Electrophoretic Focusing and Navigation for Intranasal Target Drug Delivery

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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%) of conventional devices to the olfactory region where drugs can directly enter the brain (Fig. 1a). This poor outcome is attributed to two reasons:

(1) the complexity of the nasal structure,
(2) lack of control on particle motions after administration

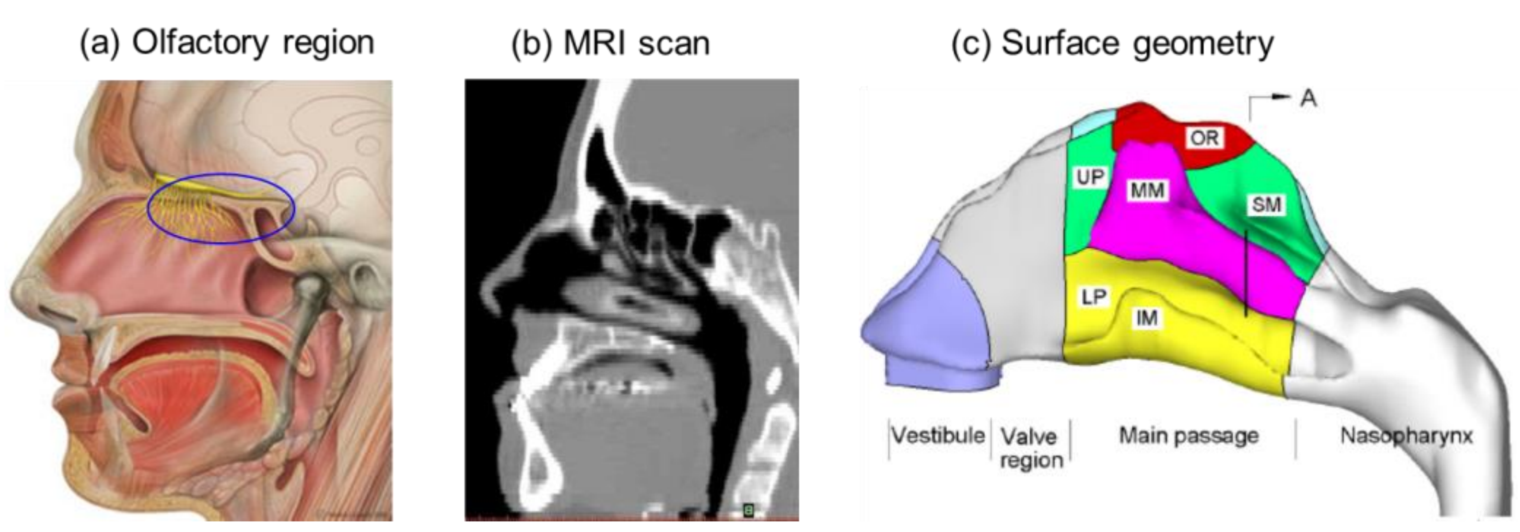

Figure 1. Nasal airway physiology: (a) anatomy; (b) MRI scan; and (c) surface model geometry

Hypothesis:

- with an appropriate external electric field, charged nanoparticles can be precisely guided via electrophoretic forces and maneuvered through the nasal passages without loss to the airway walls.
- The required electric field can be achieved by carefully arranging multiple electrodes with different electric potentials around the nose.

Objectives:

- Develop a computational fluid dynamics (CFD) model of electrophoretic-guided drug delivery;
- Numerically evaluate the efficiency of the electrophoretic-guided drug delivery in a two-dimensional nose model.

Problem Description:

1. Image-based nasal airway model

- Head MRI scans of an adult(weight 73 kg and height 173 cm) (Fig. 1b).
- Segmented using MIMICS (Materialise) into 3-D model
- internal surface geometry was constructed in Gambit (Fig. 1c).

2. Electrophoretic delivery protocol (4 components)

1) Aerosol generation (inhaler)
2) Particle charging
3) Particle focusing
4) Particle navigation

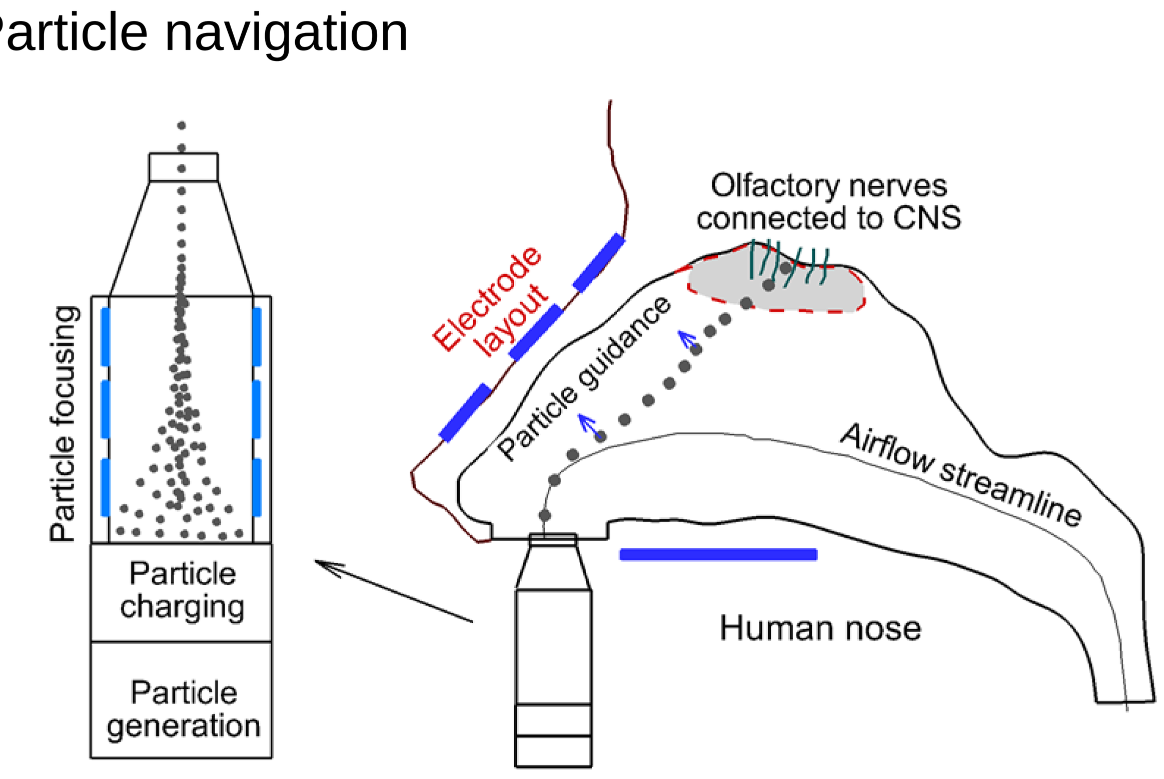

Figure 2. Diagram of electrophoretic guided drug delivery

Computational Methods:

1. Comsol Modules:

- Single phase Flow
- AC/DC
- Particle Tracing

2. Operating Conditions

- Particle: d = 0.5 µm, electric charge number = 5000.
- Electric potentials: -3 V, -8 V, -12 V, and 0 V

Results:

1. Particle Focusing and Guidance in a Curved Quadrupole

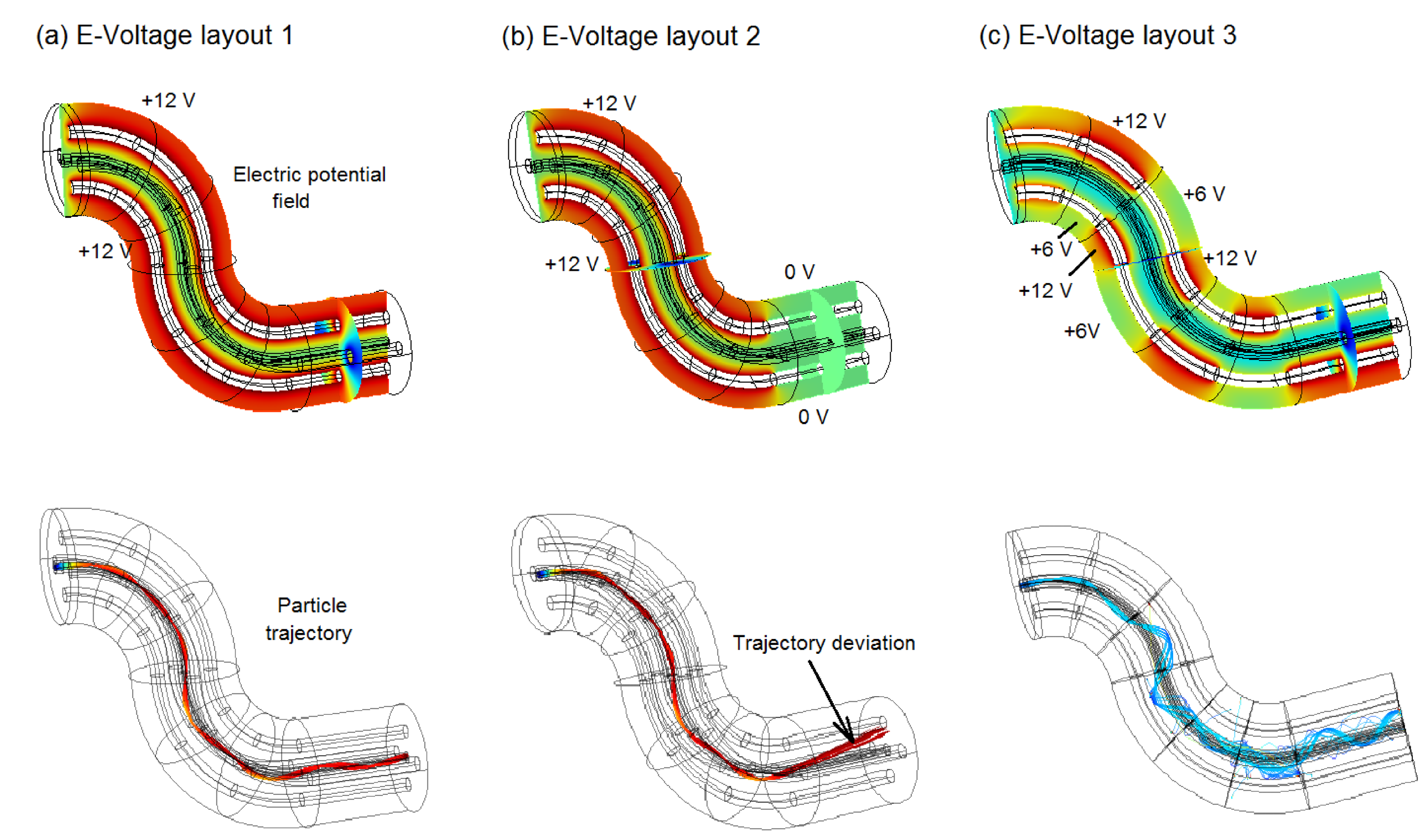

Figure 3. Electric filed and particle trajectories within the quadrupole with varying electrode voltage layouts

- 1st trial tested the sensitivity of charged particles to electrophoresis.
- 2nd trial verified the indispensability of electrophoretic forces
- 3rd trial tested the capacity of electrophoretic forces in modifying particle trajectories.

2. Particle Guidance in the Nose

- Precise control of drug particle motion is possible
- Pointed release improves targeted drug delivery

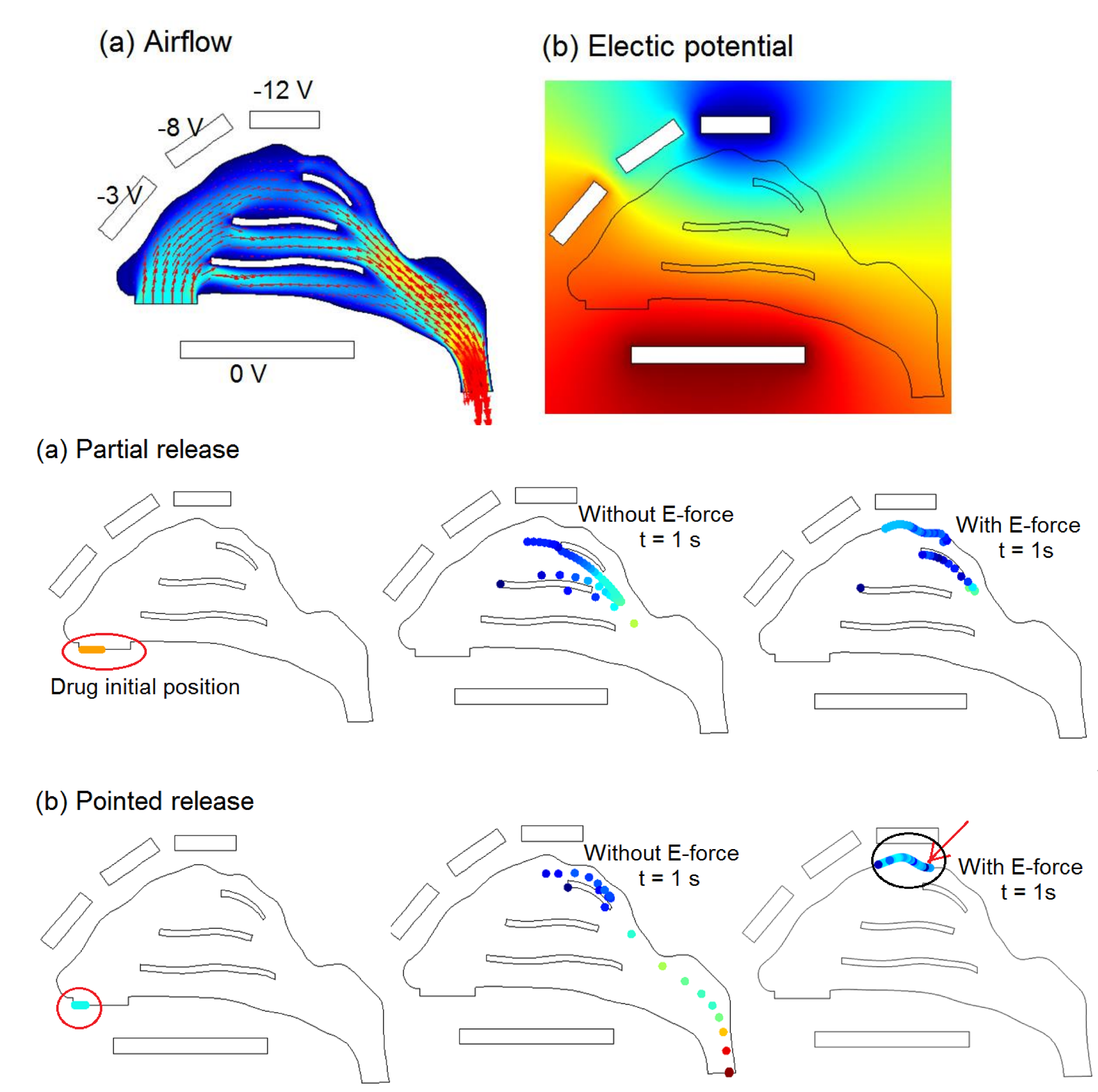

Figure 4. Nasal air flow, electric filed, and particle trajectories

Conclusions:

- It is practical to focus and guide nanoparticles with voltage that is safe to human body (<12 V).
- With appropriate electrophoretic guidance and selective drug release, significantly improved olfactory dosage could be achieved.

References:

1. Si X., Xi J., Kim J., Zhou Y., Zhong H. Modeling of release position and ventilation effects on olfactory aerosol drug delivery. *Respiratory Physiology & Neurobiology*, **186**,22-32 (2013)
2. Xi J., Longest P.W., Anderson P.J. Respiratory Aerosol Dynamics with Applications to Pharmaceutical Drug Delivery. In Fanun M (ed) Colloids in Drug Delivery. CRC Press, 501-26 (2010)

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