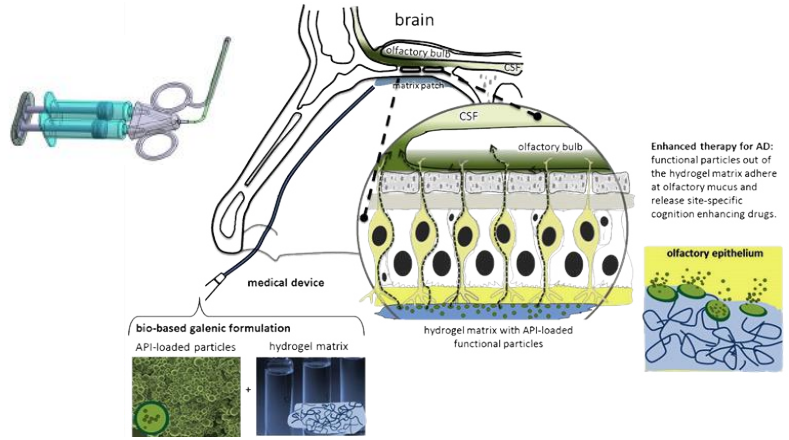
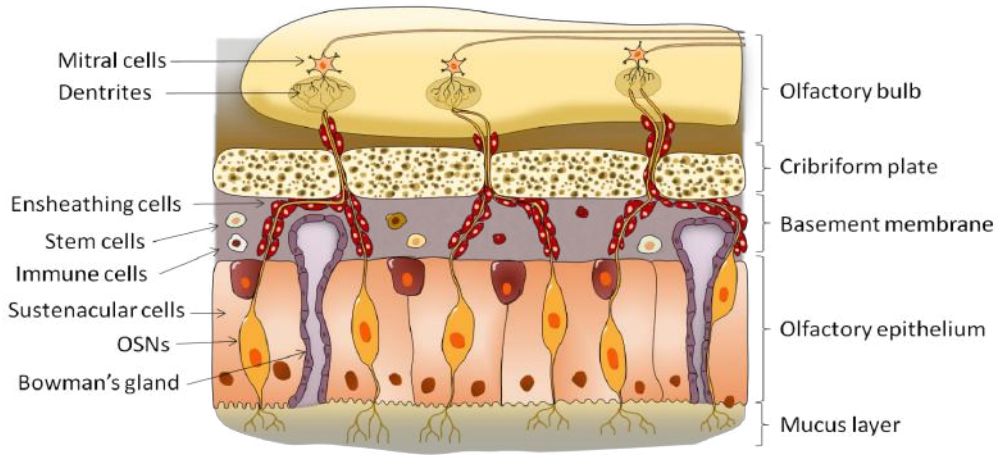
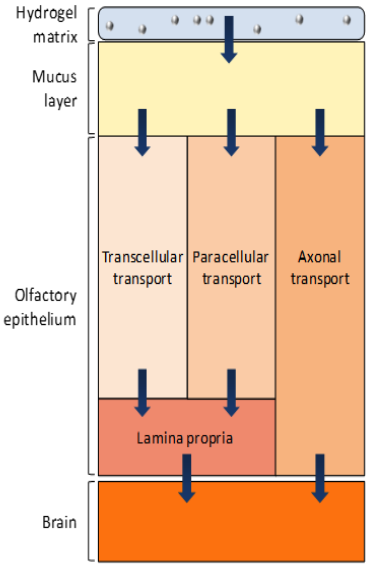
Treatment of CNS Disorders

- **N2B delivery** of medications for CNS disorders as an alternative to intravenous delivery.
- **N2B-patch:** Application of an in situ forming hydrogel containing drug loaded NPs to the olfactory epithelium via an endoscopic catheter.
- **Multiple pathways** to the brain through the olfactory region
- Very **complex problem** requiring contributions from many disciplines

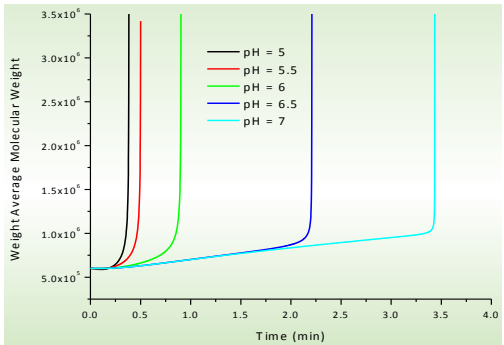




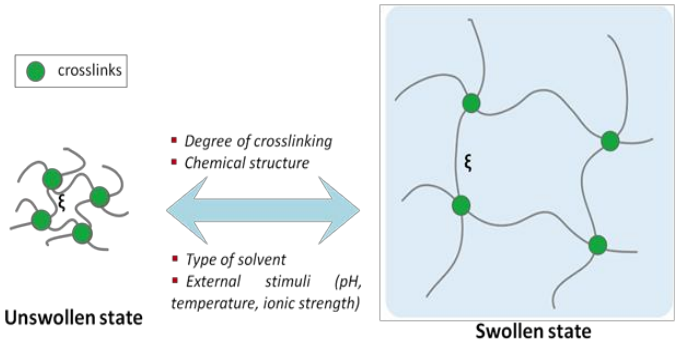


Physical Problem	Models
Hydrogel Kinetics Rheology	✓ Crosslinking and gelation kinetics (H_1) ✓ Hydrogel swelling and shrinkage (H_2) ✓ Rheological model (H_3)
Applicator Flow, Film Formation and Adhesion	✓ Reactive polymer flow in the applicator (F_1) ✓ Film formation, deposition and spreading (F_2) ✓ Hydrogel adhesion and stability (F_3)
Drug Release from Embedded NPs in the Hydrogel Matrix	✓ Particle transport in the hydrogel matrix (T_1) ✓ Drug release from embedded particles (T_2) ✓ Drug release from the hydrogel matrix to mucosa (T_3)
Drug Transfer through the Mucosa	✓ Drug transport through the olfactory mucosa (D_1) ✓ Drug transport through the olfactory epithelial cells (D_2)
Model Integration	✓ Integration of the various models

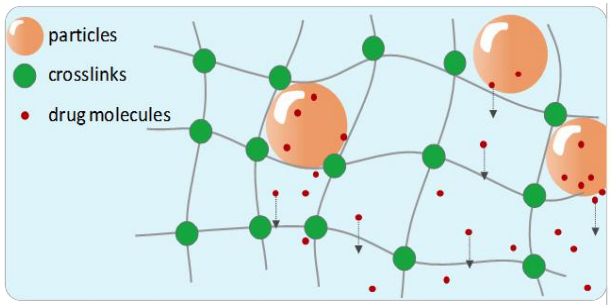
Many and Different Models!



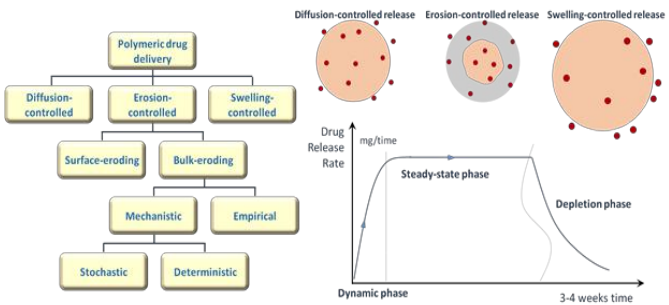
Simulation of gelation kinetics



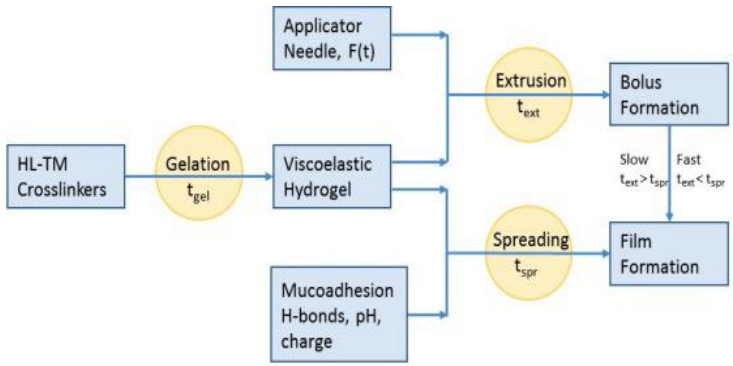
Hydrogel swelling and shrinkage



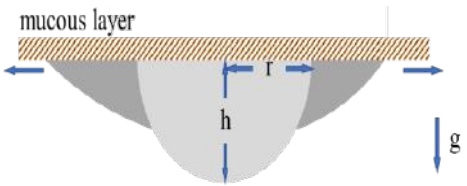
Drug release from the hydrogel to mucosa



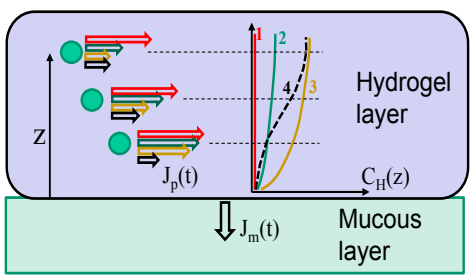
Drug release from embedded particles



Key mechanisms of hydrogel film formation



HA droplet spreading

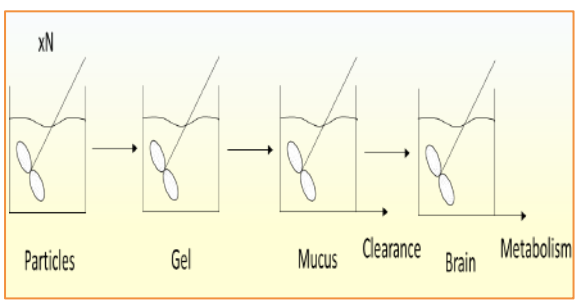


$$J_p = f\left(R(t), C(r,t), C_H(z,t)\right)$$

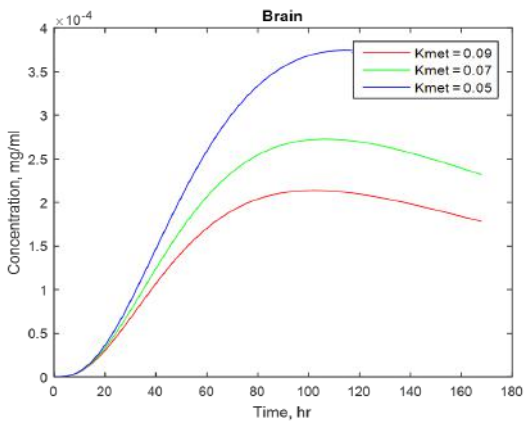
R(t) ⟹ Flux J_p

$$J_m = f\left(t, \frac{dC_H}{dz}(0,t)\right)$$

HA droplet spreading over the olfactory mucous surface



N2B Drug Transport Mechanism and drug release profile



Vocabulary in N2B-patch Modelling

Chemical Engineering

Fluid Dynamics, Rheology, Mixing, Interfacial mechanics, Mass transfer, Kinetics, Gel dynamics

Pharmacology & Biology

Toxicity, Drug Delivery, Brain penetration, Drug load, Effective dose, Drug deactivation

Medical & End-user

Effectiveness, user-friendliness, Simplicity, ease-to-use, cost, long-term effects

Miss-match and confusion in vocabulary and language !

"Languages":
Chemical Engineering
Bio-medical Engineering
Pharmacology
Biology
Materials Science
Medical
Patients

Ontological Classification

Modelling Outline in N2B-patch

Following directives of H2020 LEIT-NMBP Programme Materials and Nanotechnology Projects