SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

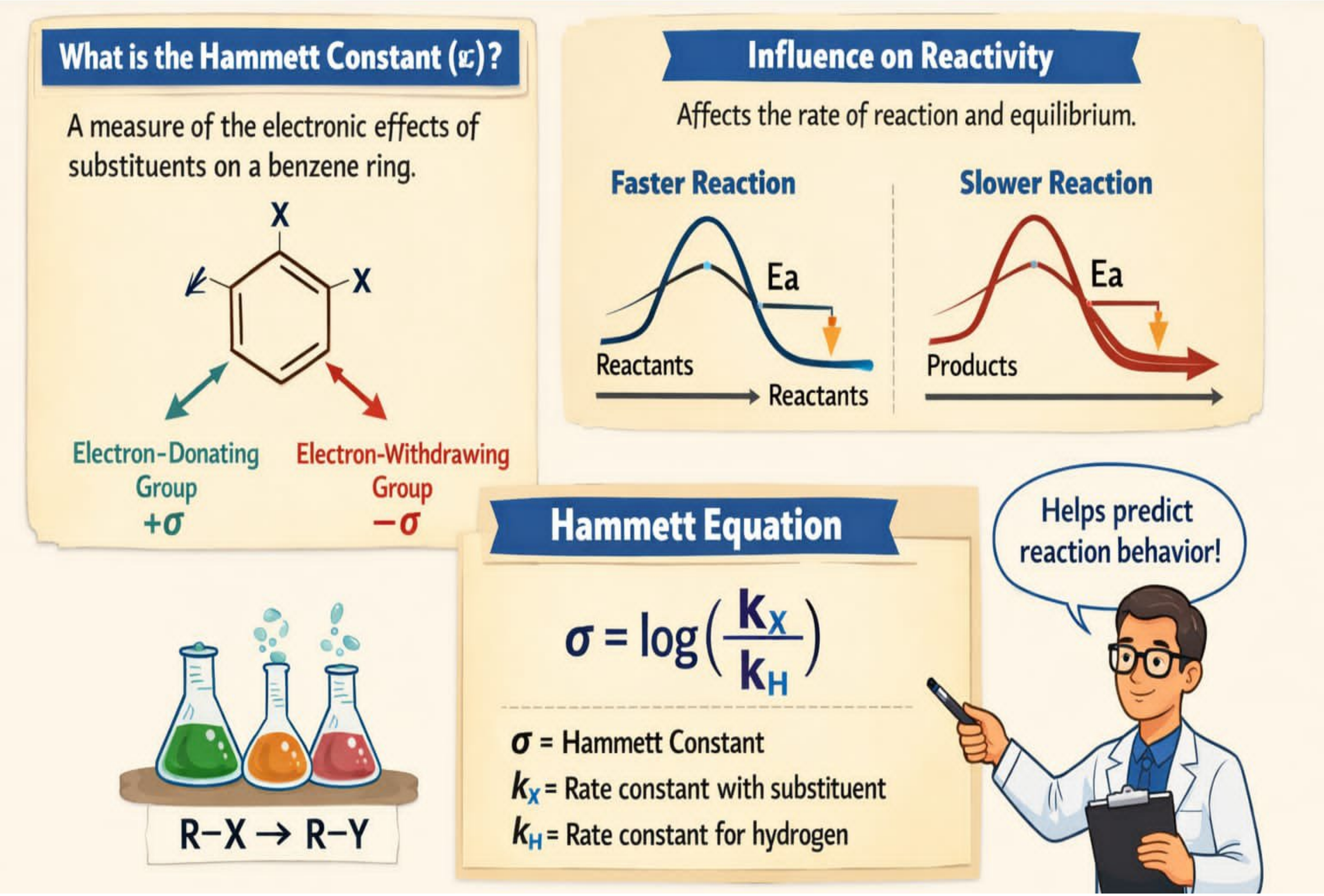
Affiliated To The Tamil Nadu Dr. MGR Medical University, Chennai
Approved by Pharmacy Council of India, New Delhi.
Coimbatore -641035

COURSE NAME : COMPUTER AIDED DRUG DESIGN(BP 807 ET)

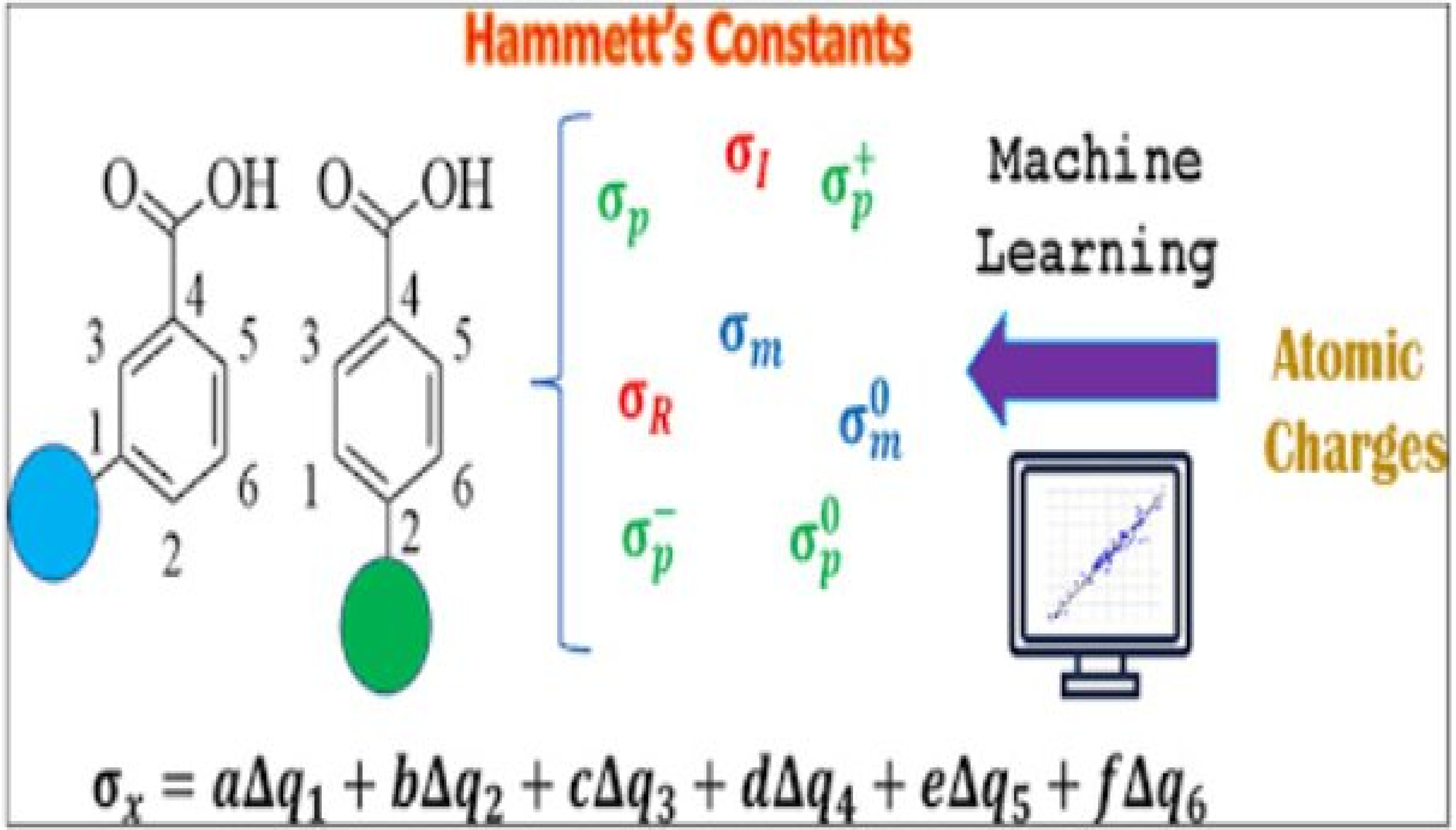
VIII SEM / IV YEAR

TOPIC : HAMMETT CONSTANT

INTRODUCTION TO HAMMETT CONSTANT

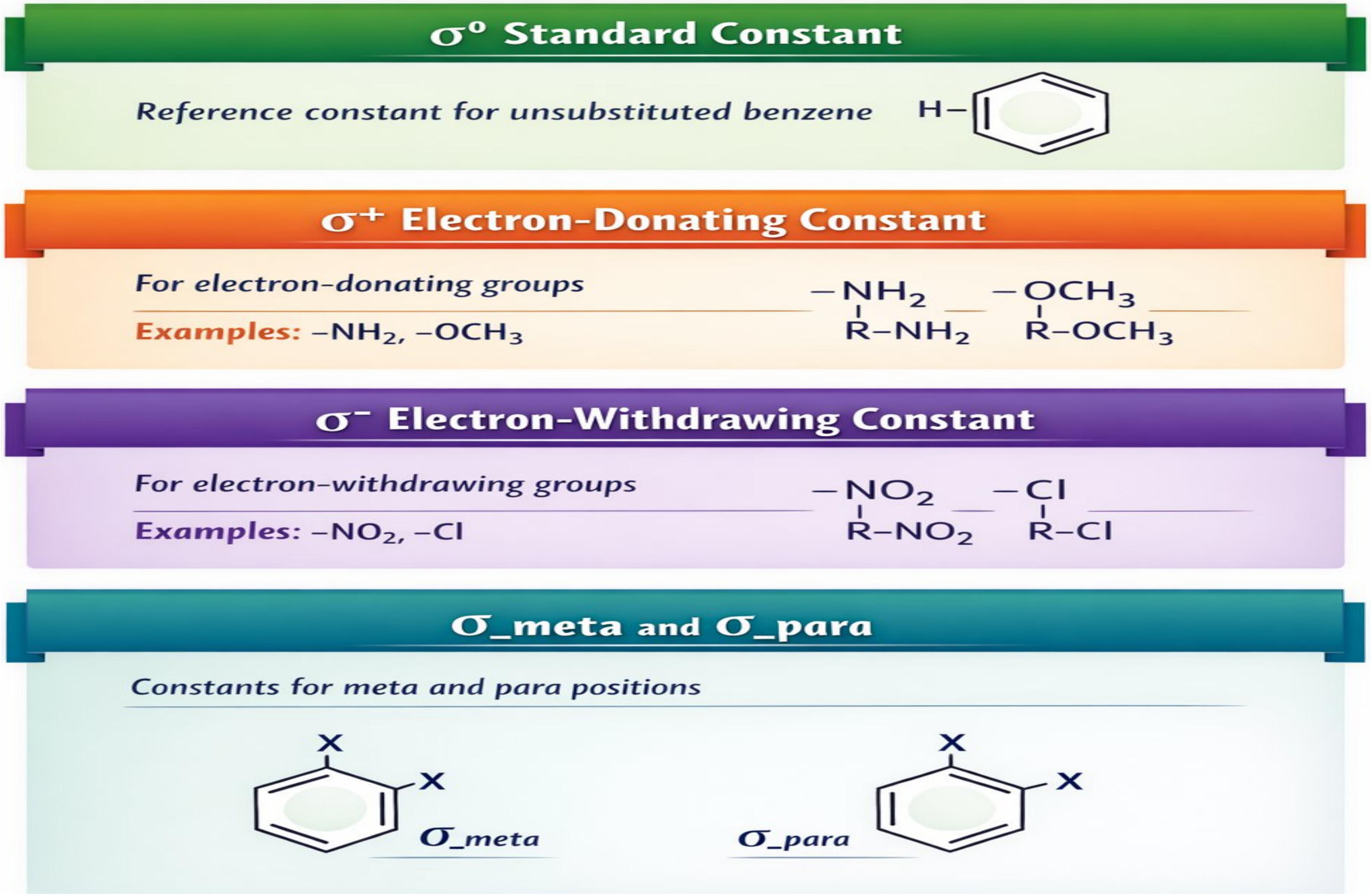


CONT...

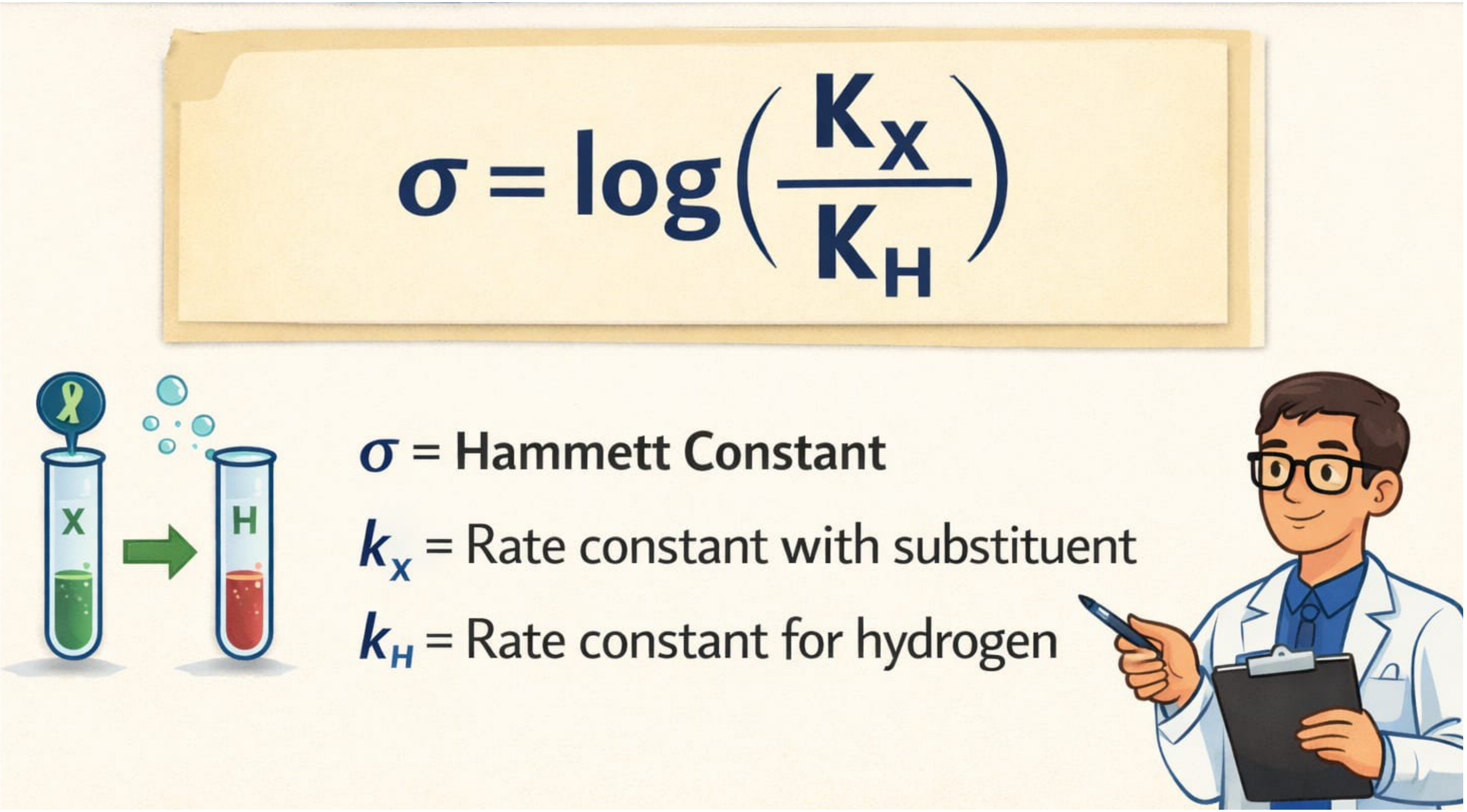


Hammett's Constants
O
OH
4
3
5
1
6
2
σ_p
σ_I
σ_p^+
σ_m
σ_R
σ_m^0
σ_p^-
σ_p^0
Machine Learning
Atomic Charges
$\sigma_x = a\Delta q_1 + b\Delta q_2 + c\Delta q_3 + d\Delta q_4 + e\Delta q_5 + f\Delta q_6$

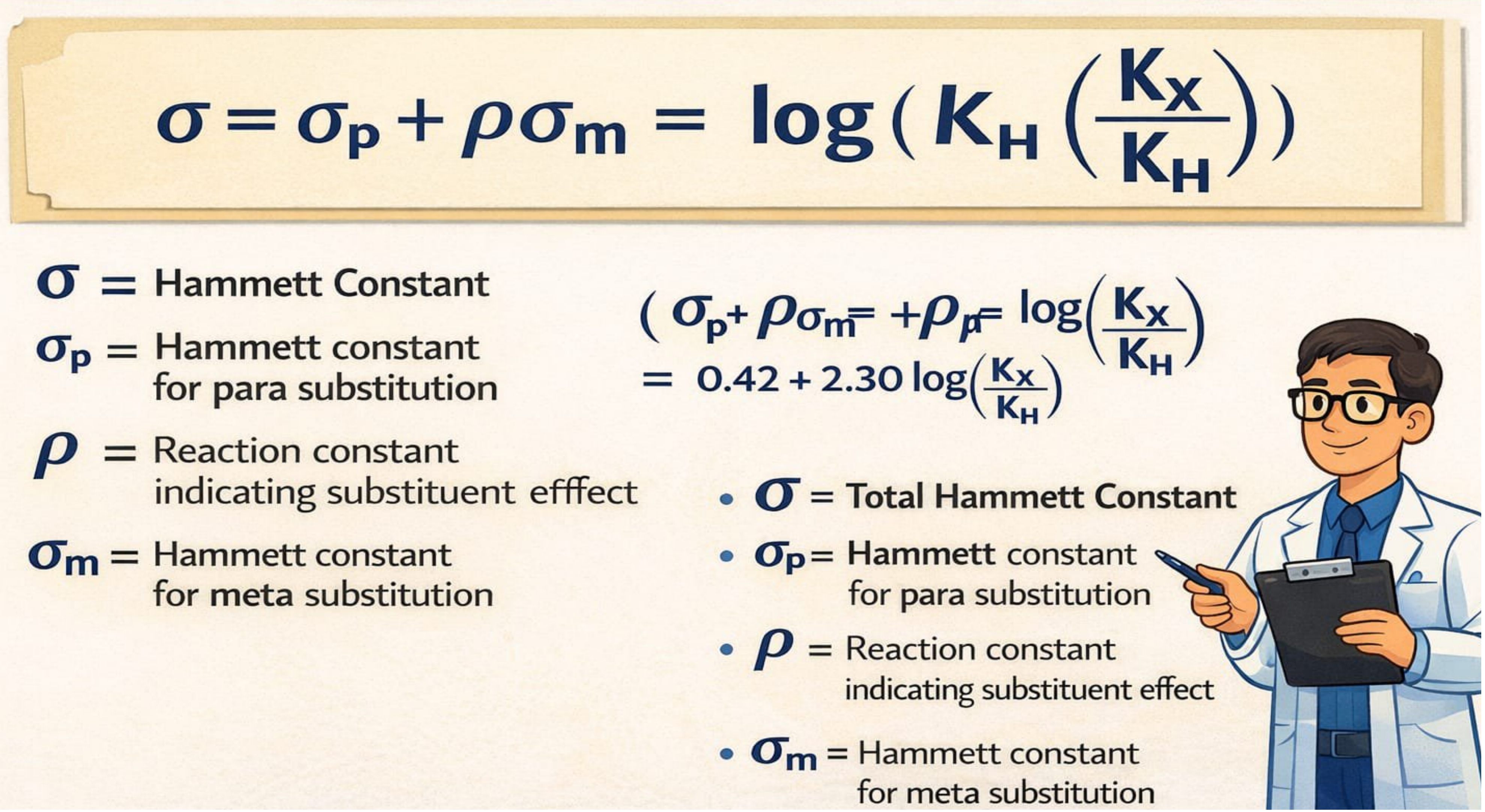
TYPES OF HAMMETT CONSTANT



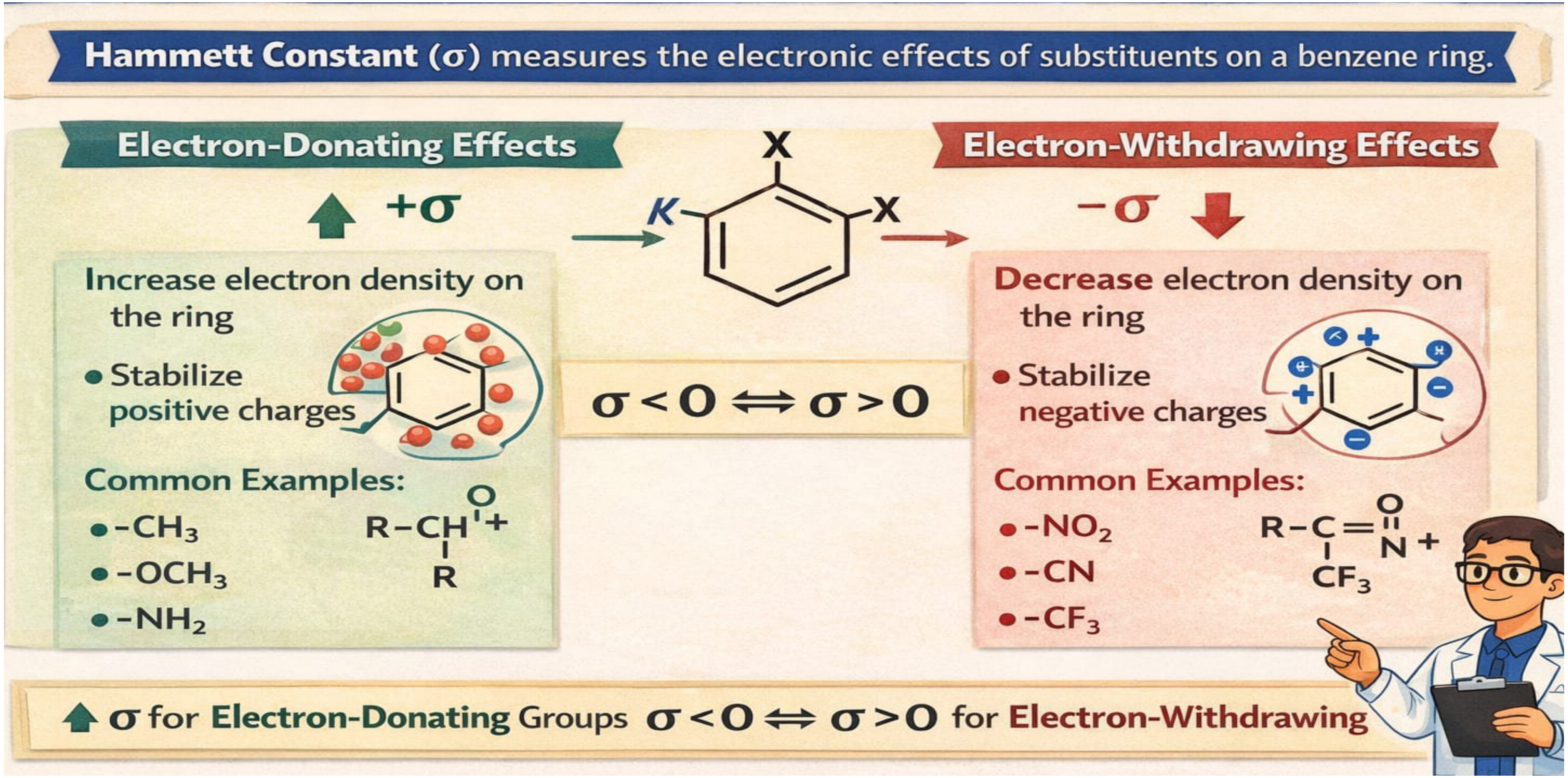
HAMMETT EQUATION



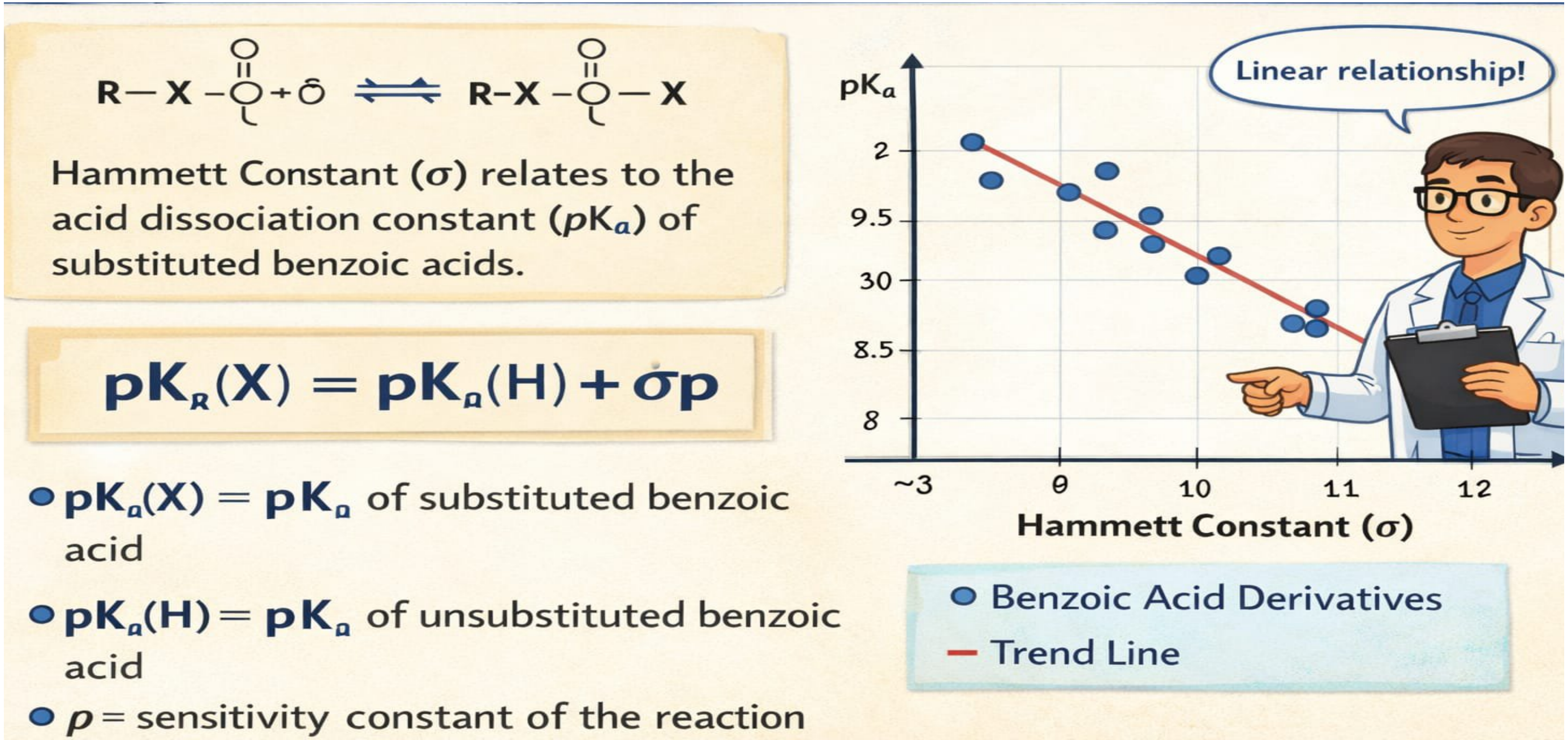
MODIFIED HAMMETT EQUATION



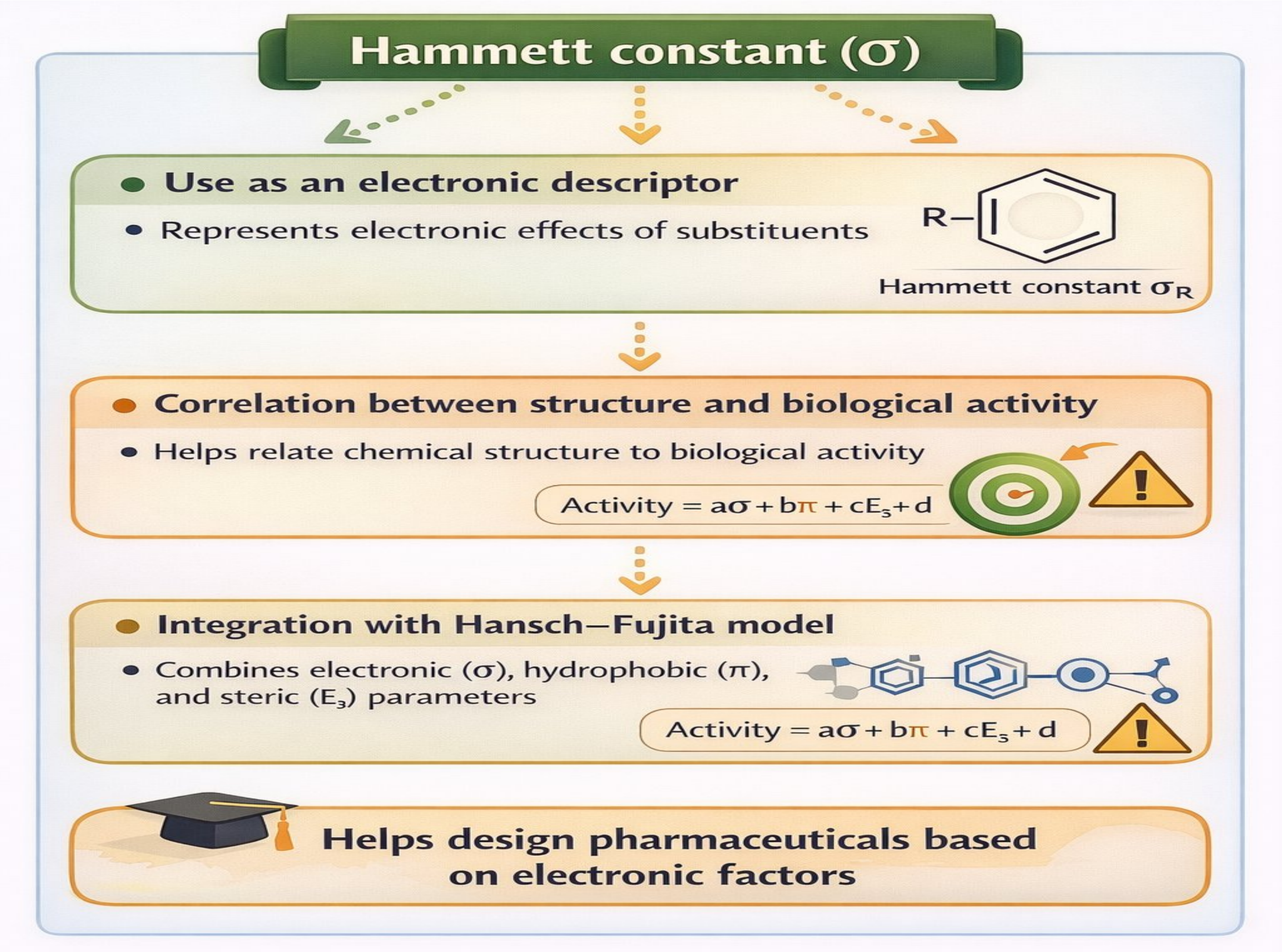
ELECTRONIC EFFECT REPRESENT OF HAMMET CONSTANT



CORRELATION OF HAMMETT CONSTANT WITH PKa



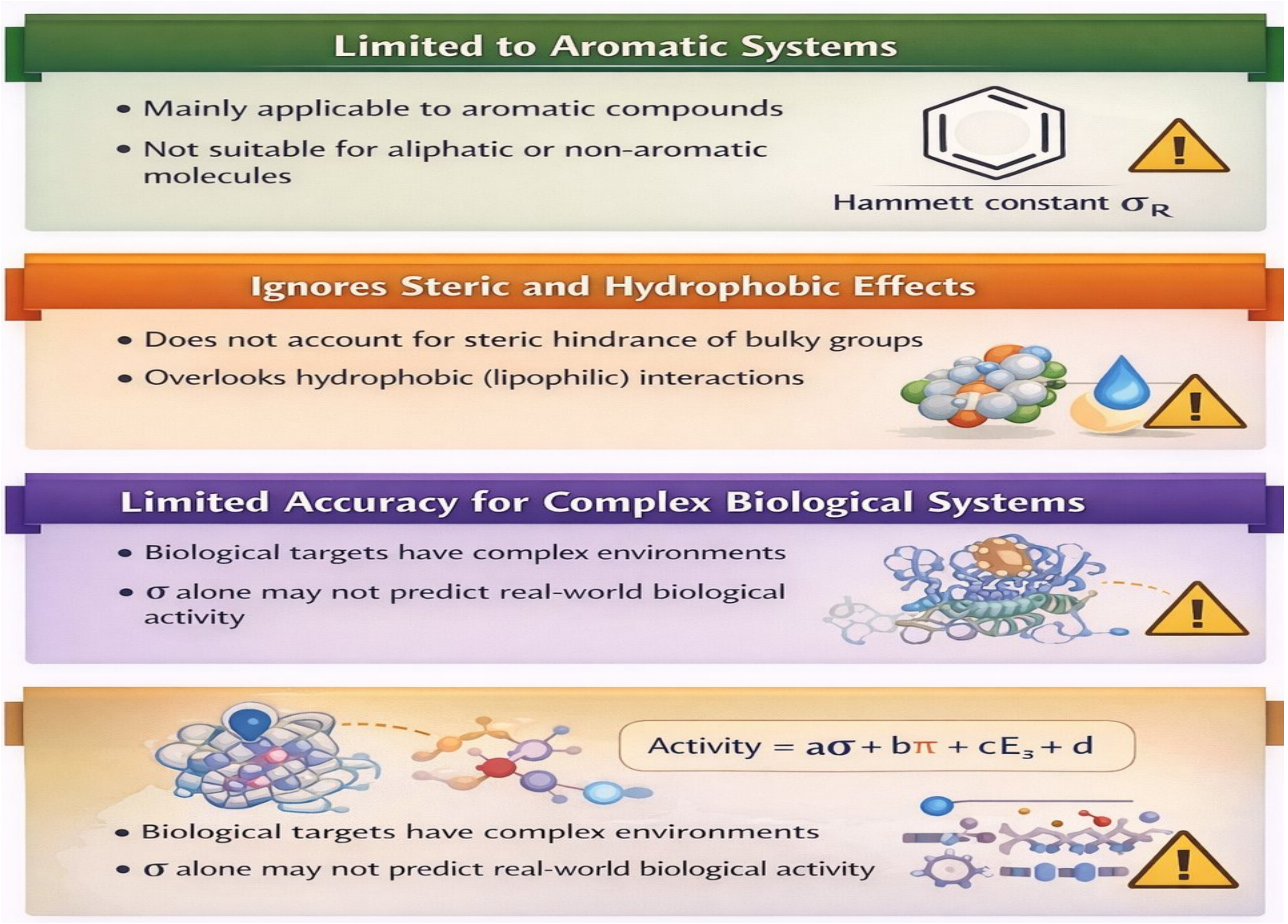
HAMMETT CONSTANT IN QSAR :



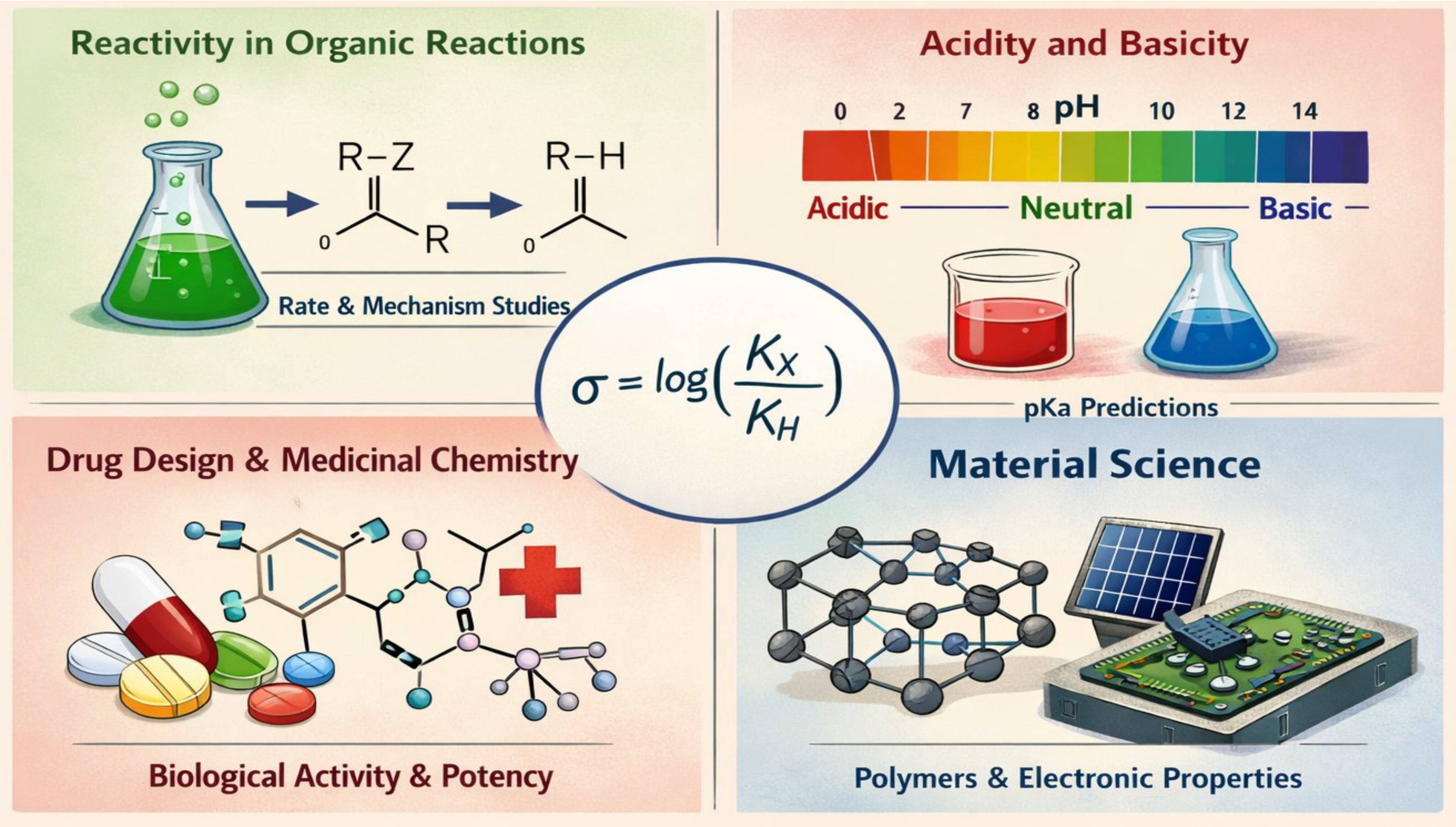
HAMMETT SUBSTITUENTS CONSTANT

Substituent	σ *para*	σ *meta*	σ^{+*}	σ^{-*}
$N{\equiv}N^{\oplus}$	1.91	1.76	—	3.43
$(CH_3)_3N^{\oplus}$	0.82	0.88	0.41	0.77
NO_2	0.78	0.71	0.79	1.27
$C{\equiv}N$	0.66	0.56	0.66	1.00
CF_3	0.54	0.43	0.61	0.65
CO_2H	0.45	0.37	0.42	0.77
$CH{=}O$	0.42	0.35	0.73	1.03
Cl	0.23	0.39	0.15	0.25
Br	0.23	0.37	0.11	0.19
$C{\equiv}CH$	0.23	0.21	0.18	0.53
I	0.18	0.35	0.14	0.27

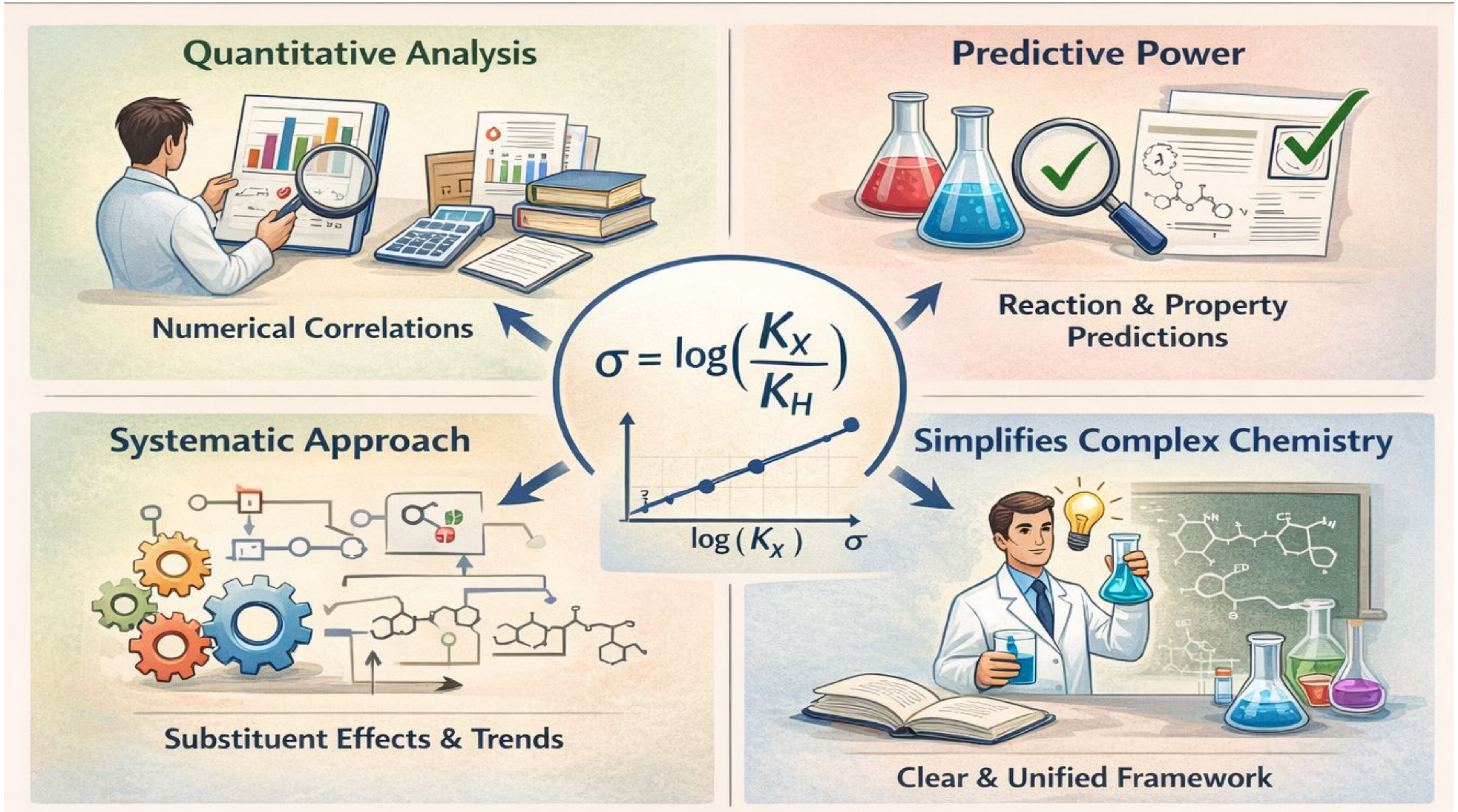
LIMITATIONS OF HAMMETT CONSTANT



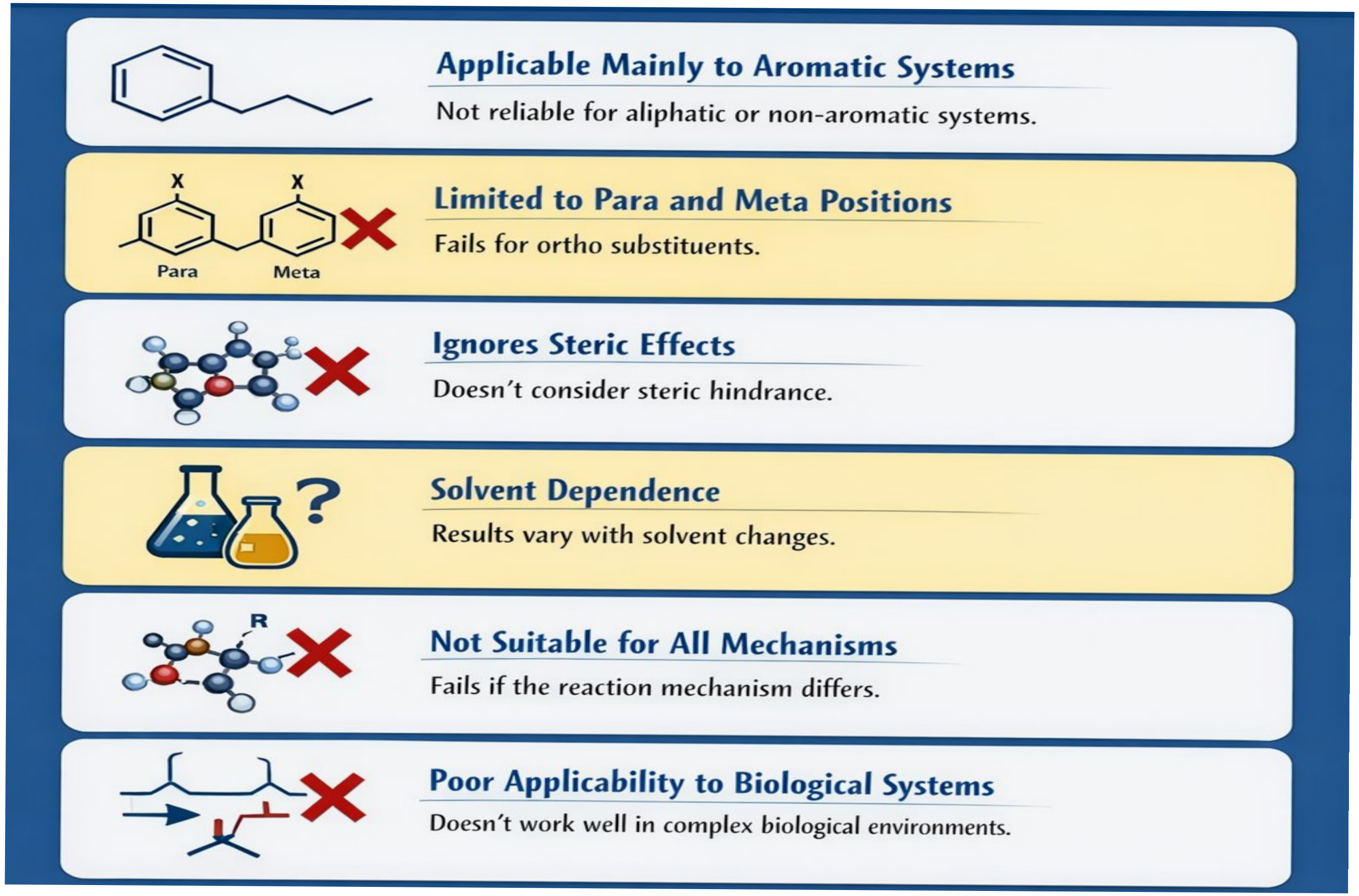
APPLICATIONS OF HAMMETT CONSTANT



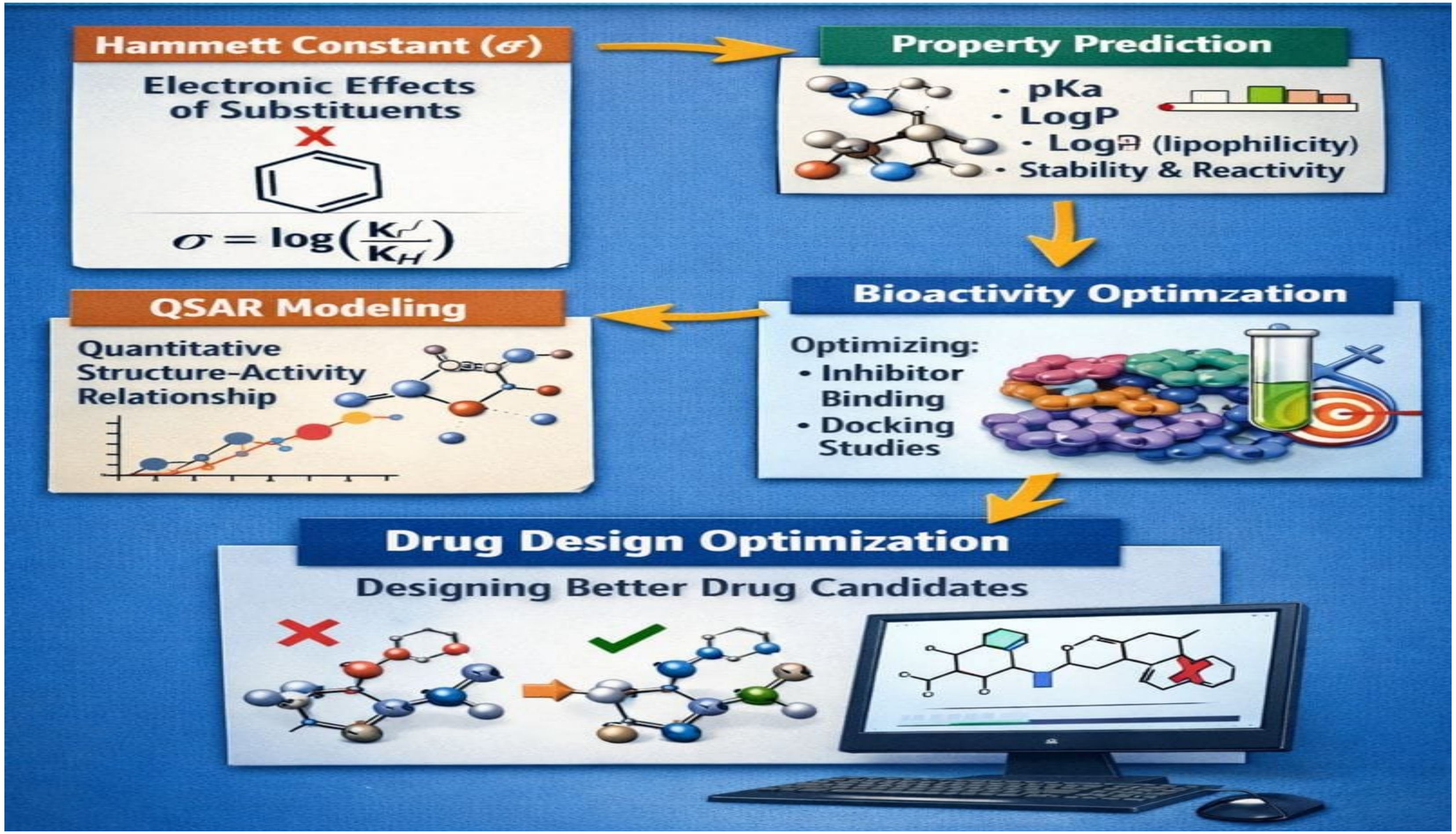
ADVANTAGES OF HAMMETT CONSTANT



DISADVANTAGES OF HAMMETT CONSTANT



ROLE OF HAMMETT CONSTANT IN CADD



ASSESMENTS

1)Which of the following is a correct form of the Hammett equation?

A) $\log(k/k_0) = \rho\sigma$

B) pKa = log(C)

C) $\Delta G = -RT \ln K$

D) $\log P = \Sigma\pi$

2)In drug design, the Hammett constant is often correlated with:

A) Drug solubility only

B) Drug reactivity, metabolism, or binding affinity

C) Molecular weight

D) Drug color

3)A substituent with a positive σ value is generally:

A) Electron-donating

B) Electron-withdrawing

C) Neutral

D) Non-polar

4) The Hammett constant (σ) is primarily used to describe:

A) Lipophilicity of a molecule

B) Electronic effects of substituents on aromatic rings

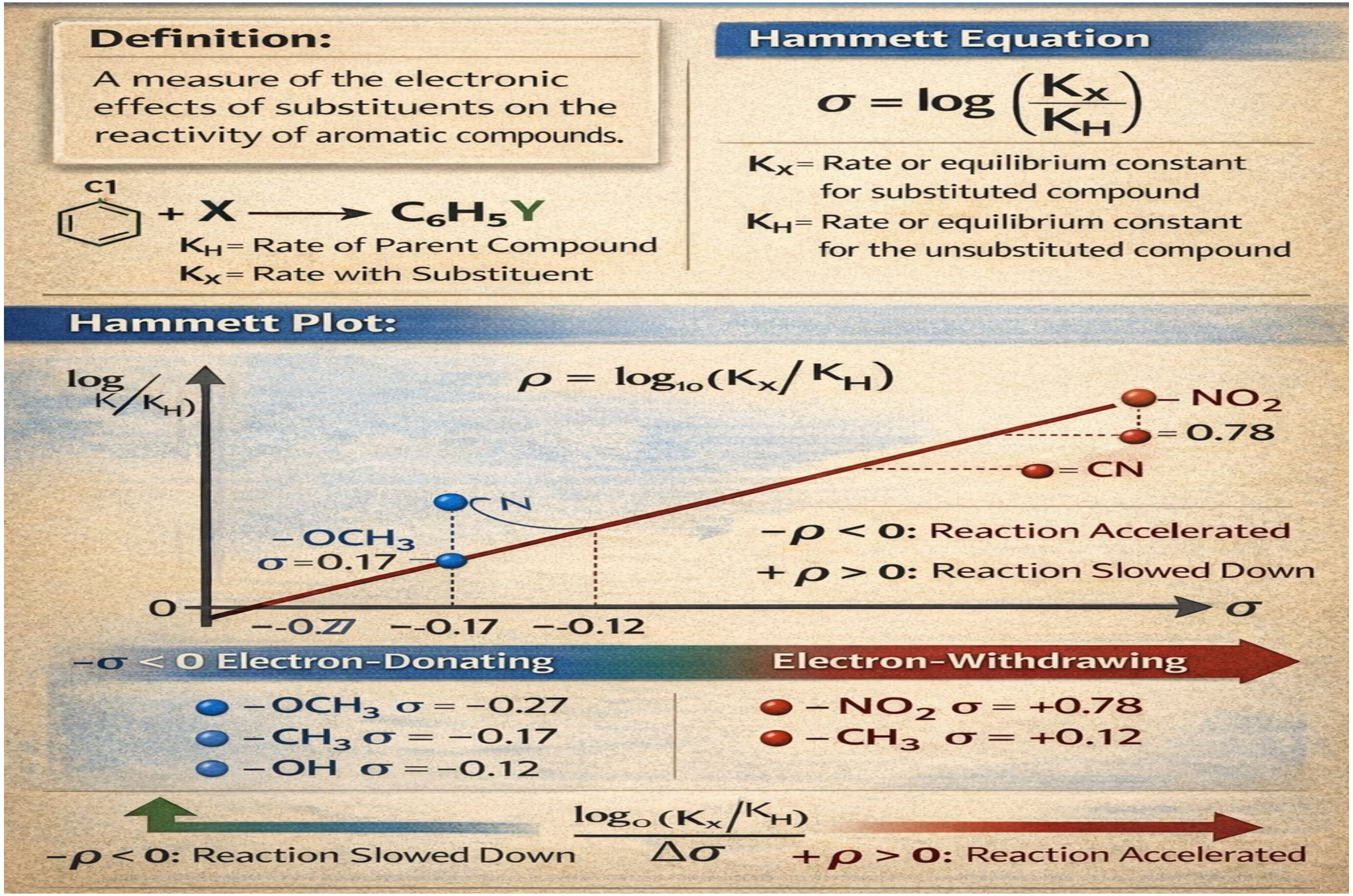
C) Molecular weight

D) Hydrogen bonding potential

5) True / False:

A negative Hammett constant ($\sigma < 0$) indicates an electron-donating substitu

SUMMARY


Definition:
A measure of the electronic effects of substituents on the reactivity of aromatic compounds.
C1
+ X ⟶ C6H5Y
KH = Rate of Parent Compound
KX = Rate with Substituent
Hammett Equation
σ = log (KX / KH)
KX = Rate or equilibrium constant for substituted compound
KH = Rate or equilibrium constant for the unsubstituted compound
Hammett Plot:
ρ = log10(KX/KH)
– NO2
= 0.78
= CN
N
– OCH3
σ = 0.17
−ρ < 0: Reaction Accelerated
+ ρ > 0: Reaction Slowed Down
0
σ
−σ < 0 Electron-Donating
Electron-Withdrawing
– OCH3 σ = −0.27
– CH3 σ = −0.17
– OH σ = −0.12
– NO2 σ = +0.78
– CH3 σ = +0.12
−ρ < 0: Reaction Slowed Down
Δσ
+ ρ > 0: Reaction Accelerated

REFERENCE

1) Hansch, C. & Leo, A. — Substituent Constants for Correlation Analysis in Chemistry and Biology

2) Hansch, C. (1971). "Quantitative Structure-Activity Relationships in Drug Design" — in Drug Design, Volume 1 (E.J. Ariëns, Ed.)

3)Martin, Y.C. — Quantitative Drug Design: A Critical Introduction


Thank You!