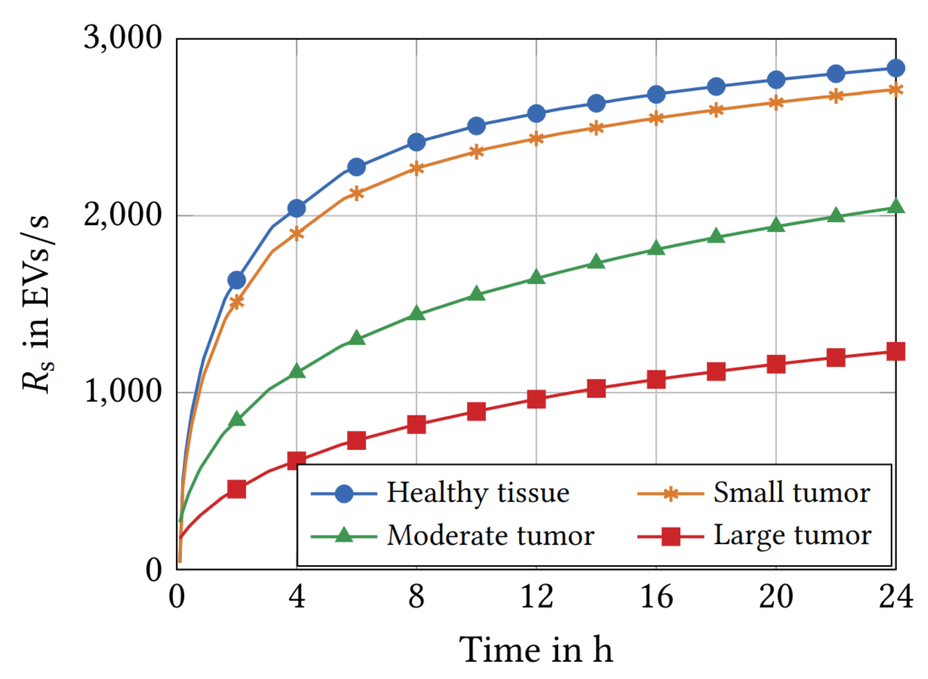


Figure 3



Quellen

[1] Laszlo Gulyas, Richard Legendi: ***Effects of Sample Duration on Network Statistics in Elementary Models of Dynamic Networks***, International Conference on Computational Science, Singapore (2011)