Improving Intranasal Drug Delivery to the Olfactory Region Using Magnetophoretic Guidance

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Introduction:

Although direct nose-to-brain drug delivery has multiple advantages, its application is limited by the extremely low delivery efficiency (<1%) [1]. It is critical to search for more effective methods to deliver drugs to the olfactory region.

Two known factors keep nasally administered drug from effective olfactory delivery:

(1) the complex nasal structure, which traps particles reaching the olfactory receptor (Fig. 1),

(2) the lack of control on particle motions after their release at the nostrils.

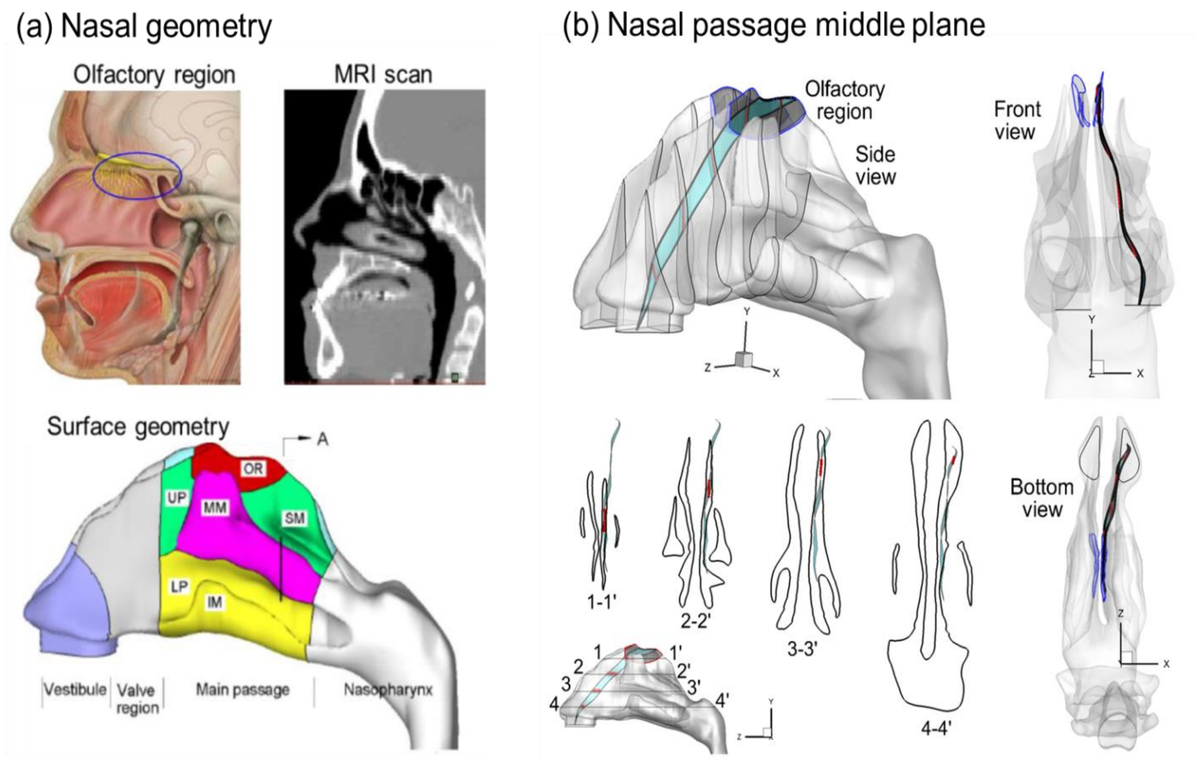

Figure 1. Nasal Complexity and narrowness prevents effective intranasal drug delivery.

Computational Methods:

In this study, we introduced a delivery method that utilized magnetophoretic forces to steer ferromagnetic drug particles to the olfactory region. The feasibility of this method was numerically evaluated in both idealized 2-D and anatomically accurate 3-D nose models using COMSOL. The influences of particle relative permeability, particle diameter, and drug release position on the olfactory delivery were also studied.

Comsol Modules: Airflow, Manetophoretic force, Particle tracing

Geometries

- Two plate channel
- Idealized 2-D nose geometry [2,3]
- Image-based 3-D geometry [3]

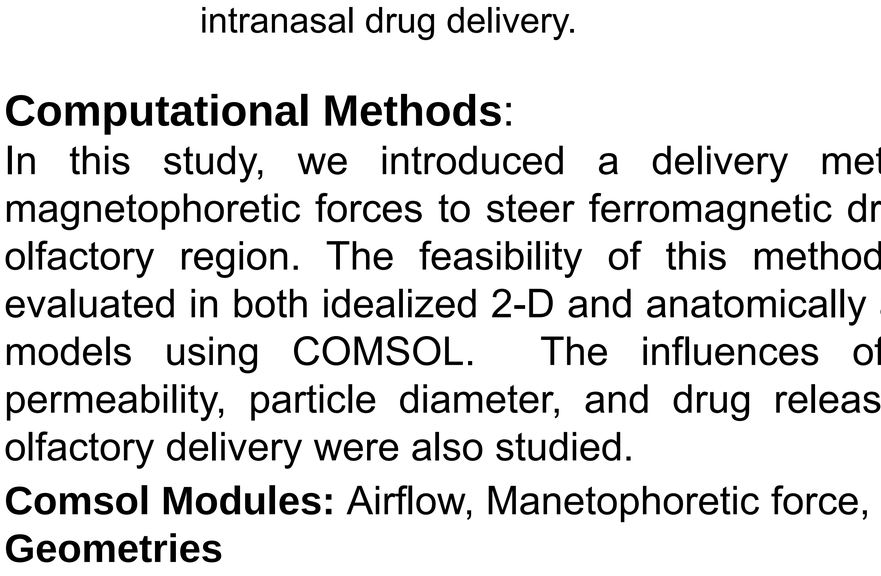

Figure 2. Trajectories of ferromagnetic particles in the two-plate channel under various magnetic field.

Results:

1. In the two-plate channel, ferromagnetic particles behaves differently with and without a external magnetic field. By changing magnets arrangement, the trajectories of drug particles can manipulated (Fig. 2).

2. 2-D nose model

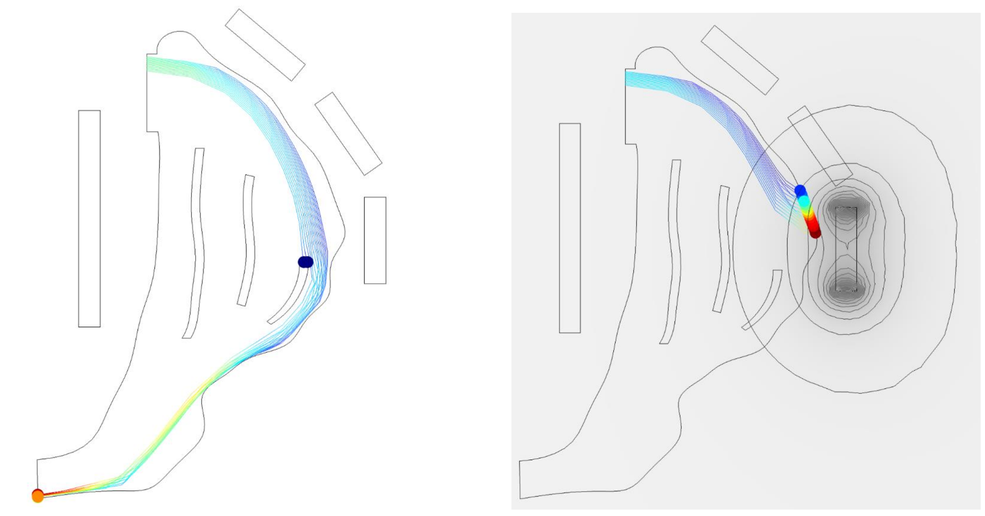

Figure 3. Deposition without and with a external magnetic field

2. Image-based 3-D nose model

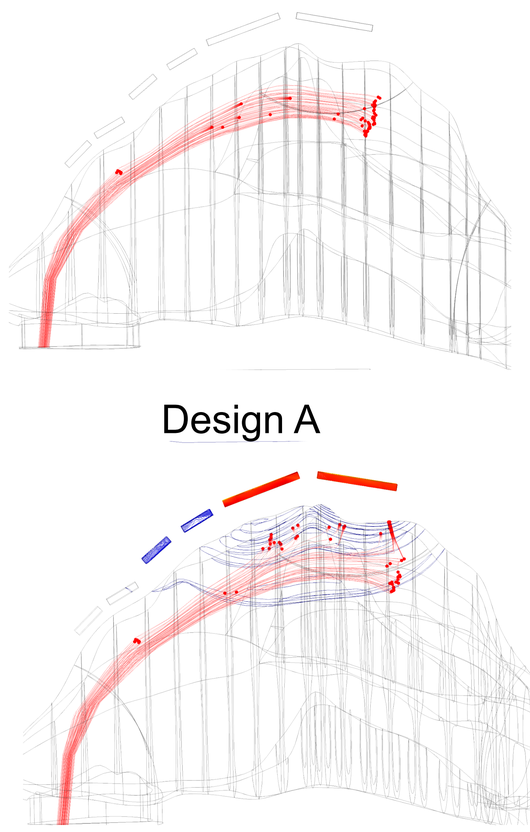

Figure 4. Deposition (a) without M-field, and with different arrangements of magnets.

Conclusions:

- It is feasible to focus and guide nanoparticles with permanent magnets and ferromagnetic particles to achieve clinically significant olfactory dosages.
- With appropriate magnetophoretic guidance and selective drug release, an olfactory delivery efficiency of more than 20% can be achieved.
- The optimal particle size range for magnetophoretic guidance is 10−15 μm.

References:

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