

# Student Research Group

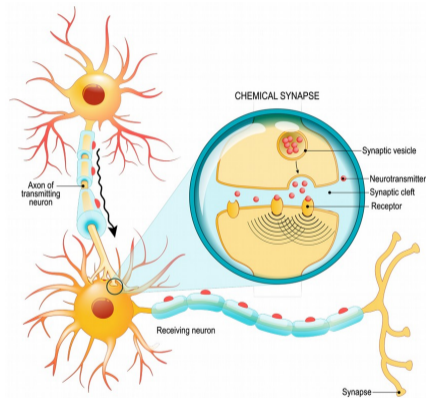
## Estimating pH-dependent rates by machine learning techniques

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Modeling and Simulation of Complex Processes  
Computational Molecular Design

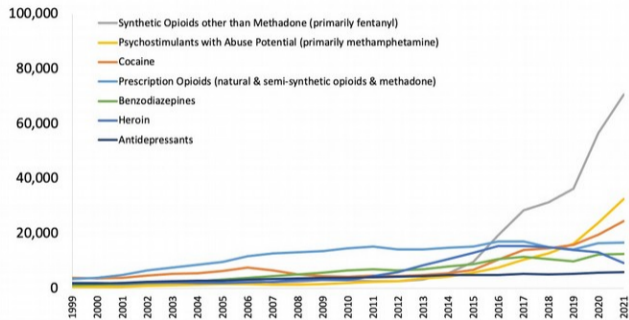
12 May 2023

- Opioid receptors are responsible for regulating the human body's response to most hormones, neurotransmitters, drugs, and are involved in sensory perception of vision, taste, and olfaction.
- There exist three classes of opioid receptors:  $\mu$ ,  $\delta$  and  $\kappa$ .
- Opioid receptors are located in both peripheral and central nervous system.
- The  $\mu$ -opioid receptors are the most important as are involved in pain relief and can be activated by pharmaceutical drugs.



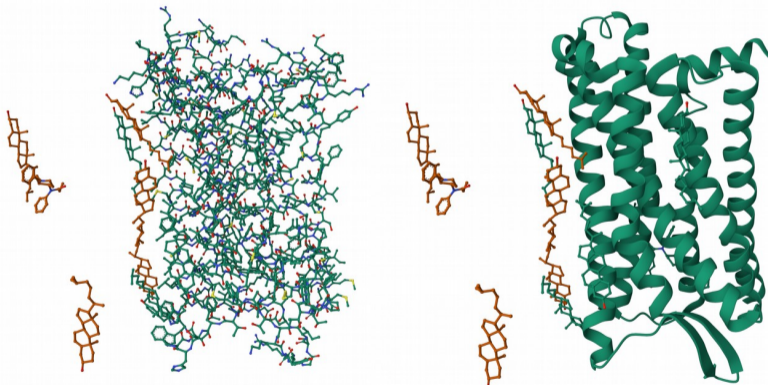
- Opioids are responsible of undesirable side effects.
- Opioid misuse and addiction is a major public health crisis.
- The number of drug overdose deaths increased by nearly 30% from 2019 to 2020 and has quintupled since 1999.

Figure 2. National Drug-Involved Overdose Deaths\*, Number Among All Ages, 1999-2021



\*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999–2021 on CDC WONDER Online Database, released 1/2023.

Fentanyl – bound mu – opioid receptor – Gi complex  
ball and stick representation (left); cartoon representation (right)



- The dynamics of ligand-receptor systems are influenced by the acidity of the cellular membranes.
- A pH change involves quantum mechanical (QM) mechanisms: bond breaking (deprotonation) and bond formation (protonation).
- QM simulations are impractical for large molecular systems.

Video

- The dynamics of a ligand-receptor system is "complex", in the sense that it exhibits a chaotic and non-linear behavior.
- We can produce "trajectories" by means of computer simulations, but the analysis of trajectories makes use of tools based on probability theory and statistics.

- ① Theory: Hamiltonian Dynamics, Langevin Dynamics, Probability Theory.
- ② Methods: tools to produce and analyze trajectories. This will require the use of Python, please install Anaconda (see instructions in Exercise 1).
- ③ Research objective: use of Machine Learning techniques to estimate rates.

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