

The Effect of Functionalization on Cation-Pi interaction

By: Dhyey Ray

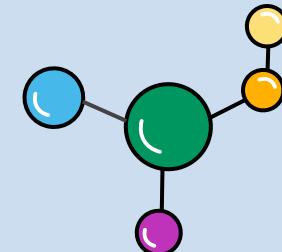
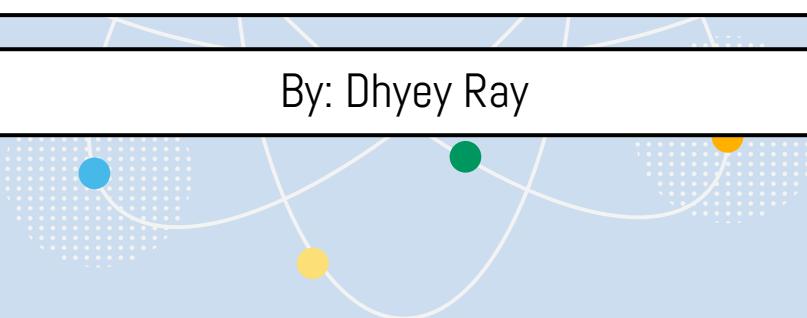
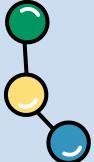




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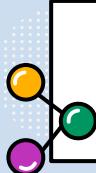
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Background

Kumar Paper and Experimental Goals



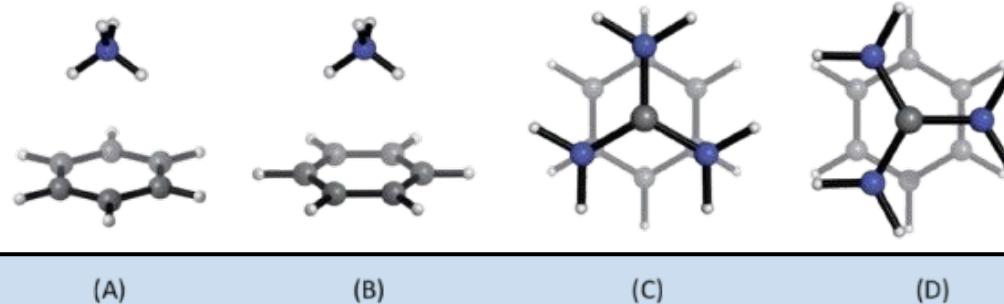
Cation–p interactions in protein–ligand binding: theory and data-mining reveal different roles for lysine and arginine

Goal:

- Determine the interaction energy between benzene (model aromatic system) and the cationic amino acids lysine, arginine, and histidine.

Methods:

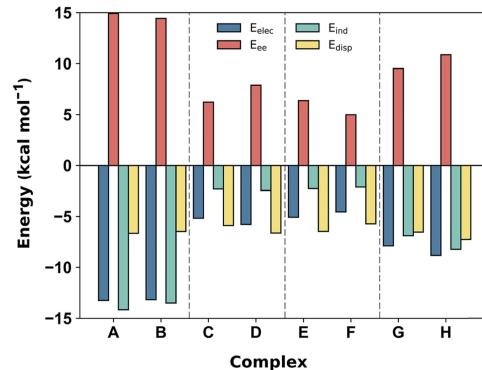
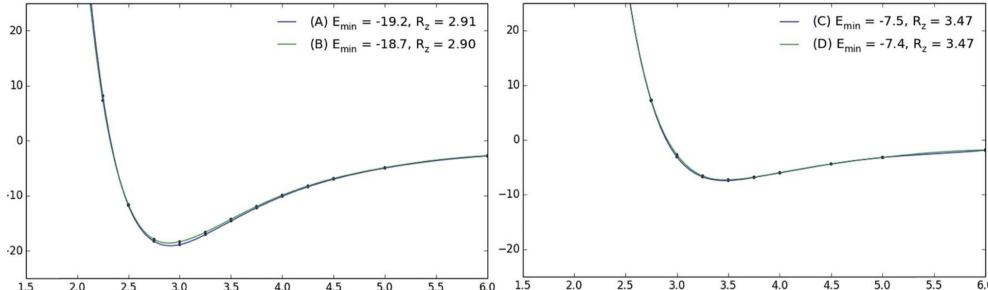
- Geometry Selection: Performed on benzene and cationic groups using MP2.
- Energy Calculations: Ground state interaction energies calculated using DLPNO-CCSD(T) in ORCA, with systematic variation of the cationic group position relative to benzene.
- Energy Decomposition: SAPT (via PSI4) used to break down interaction energies into components: exchange, induction, dispersion, and electrostatics.
- Solvent Effects: Interaction energies recalculated using dielectric constants to model solvent effects.



Results

Results:

1. In the gas phase, lysine shows the strongest interaction with benzene due to dominant electrostatic forces than arginine's interaction, which is a balance of electrostatics and dispersion forces
2. Solvent effects (e.g., higher dielectric) weaken lysine's electrostatic interaction significantly, making it less favorable.
3. Empirical Protein Data Bank (PDB) data supports this trend, with arginine being more frequently involved in cation– π interactions than lysine.



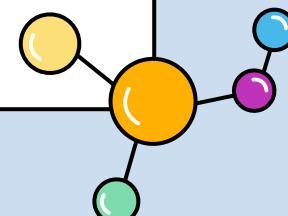
Our Experimental Goal

Let's see how functionalization of the benzene ring affects lysine-benzene interaction energy and how DFT and DLPNO-CCSD(T) compare in the analysis.

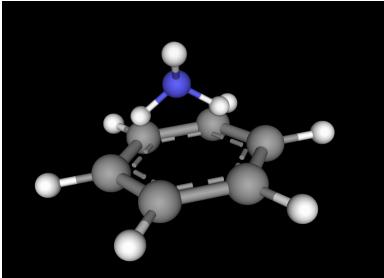
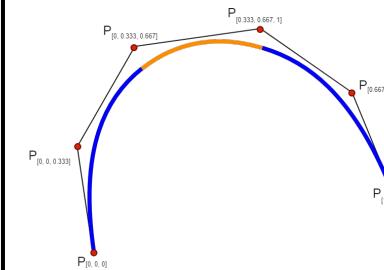
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Methodology

Python!!!

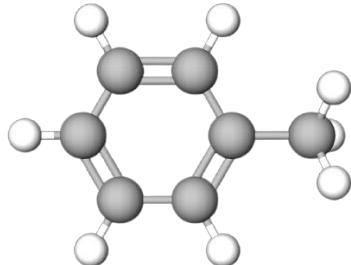


Steps

Optimized Structures	Preparation	Quantum Fun	Data Analysis
 National Institute of Standards and Technology U.S. Department of Commerce		$\hat{H} \Psi = E \Psi$ <p>Hamiltonian Operator (Energy operator) Energy eigenvalue</p>	
Obtain the optimized structure of the aromatic system from CCCBDB	Perform necessary rotations to align aromatic system and NH3 so that NH3 is in the center and atom aligned.	Run the optimization by lowering NH3 towards ring on Orca using DLPNO-CCSD(T) and DFT on PSI-4.	Create Graphs and find minima using Cubic Spline Interpolation.

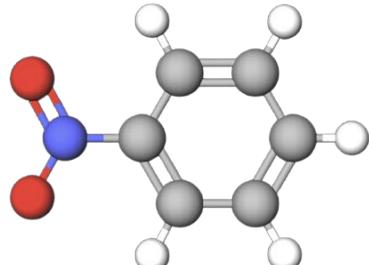
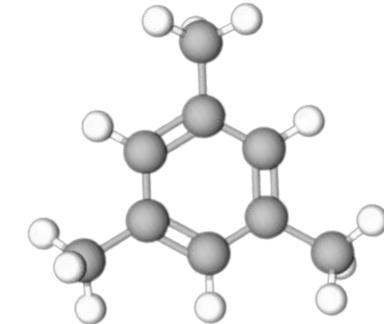


Meet our Aromatic Systems and Predictions



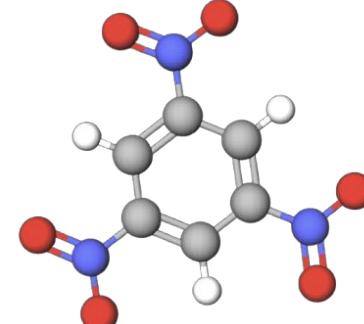
Toluene

I,3,5
Trimethyl
Benzene

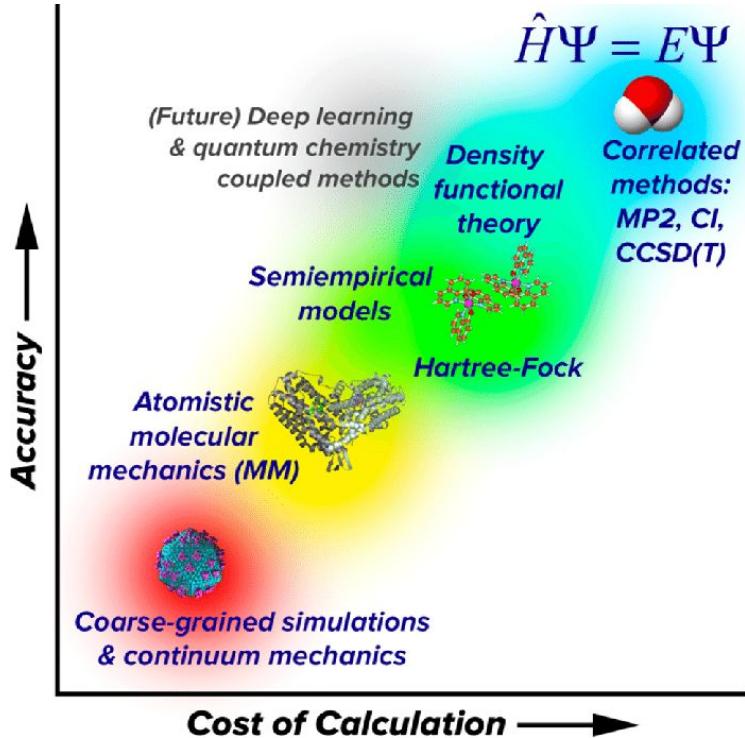


Nitrobenzene

I,3,5
Trinitro
Benzene



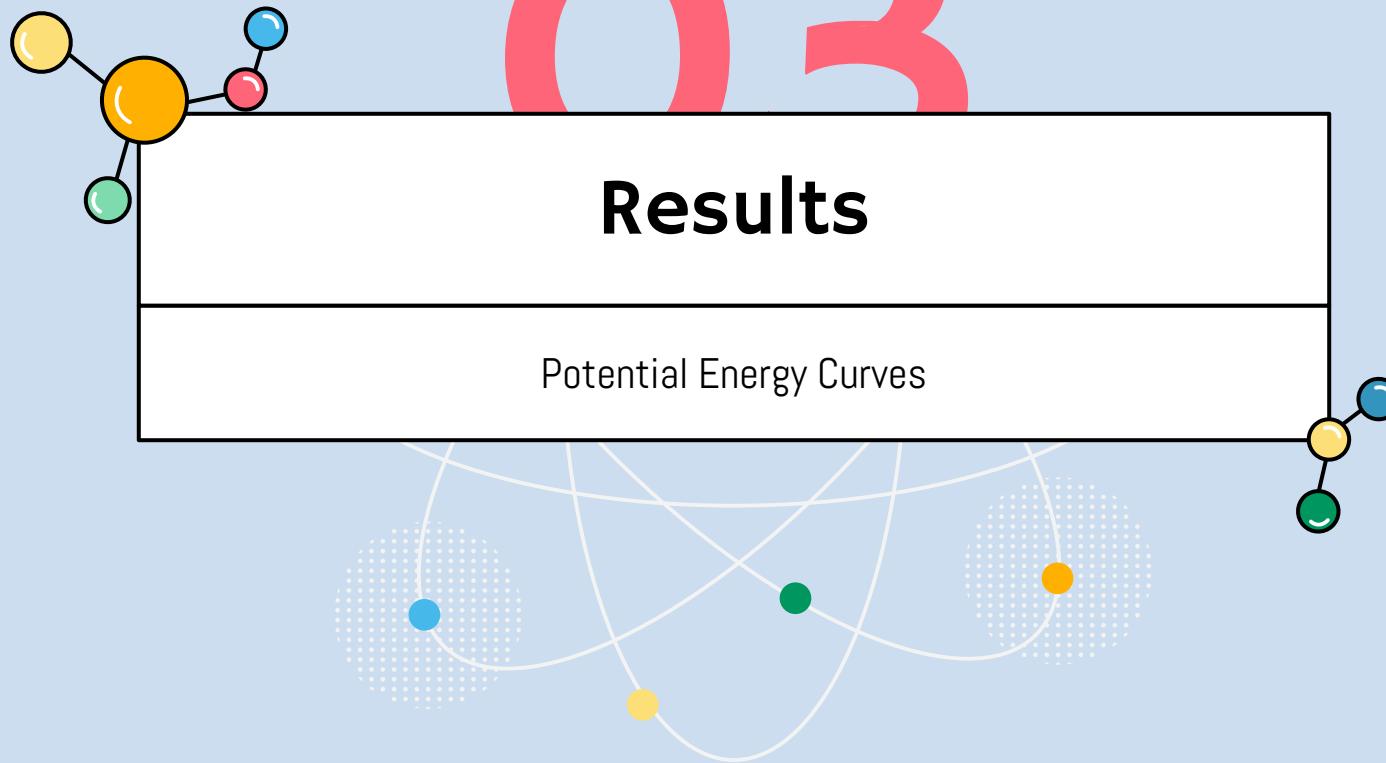
Computational Cost vs. Accuracy



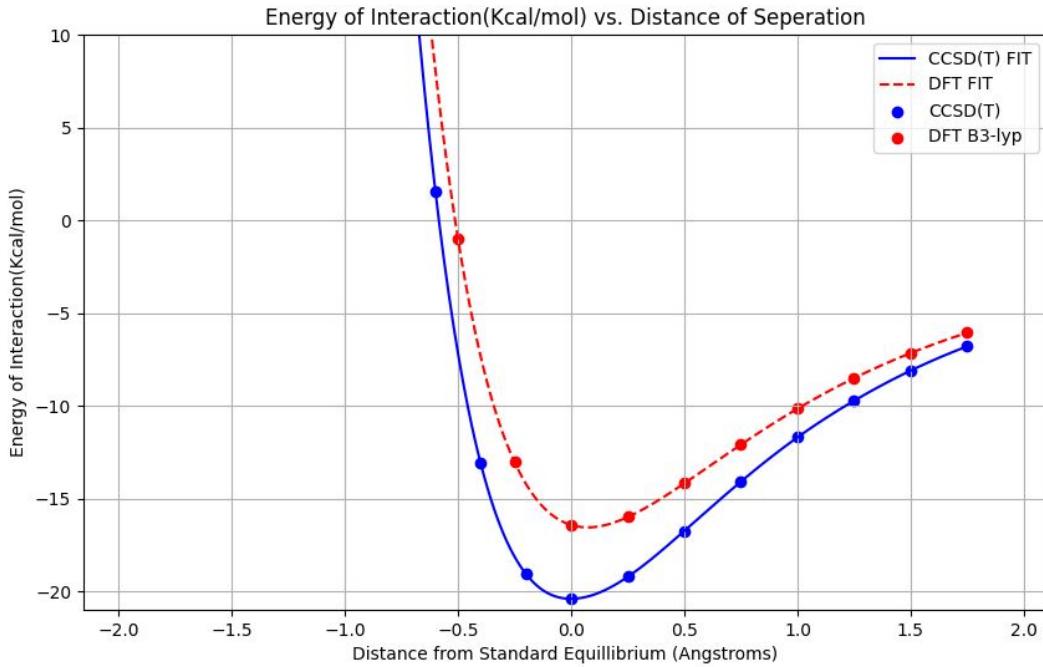
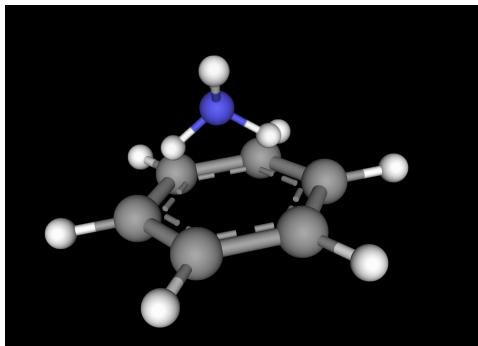
O3

Results

Potential Energy Curves



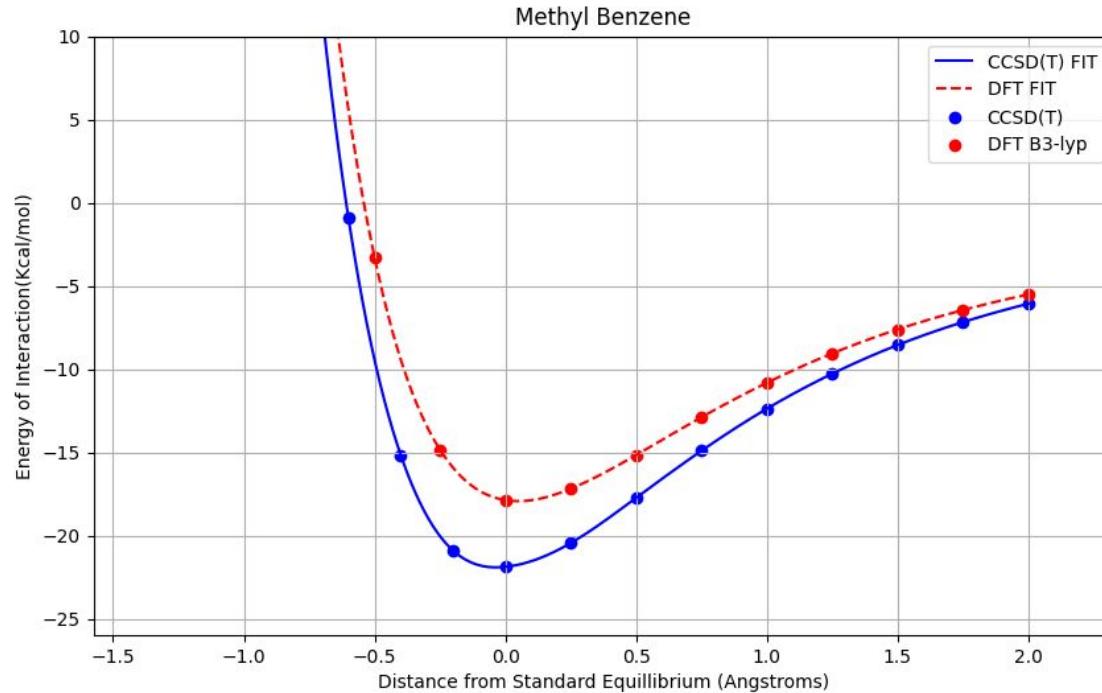
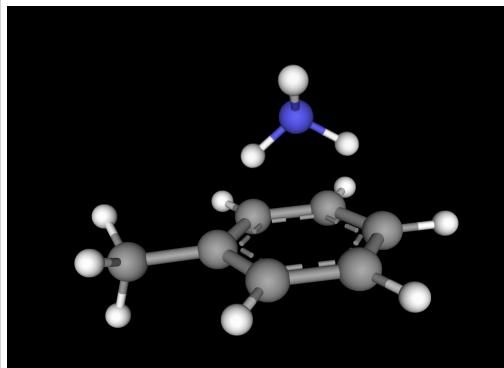
Lys/Benzene:



CCSD(T) minimum: $x = -0.000100$, $y = -20.404561$

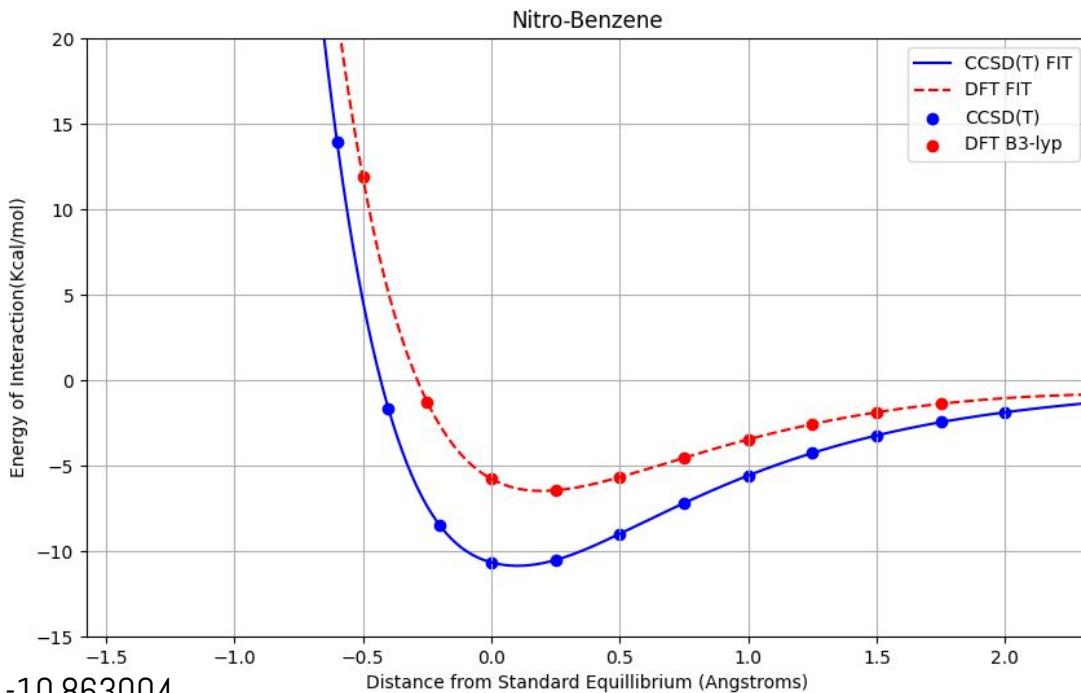
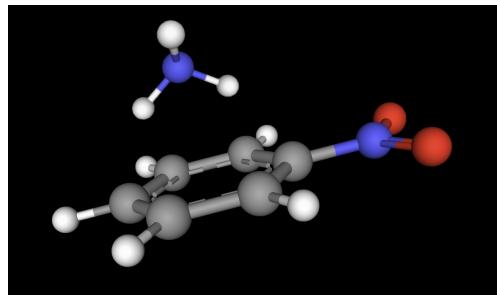
DFT FIT minimum: $x = 0.072645$, $y = -16.557487$

Lys/Toluene:



CCSD(T) minimum: $x = -0.036874$, $y = -21.909502$
DFT FIT minimum: $x = 0.052605$, $y = -17.929000$

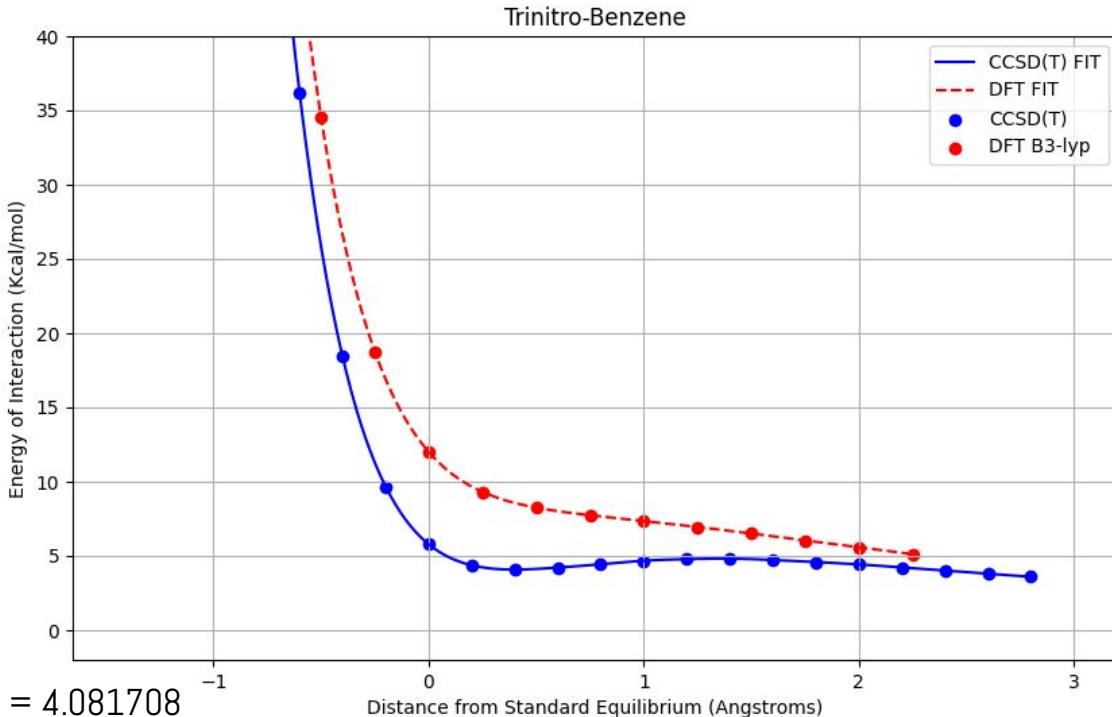
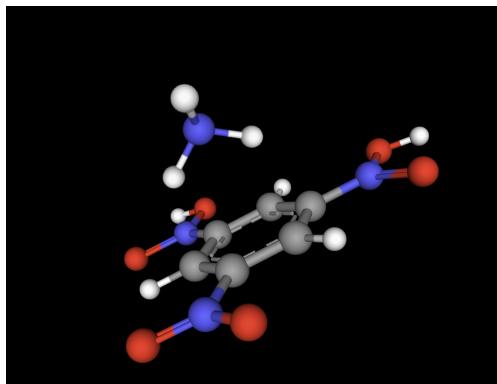
Nitro/Lys:



CCSD(T) minimum: $x = 0.104609$, $y = -10.863004$

DFT FIT minimum: $x = 0.194890$, $y = -6.482986$

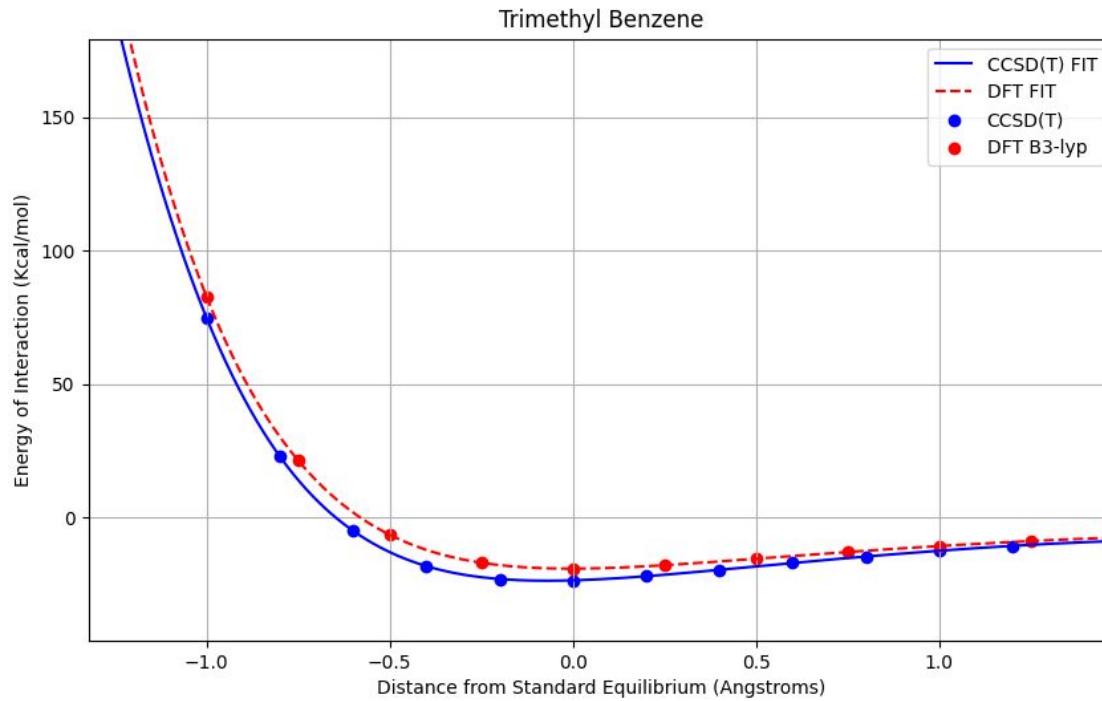
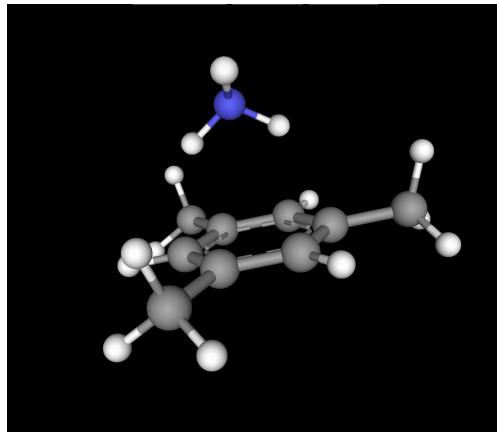
Trinitro/Lys:



CCSD(T) minimum: x = 0.397595, y = 4.081708

DFT FIT minimum: x = 2.250000, y = 5.125369

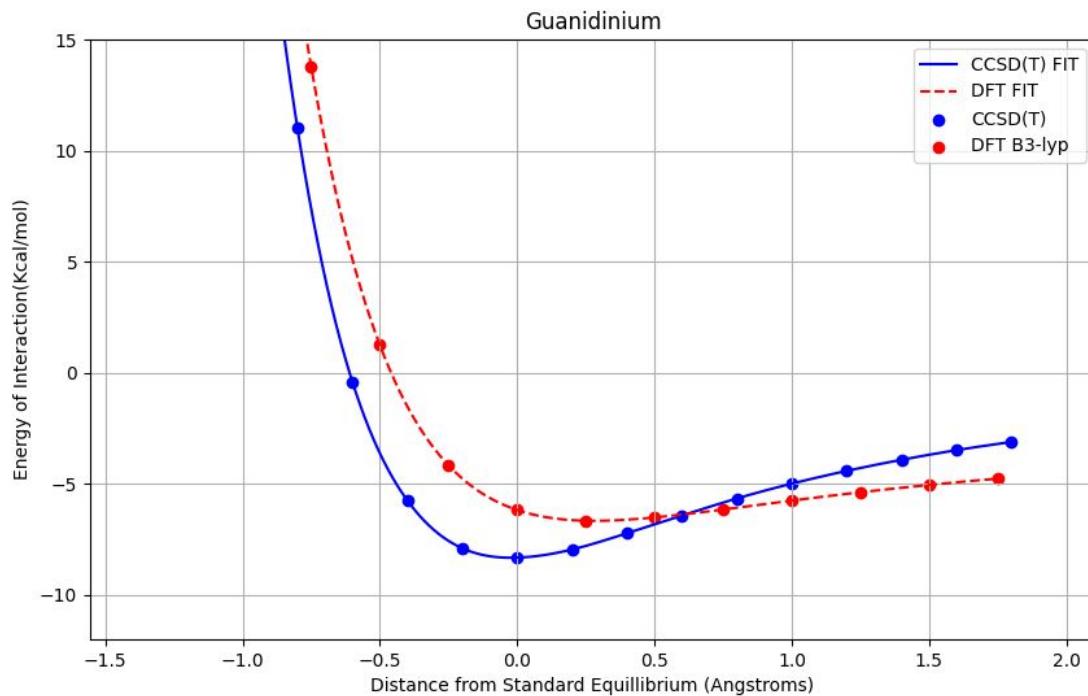
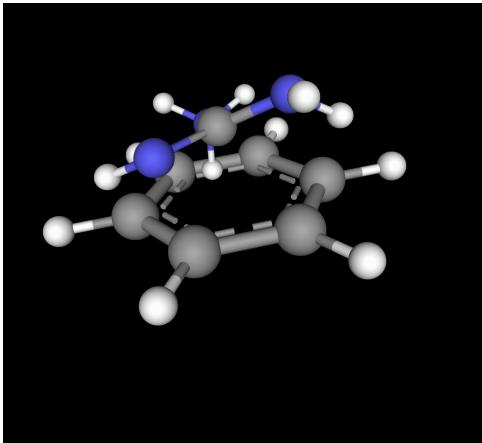
Trimethyl/Lys:



CCSD(T) minimum: $x = -0.072545$, $y = -23.577745$

DFT FIT minimum: $x = -0.004509$, $y = -19.054448$

Benzene/Arg:



CCSD(T) minimum: x = -0.023647, y = -8.328307

DFT FIT minimum: x = 0.283066, y = -6.666472

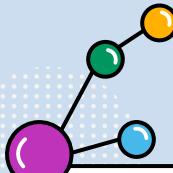


Summary

Data	Trinitro	Nitro	Benzene	Toluene	Trimethyl
Equilibrium Position Coupled Cluster(Å)	3.89	3.6	3.50	3.47	3.43
Equilibrium Position DFT (Å)	N/A	3.69	3.57	3.55	3.5
Interaction Energy Coupled Cluster(Kcal/mol)	-4.08	-10.86	-20.4	-21.9	-23.6
Interaction Energy DFT(Kcal/mol)	N/A	-6.48	-16.5	-17.9	-19



Computational Cost



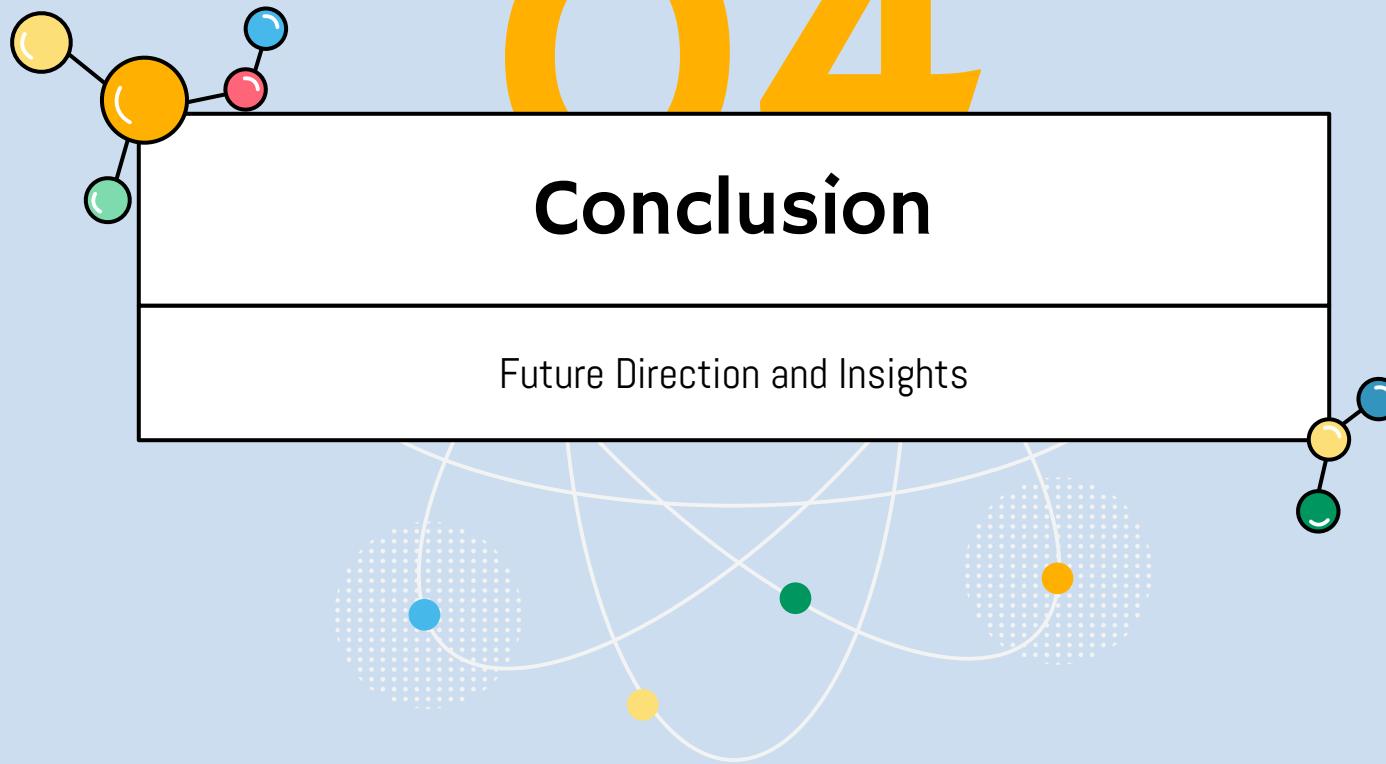
Name of Method	Trinitro	Trimethyl	Toluene	Nitro	Guanidinium
PSI4 DFT(Either Functional) 60 CPU Core	2:40	1:30	>1minute	>1minute	1.40
ORCA DLPNO CCSD(T) 60 CPU Core	18.30	15	11	6:42	5:47



Q4

Conclusion

Future Direction and Insights

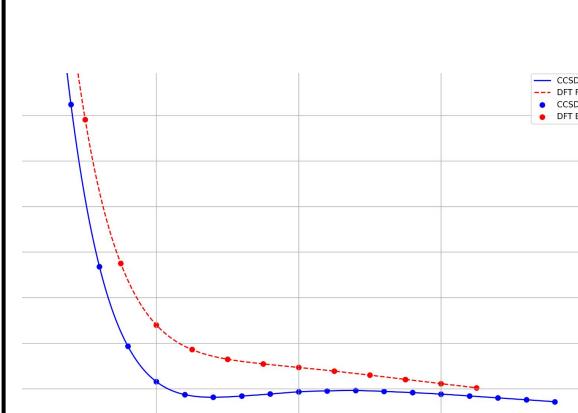
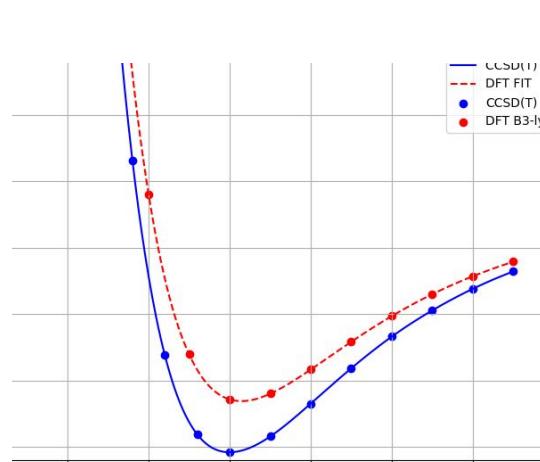
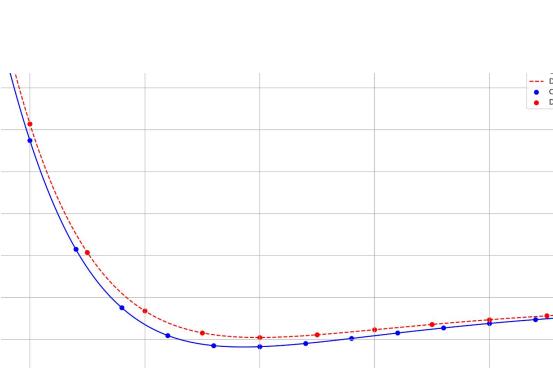


Accuracy of DFT

Toluene

Benzene

Nitro-Benzene



Lots of Correlation
High Accuracy

Normal Correlation
Steepness Lowered

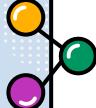
Low Correlation
Wrong Shape

DFT (Density Functional Theory) vs. CCSD

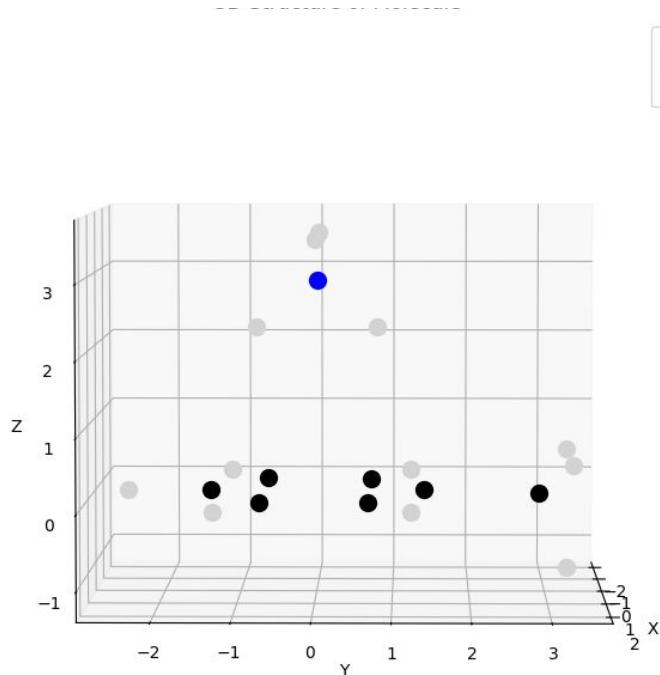
The functionals in this study are LDA based, so they over correlate because they don't do well with non-smooth electron densities. This causes inaccuracies whereas Couple Cluster does a Hartree Fock then introduces an excitation operation that accounts for single, double and in this case triple excitations, which encapsulates correlation more accurately. The first excitation account for orbital relaxation, the second excitation account for

$$\left[-\frac{\hbar^2}{2m} \nabla^2 + V_s(\mathbf{r}) \right] \varphi_i(\mathbf{r}) = \varepsilon_i \varphi_i(\mathbf{r}) \quad V_s(\mathbf{r}) = V(\mathbf{r}) + \int \frac{n(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} d^3\mathbf{r}' + V_{XC}[n(\mathbf{r})],$$

$$\begin{aligned} |\Psi\rangle &= e^{\hat{T}} |\Phi_0\rangle \\ &= \left(1 + \hat{T} + \frac{1}{2} \hat{T}^2 + \frac{1}{3!} \hat{T}^3 + \dots \right) |\Phi_0\rangle, \end{aligned}$$



Optimization of Uneven Functionalizations



1. Free Geometry
Minimization of the unsymmetrical aromatic complexes using DFT B3LYP
2. Finding the energy of the complex, and individual molecules using CCSD(T)

Future Directions

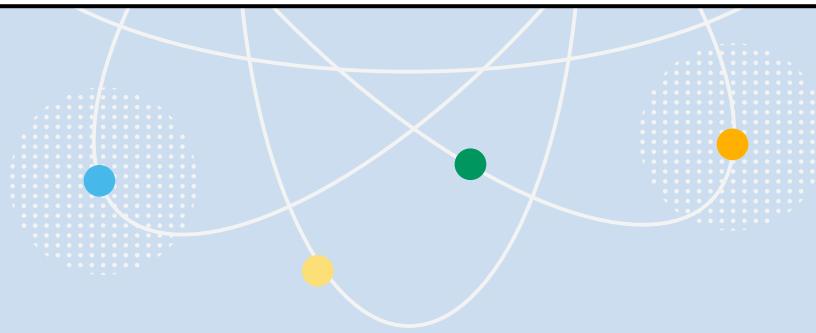
1. Compute potential energy surfaces for (Arg/Lys–Phe/Tyr) with solvent effects.
2. Compute potential energy surfaces for (Phe/Tyr–Phe/Tyr) with solvent effects.
3. Parametrize a Coarse grain model with PEC data

Citation

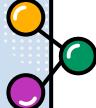
Kiran Kumar, M. Woo, S., Thomas Siu, A. Cortopassi, W., Fernanda Duarte, & S. Paton, R. (2018, January 31). *Cation–π interactions in protein–ligand binding: Theory and data-mining reveal different roles for lysine and arginine.* Chemical Science. <https://pubs.rsc.org/en/content/articlehtml/2018/sc/c7sc04905f>

THANKS

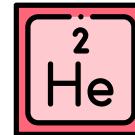
Questions? Comments? Suggestions?







TWO COLUMNS



HYDROGEN

Mercury is the closest planet to the Sun and the smallest one in the Solar System—it's only a bit larger than the Moon

HELIUM

Venus has a beautiful name and is the second planet from the Sun. It's hot and has a poisonous atmosphere

THE STRUCTURE OF THE ATOM: CARBON ATOM

ELECTRON

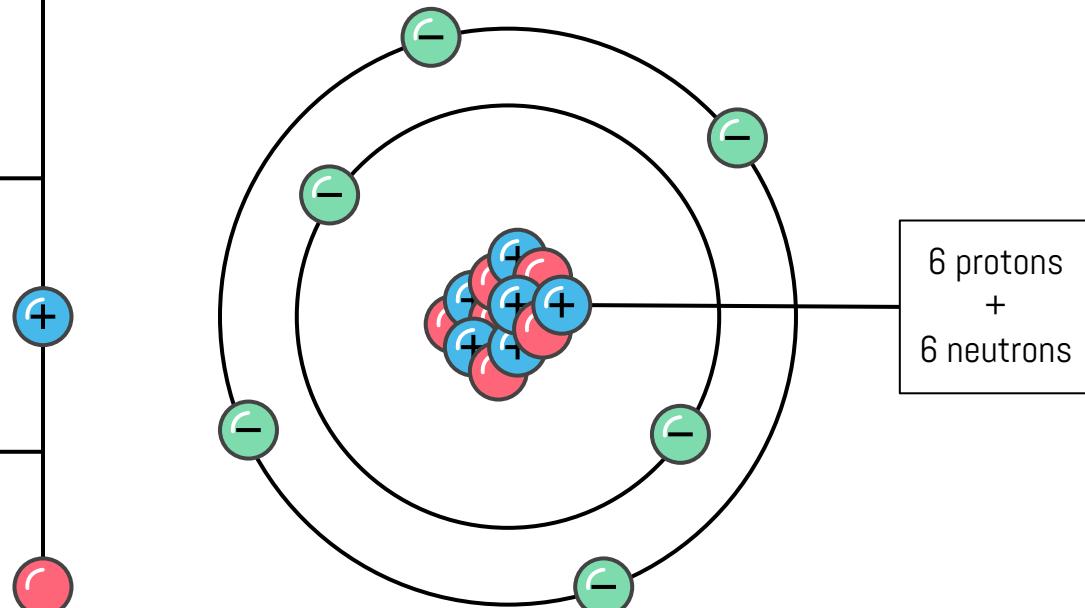
Mercury is the closest planet to the Sun

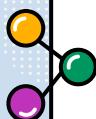
PROTON

Venus is the second planet from the sun

NEUTRON

Despite being red, Mars is a cold place





TWO COLUMNS



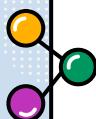
LITHIUM

Mercury is the closest planet to the Sun and the smallest one in the Solar System—it's only a bit larger than the Moon

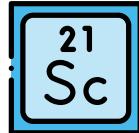
BERYLLIUM

Venus has a beautiful name and is the second planet from the Sun. It's hot and has a poisonous atmosphere



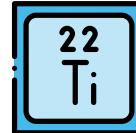


TRANSITION METALS



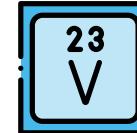
SCANDIUM

Mercury is the closest planet to the Sun



TITANIUM

Venus is the second planet from the Sun



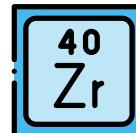
VANADIUM

Despite being red, Mars is actually a very cold place



YTTRIUM

Jupiter is the biggest planet of them all



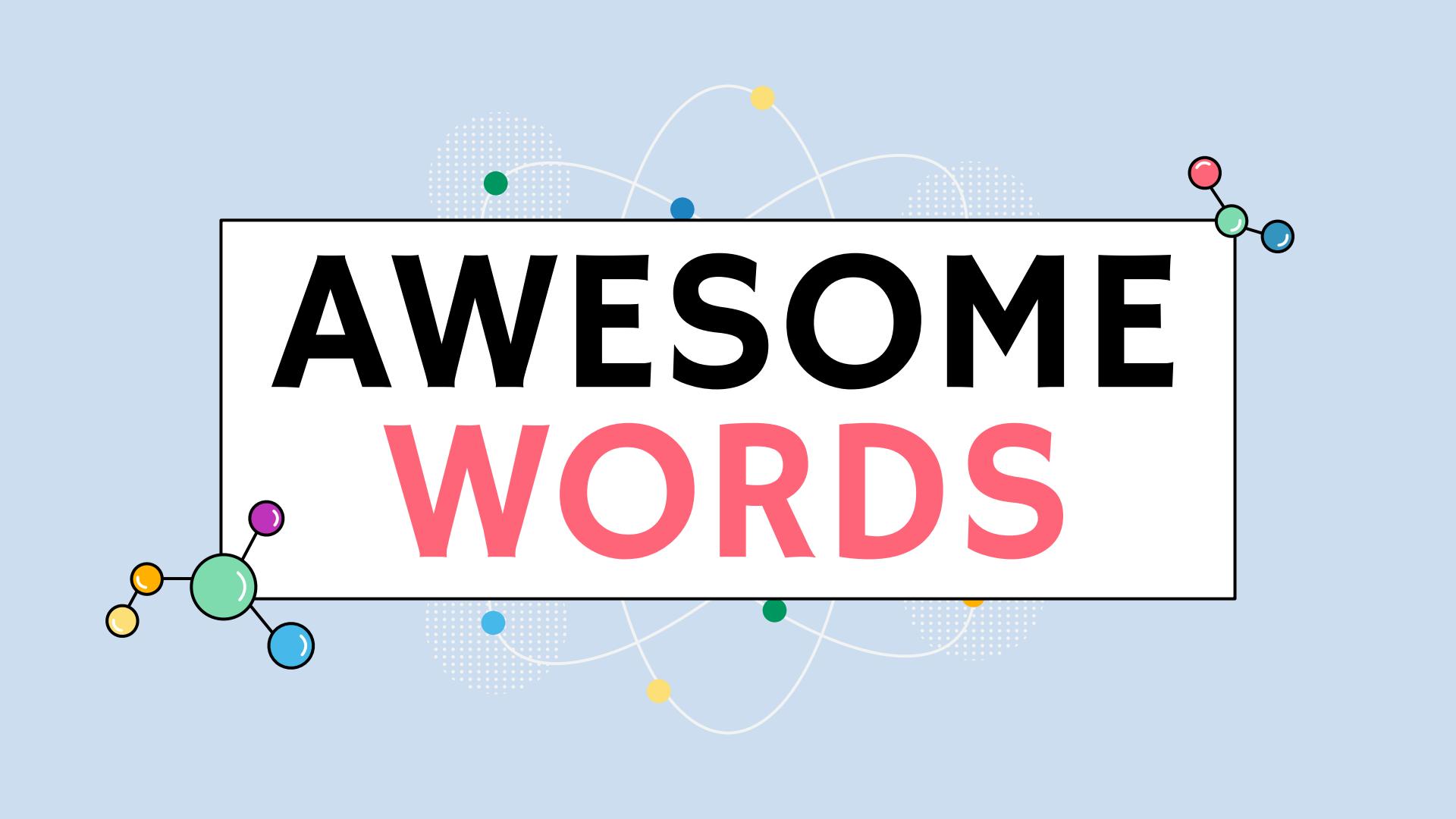
ZIRCONIUM

Saturn is composed of hydrogen and helium



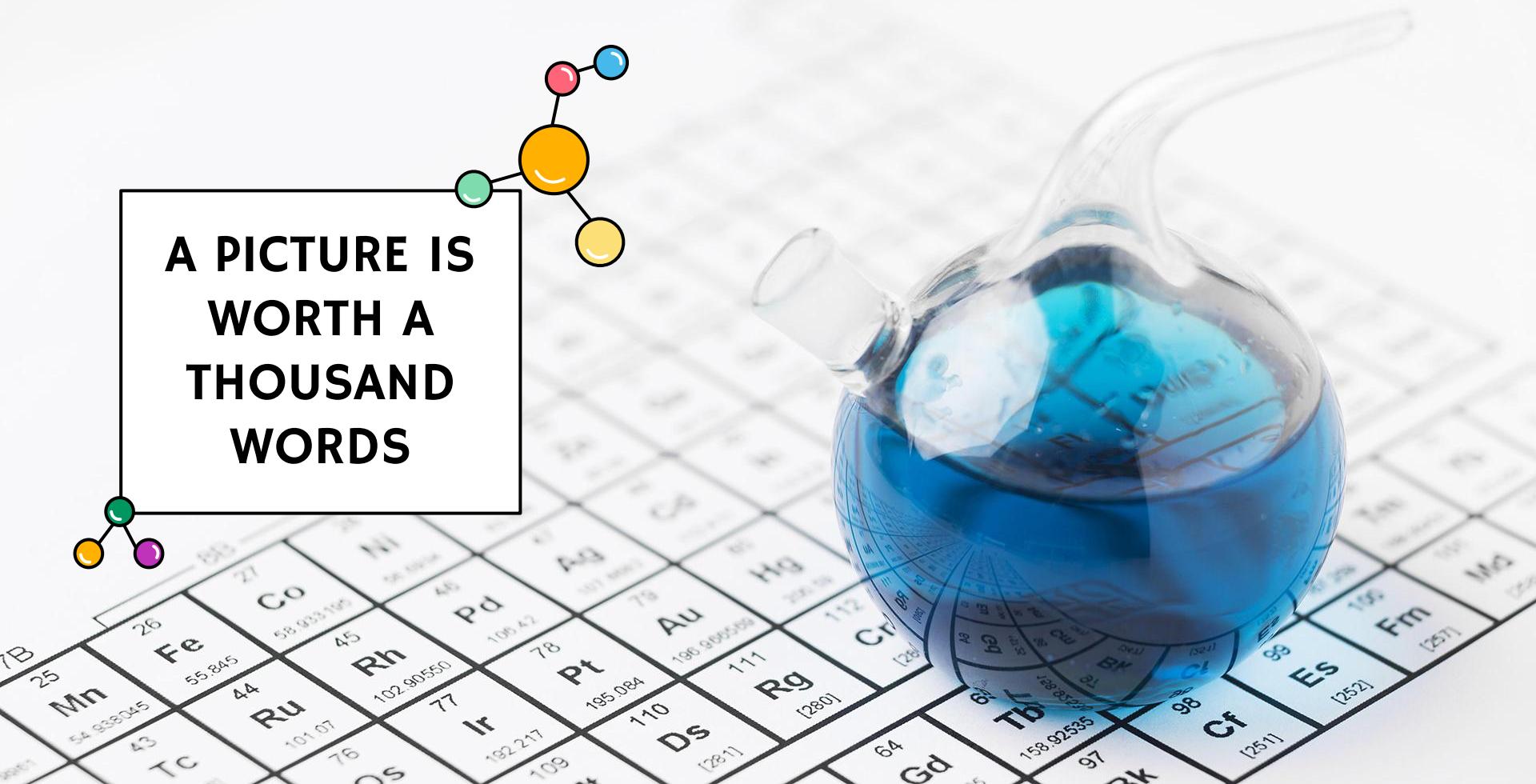
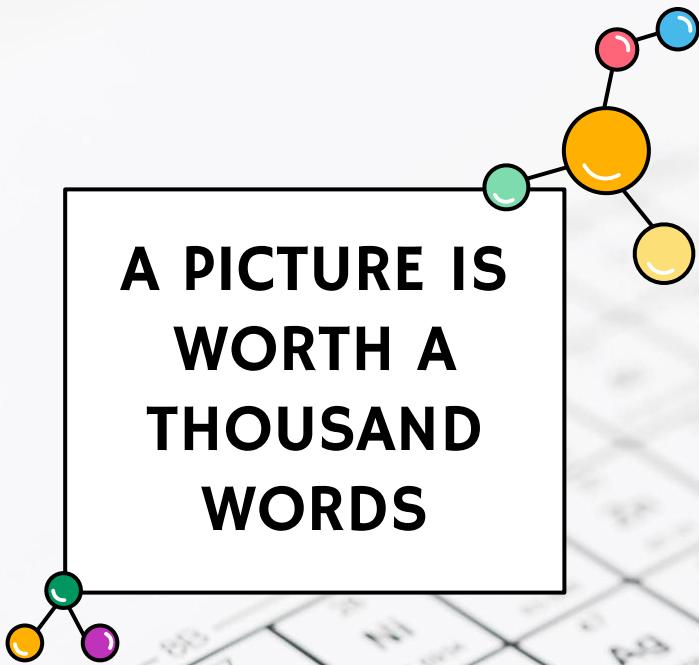
NIOBIUM

Neptune is the farthest planet from the Sun



AWESOME **WORDS**

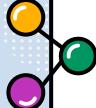
A PICTURE IS
WORTH A
THOUSAND
WORDS



TEXT AND PHOTO

You can give a brief description of the topic you want to talk about here. For example, if you want to talk about Mercury, you can say that it's the smallest planet in the entire Solar System

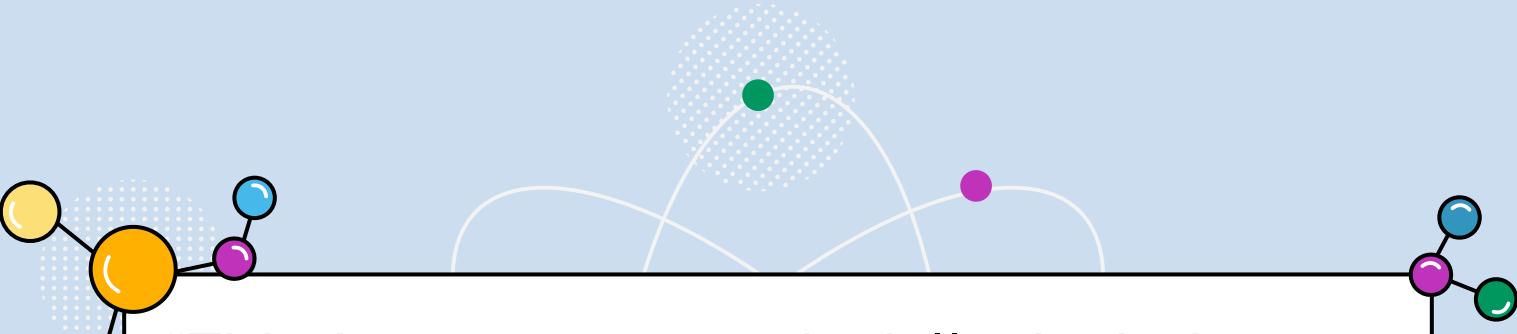




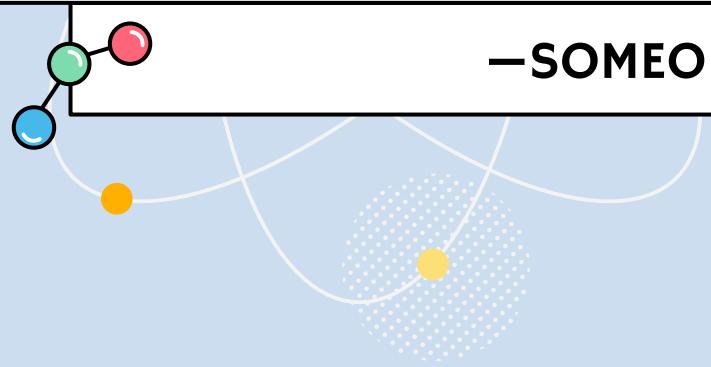
TEXT AND PHOTO 3



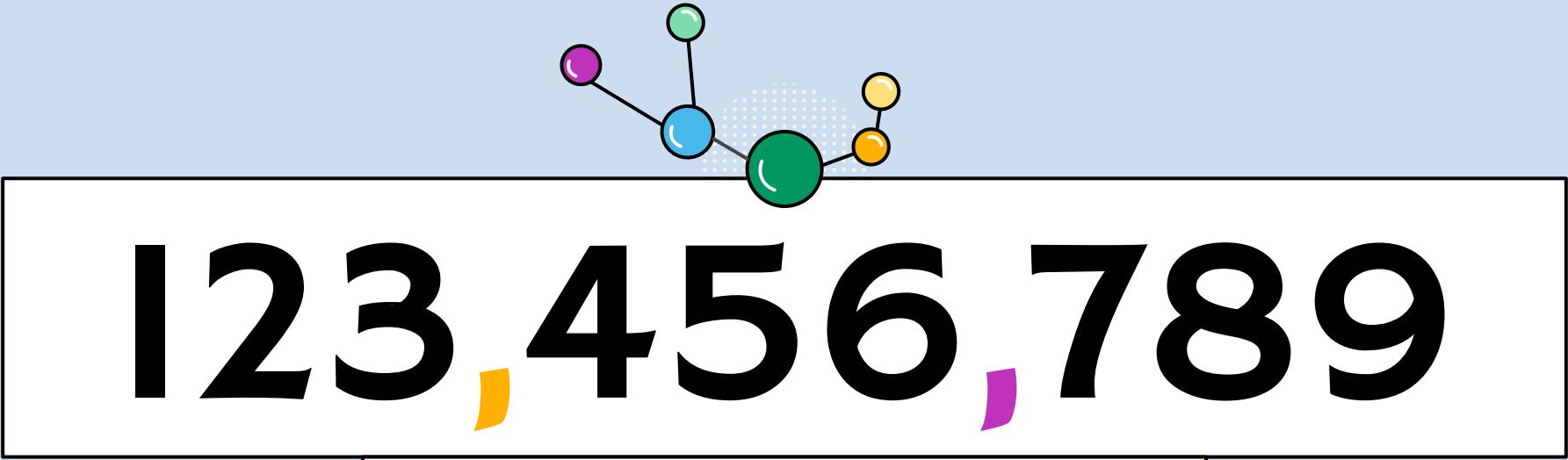
You can give a brief description of the topic you want to talk about here.
For example, if you want to talk about Mercury, you can say that it's the
smallest planet in the entire Solar System



“This is a quote, words full of wisdom
that someone important said and can
make the reader get inspired.”

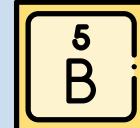


—SOMEONE FAMOUS



123,456,789

Big numbers catch your audience's attention



10.811 u

It's the atomic mass of Boron



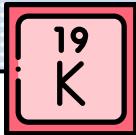
22.990 u

It's the atomic mass of Sodium



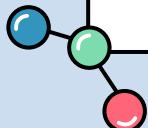
51.996 u

It's the atomic mass of Chromium



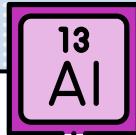
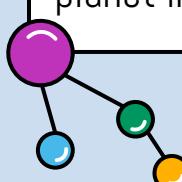
23%

Venus is the second planet from the Sun



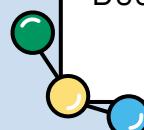
45%

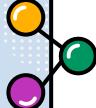
Jupiter is the biggest planet in the Solar System



78%

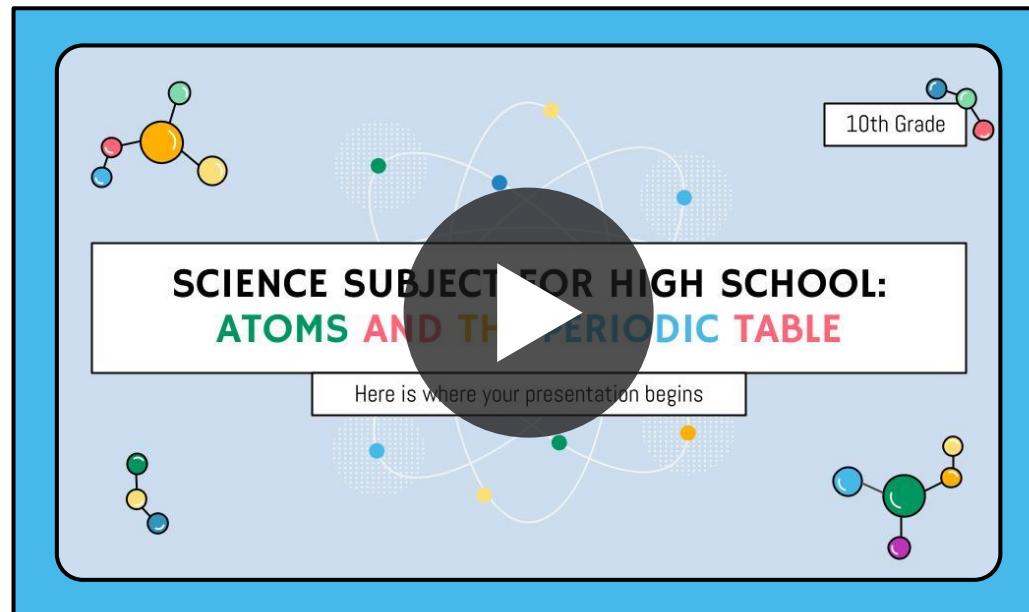
Despite being red, Mars is a cold place

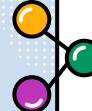




VIDEO TUTORIAL

You can replace the image on the screen with your own work. Just right-click on it and select "Replace image"

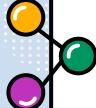




TABLET Screenshot



You can replace the image on the screen with your own work. Just right-click on it and select "Replace image"

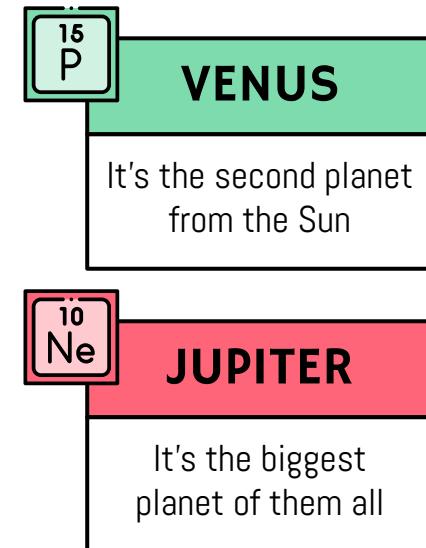
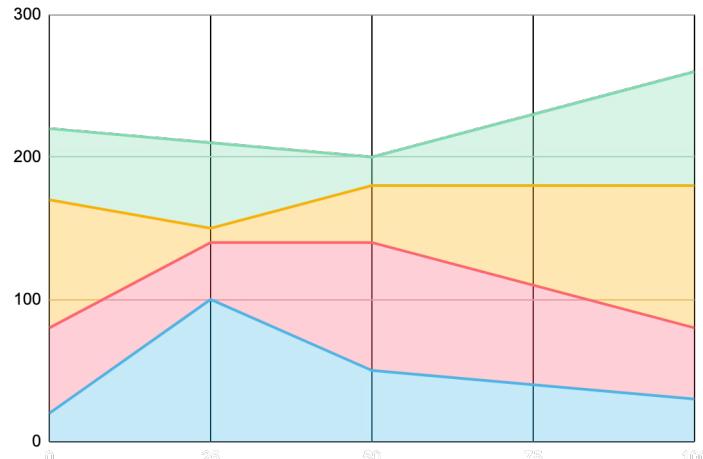
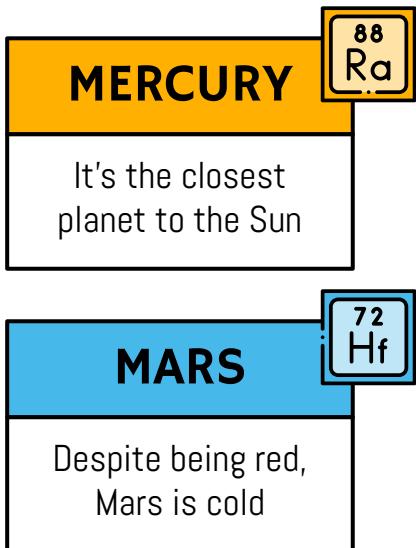


PHONE SCREENSHOT

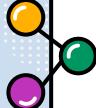
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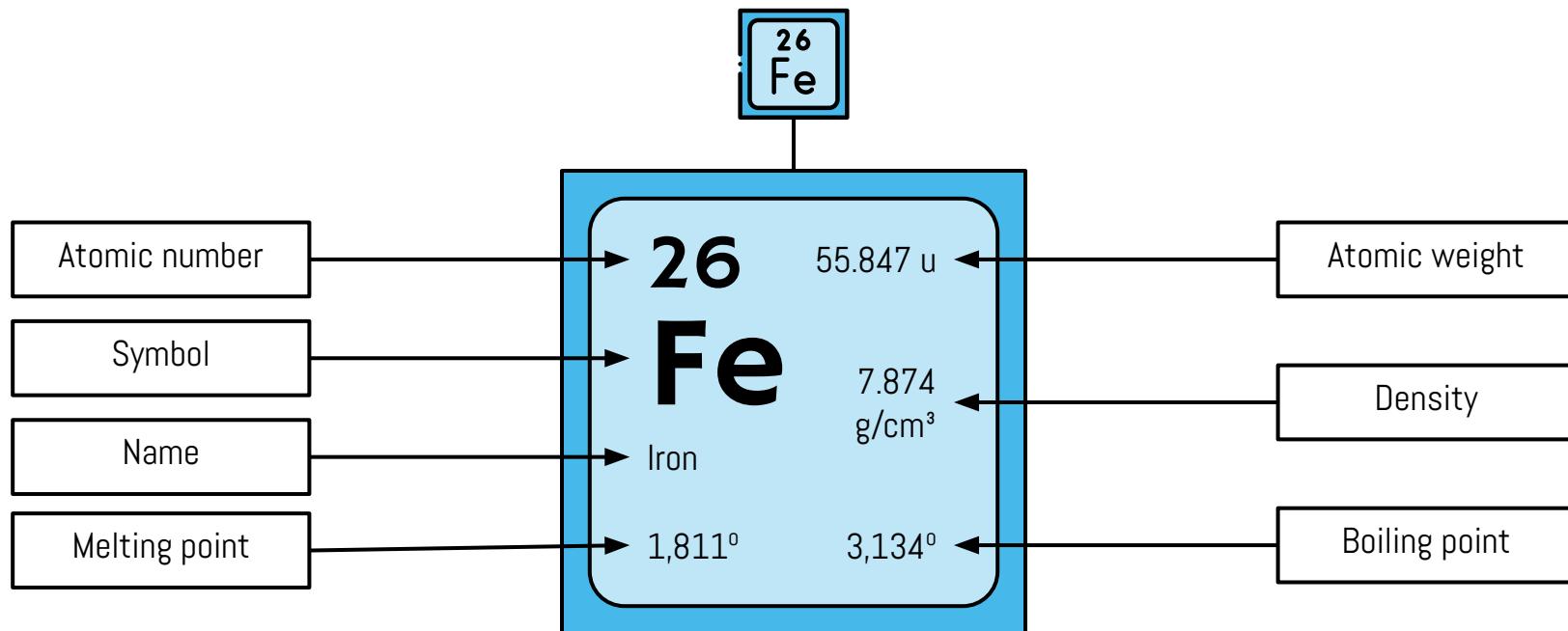
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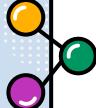


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ELEMENT INFORMATION





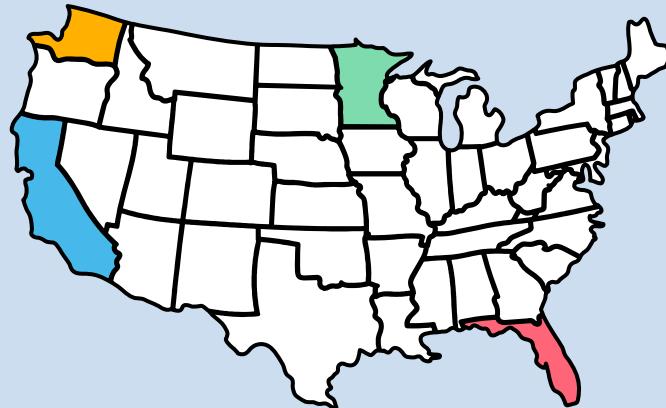
BEST CHEMISTRY SCHOOLS

MERCURY

It's the closest planet to the Sun

MARS

Despite being red, Mars is cold

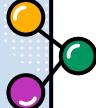


VENUS

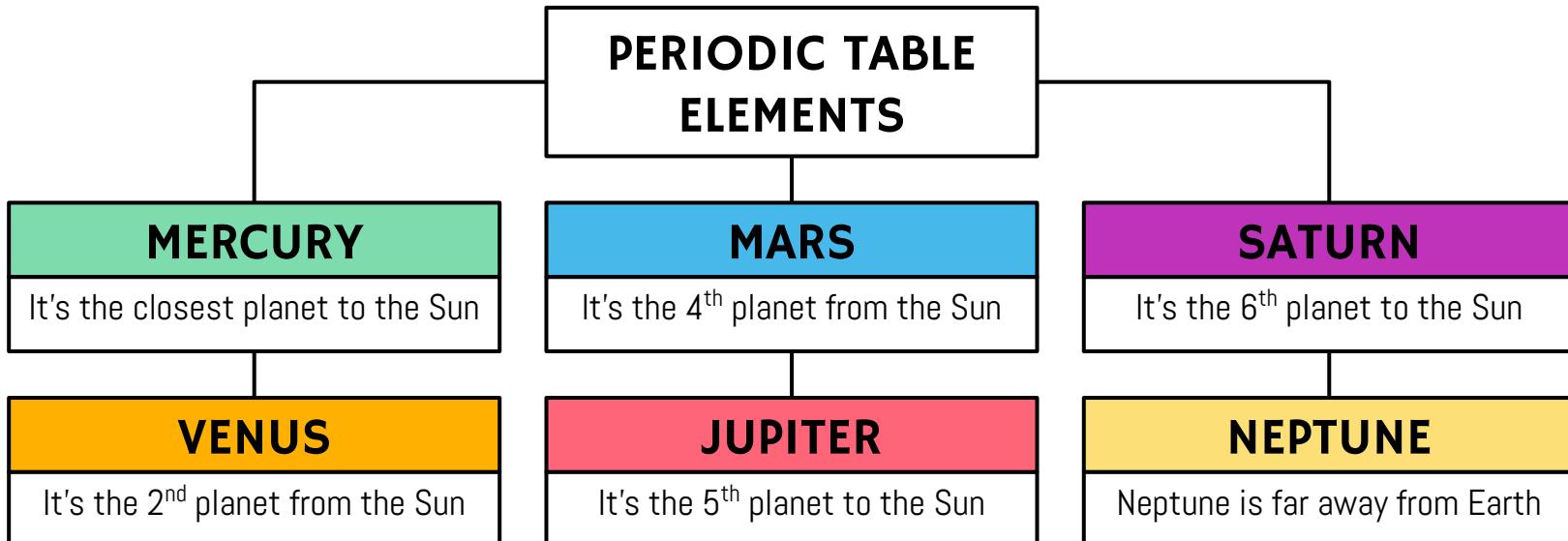
It's the second planet from the Sun

JUPITER

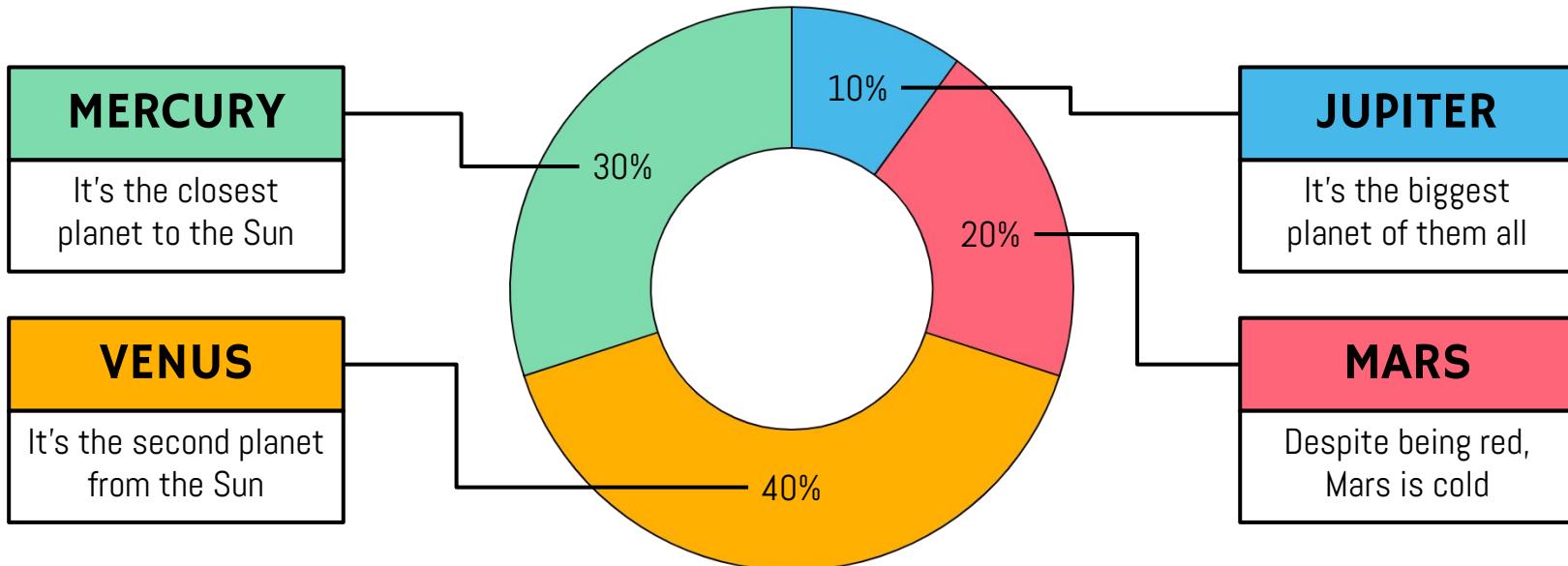
It's the biggest planet of them all



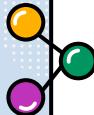
INFOGRAPHIC DIAGRAM



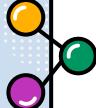
THIS IS ANOTHER GRAPH



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ICON PACK: PERIODIC TABLE

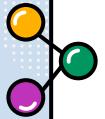


ALTERNATIVE RESOURCES

Here's an assortment of alternative resources whose style fits the one of this template:

Photos

- Man in lab doing experiments
- Still life arrangement of test tubes
- Senior woman teaching english
- Teacher standing and holding tablet
- Close up scientist wearing face mask
- Children learning more about chemistry in class
- Scientist working with chemical substances
- Girls learning more about chemistry in class
- Chemistry class elements with copy space
- Still life assortment of test tubes



RESOURCES

Did you like the resources on this template? Get them for free at our other websites:

Photos

- Top view world science day arrangement
- Front view science elements with chemicals assortment
- Male researcher in the biotechnology laboratory with tablet
- Side view of female scientist holding lab substance
- Medium shot woman with chemical substance
- Pretty girl learning more about chemistry in class
- Top view science elements
- High angle science elements composition
- High angle science elements with chemicals composition
- High angle science elements with chemicals assortment

Icons

- Icon pack: Periodic table

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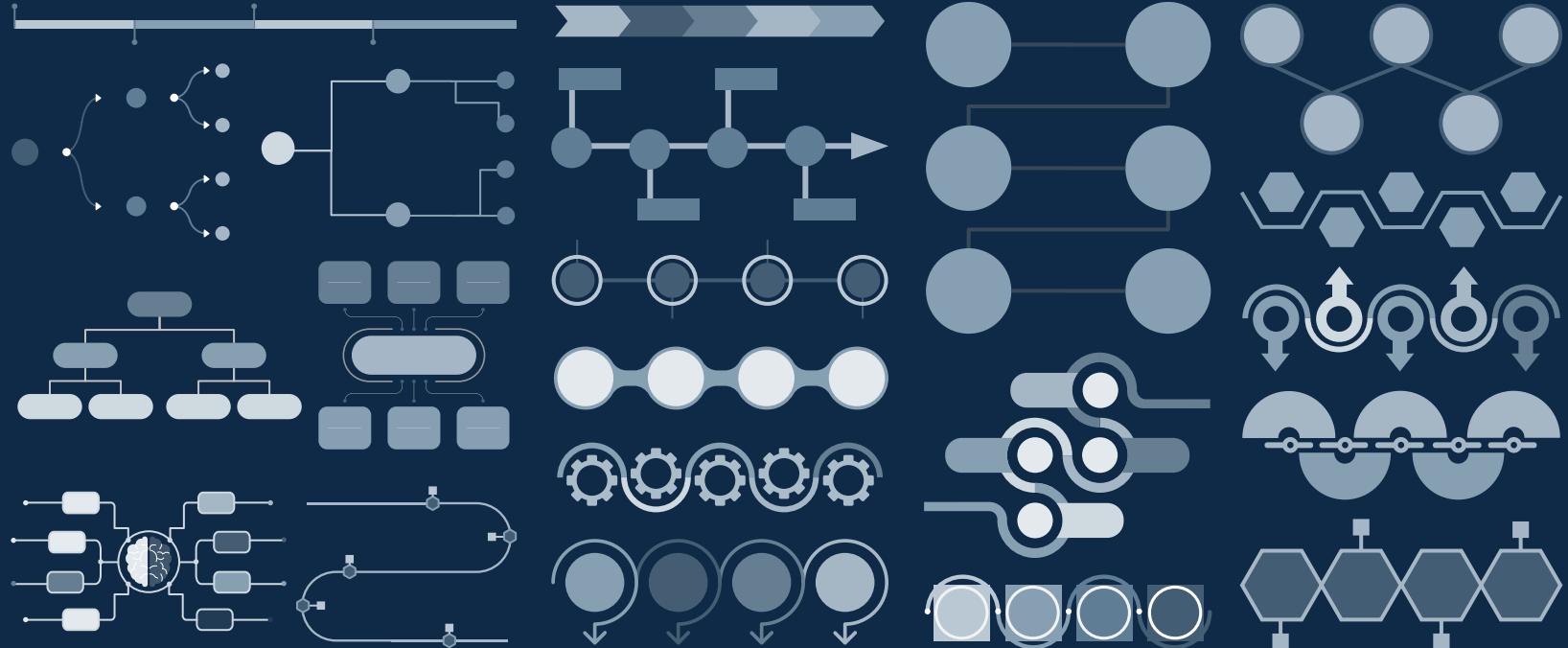
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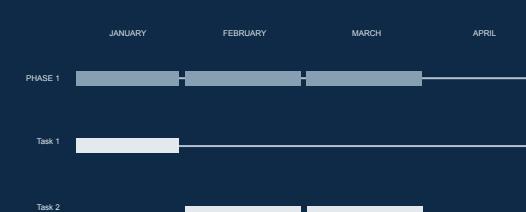
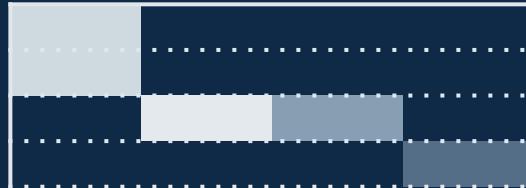
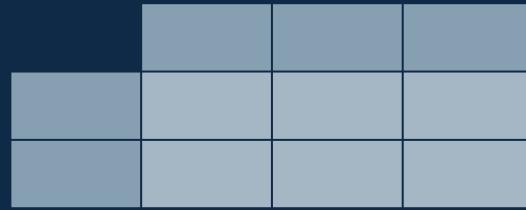
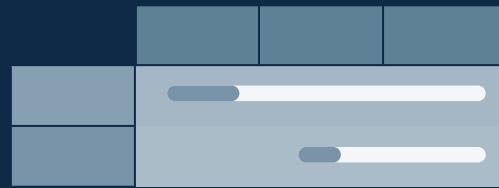
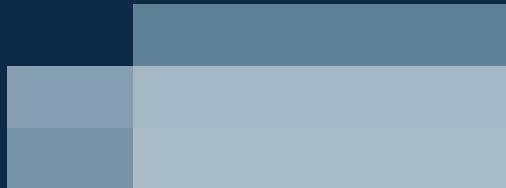
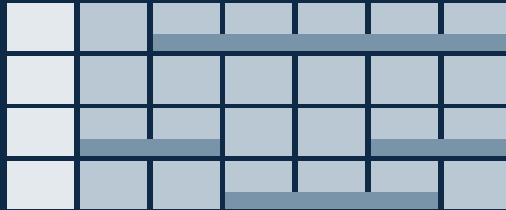
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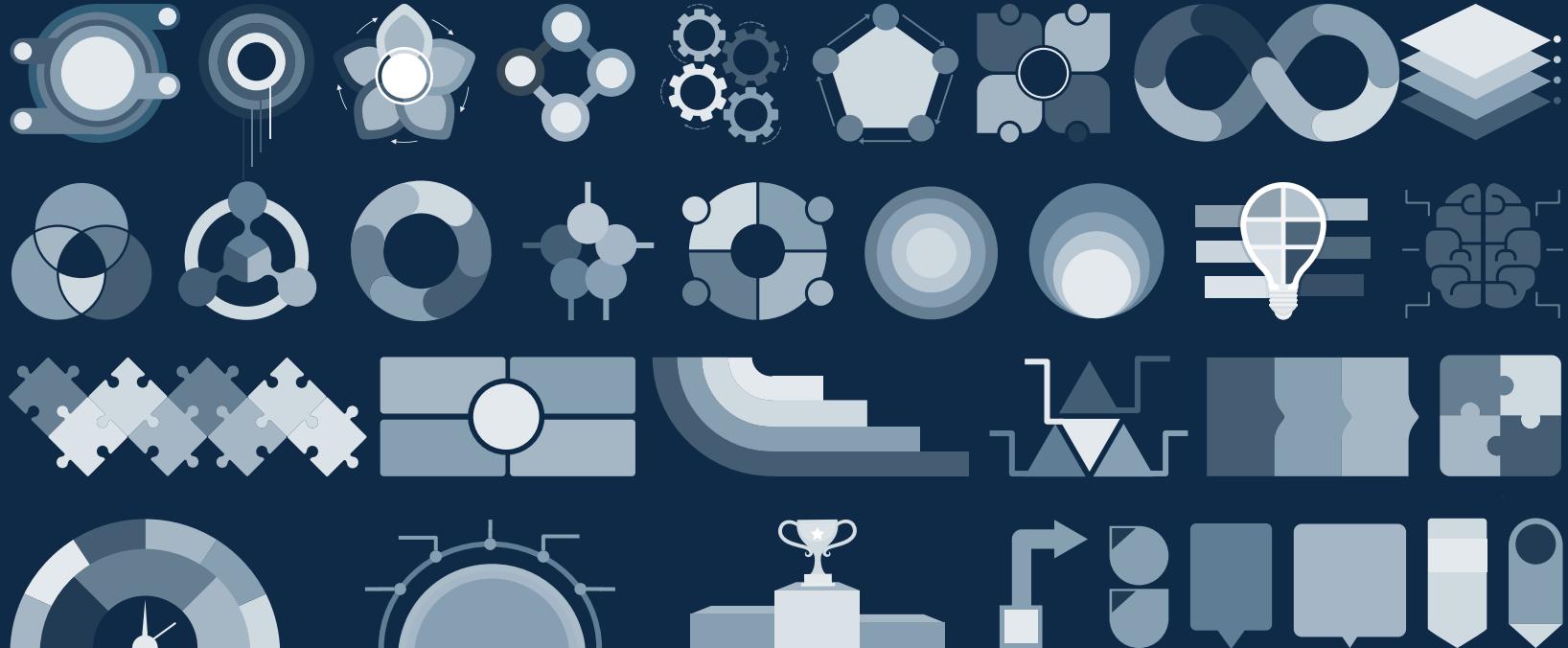
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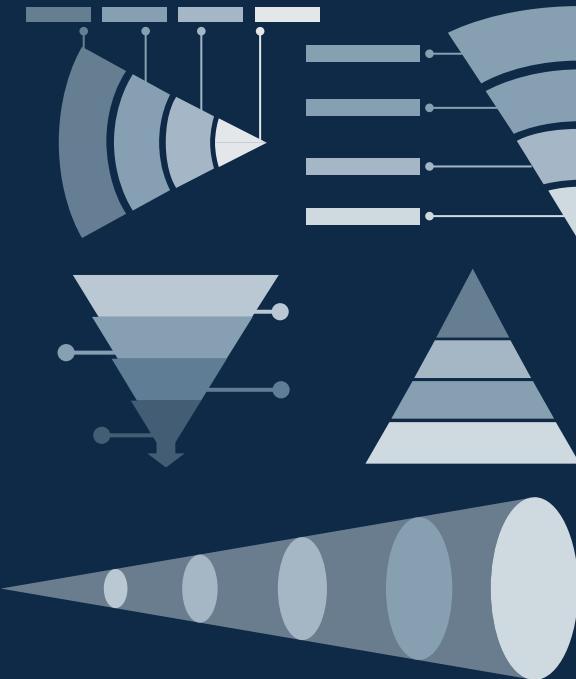
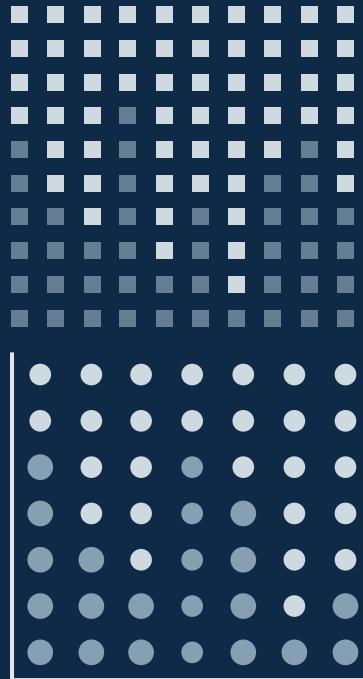












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