Quantum Mechanical Simulation of Fluorine-Containing Biomolecules

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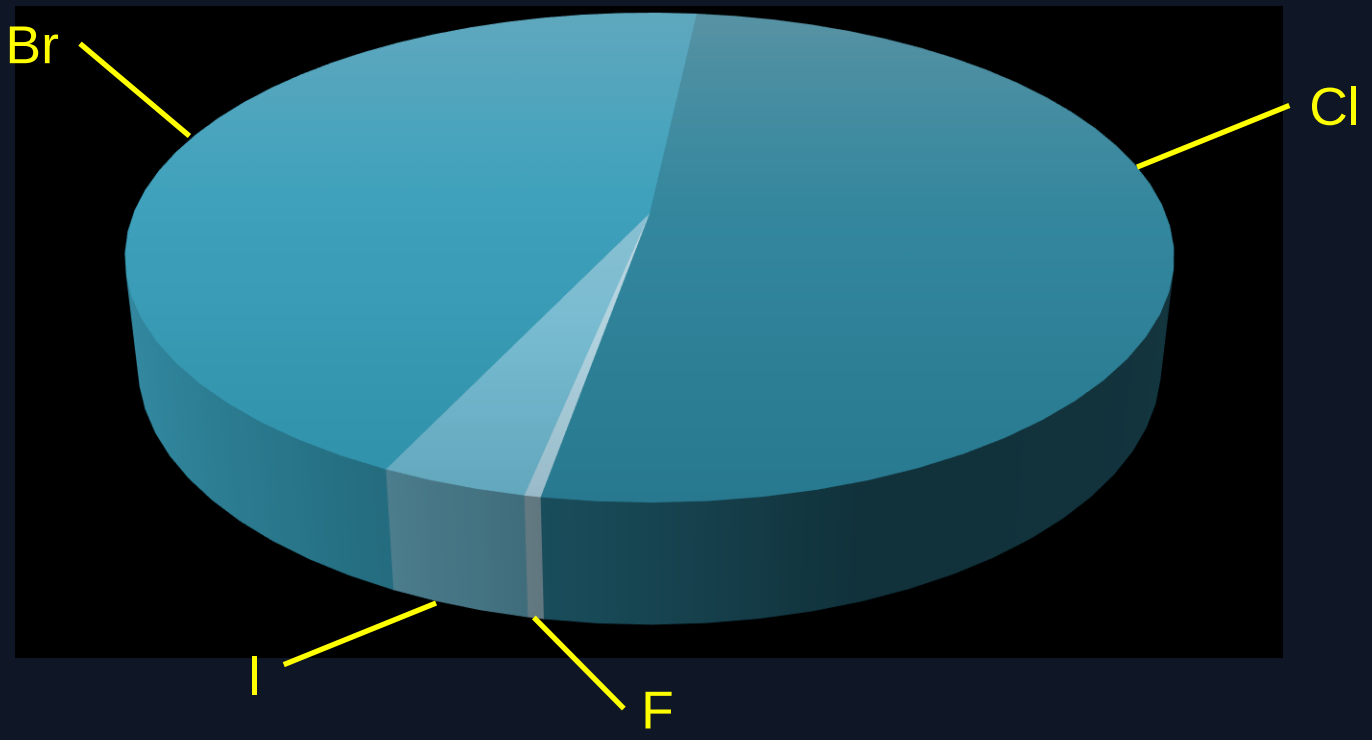
Fluorine plays almost no role in biosphere

There are about 4700 naturally occurring organohalogen compounds



Chlorine-containing: 2400
Bromine-containing: 2100
Iodine-containing: 180
Fluorine-containing: 20

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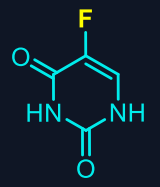
G. W. Gribble, *J. Chem. Educ.* **2004**, *81*, 1441; G. W. Gribble, *Naturally Occurring Organohalogen Compounds-A Comprehensive Update* **2010**, 1; M. C. Walker, M. C. Y. Chang, *Chem. Soc. Rev.* **2014**, *43*, 6527; L. Wang, X. Zhou, M. Fredimoses, S. Liao, Y. Liu, *RSC Advances* **2014**, *4*, 57350. K. K. J. Chan, D. O'Hagan, *in Methods Enzymol.*, 516, Academic Press, **2012**, 219.

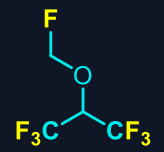
Fluorine is commonly used in bioactive molecules

To date, 20% of drugs and 30% of agrochemicals contain fluorine.

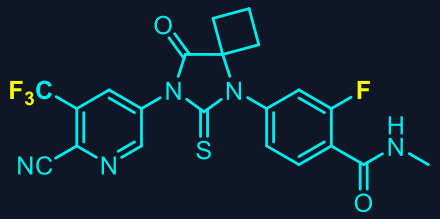


Fluorouracil
(5-FU, antitumor)

Isoflurane
(anesthetic)

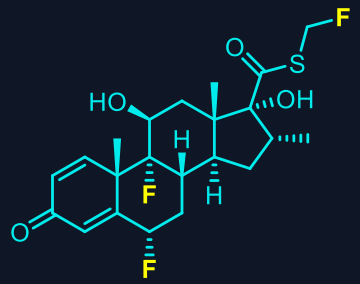


Sevoflurane
(anesthetic)

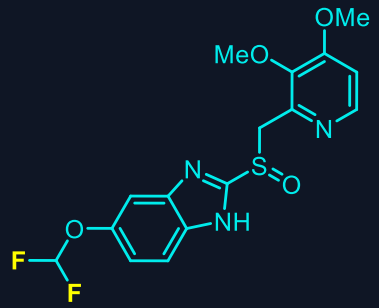


Erleada
(nonsteroidal antiandrogen)

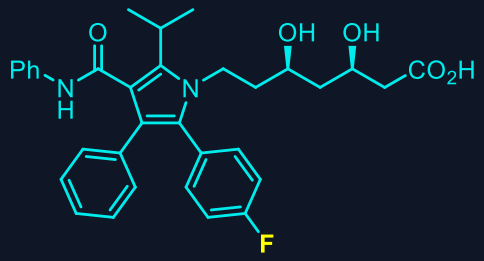
Efavirenz
(HIV-RT inhibitor)



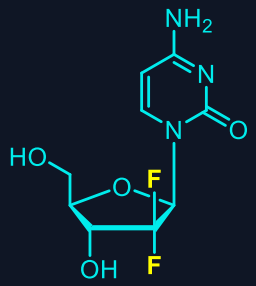
Fluticasone
(anti-inflammatory)



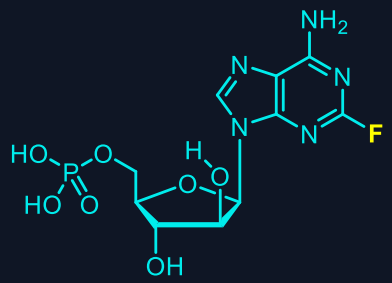
Pantoprazole
(treating stomach ulcers)



Lipitor
(treating high cholesterol)



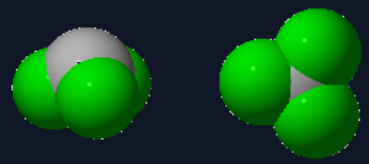
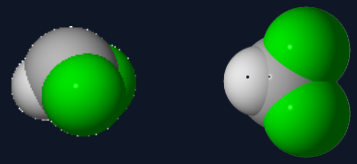
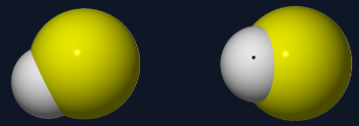
Gemcitabine
(chemotherapy drug)

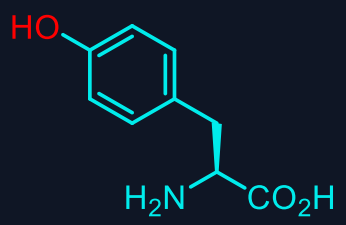


Fludarabine
(chemotherapy drug)

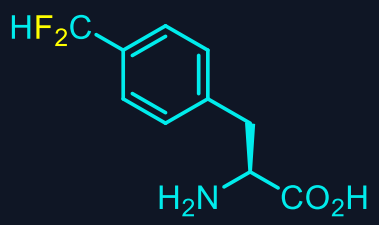
C. Ni, J. Hu, *Synlett* **2011,** 770-782, G. K. S. Prakash, **F. Wang**, *Chimica Oggi,* **2012**, *30*, No. 5.

Fluorine-containing moieties can be used to mimic other functional groups

substituent	electronegativity	*space filling model*
$-CF_3$ (trifluoromethyl)	3.46	
$-CF_2H$ (diifluoromethyl)	3.00	
–SH (thiol)	2.32	
–OH (hydroxyl)	3.51	
$-CH_3$ (methyl)	2.27	



Tyrosine
(naturally occurring amino acid)



Fluorinated tyrosine mimic
(fluorine-containing amino acid)

Quantum Mechanical Simulation of Fluorine-Containing Biomolecules

- Goals
  - Compute the physicochemical properties of fluorine-substituted amino acids using Density Functional Theory (DFT)
  - Compare these simulations to experimental results obtained in the lab
  - Create a model to predict the properties and interactions of these molecules

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Quantum Mechanical Simulation of Fluorine-Containing Biomolecules

- Timeframe
  - Start date: October 1st, 2023
  - End date: April 1st, 2024

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Quantum Mechanical Simulation of Fluorine-Containing Biomolecules

- What I hope to learn
  - Become familiar with the HPC system
  - Expand knowledge of Density Functional Theory, specifically within key molecules of a biological system
  - Gain insights into how fluorine can function in an amino acid to confer desired properties

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Quantum Mechanical Simulation of Fluorine-Containing Biomolecules

- Goals for Next Month
  - Finish running simulations on basic models to become familiar with the calculations and analysis
  - Begin performing simulations and calculations on fluorinated amino acids
  - Begin obtaining experimental data for comparison

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- Help needed (if any)
  - N/A