

# Tricks and Tips for Prompt Engineering in the Era of LLMs

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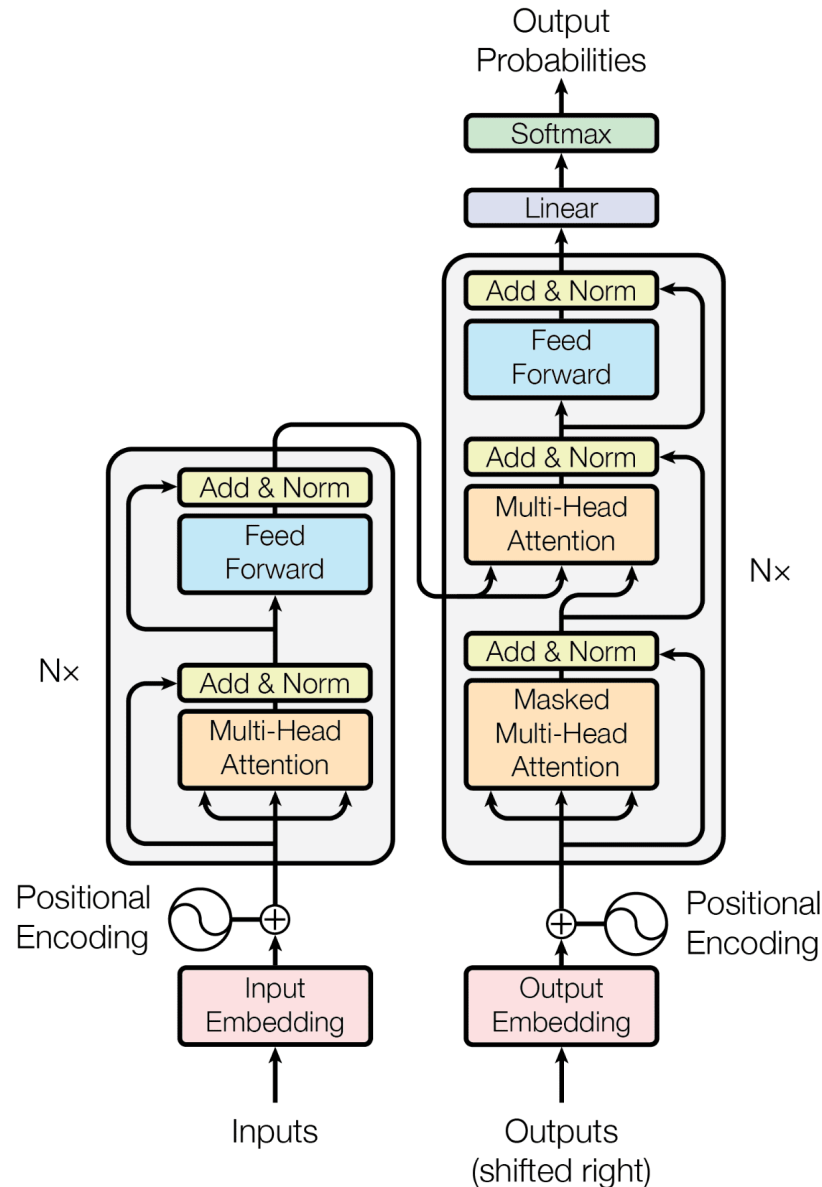
May 22, 2025

# Agenda

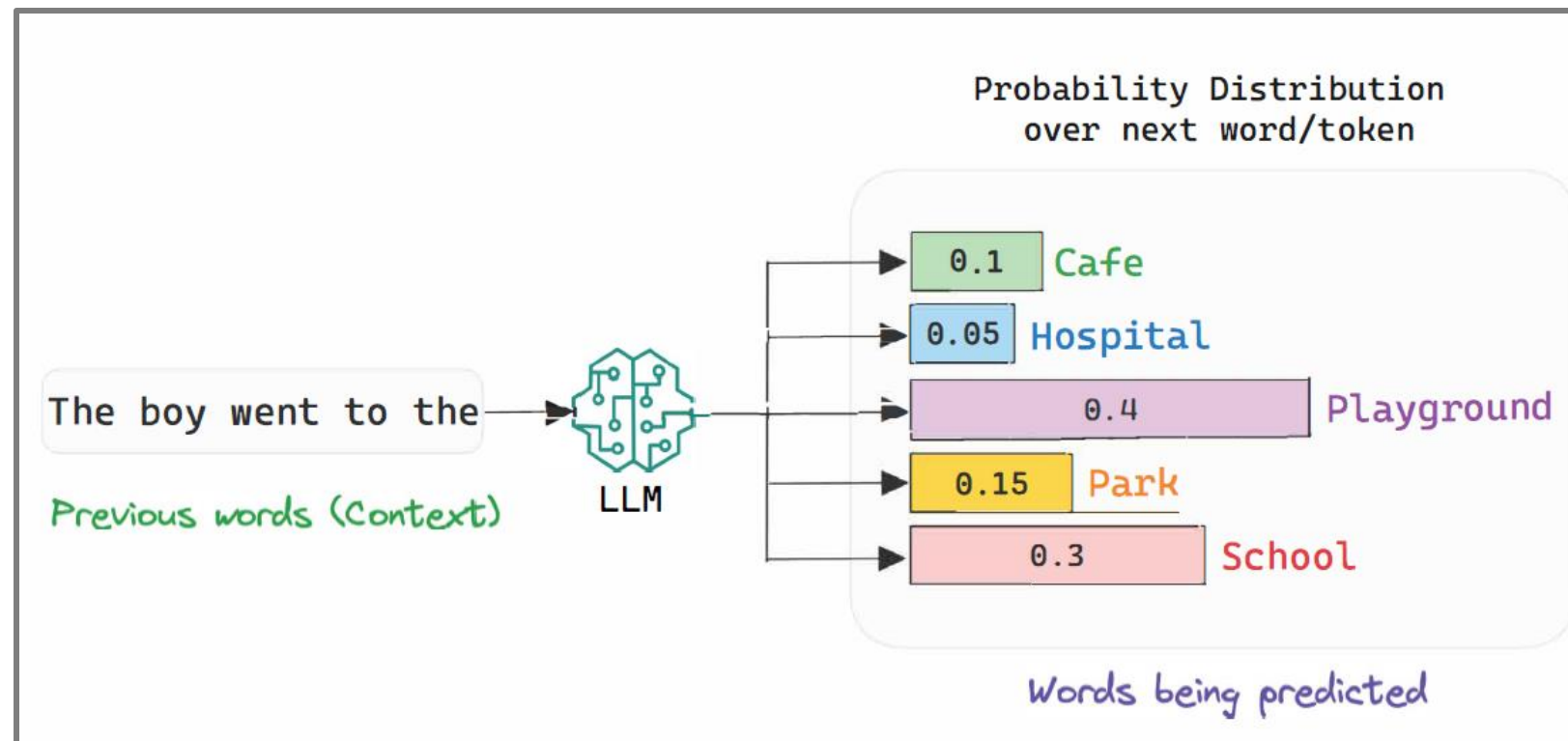
- Large Language Models (LLMs)
- Prompt Engineering
  - Principles & Strategies
- Ethical Use of LLMs
- Case Studies
- Resources



# Large Language Models (LLMs)



**GPT**  
generative pre-trained transformer

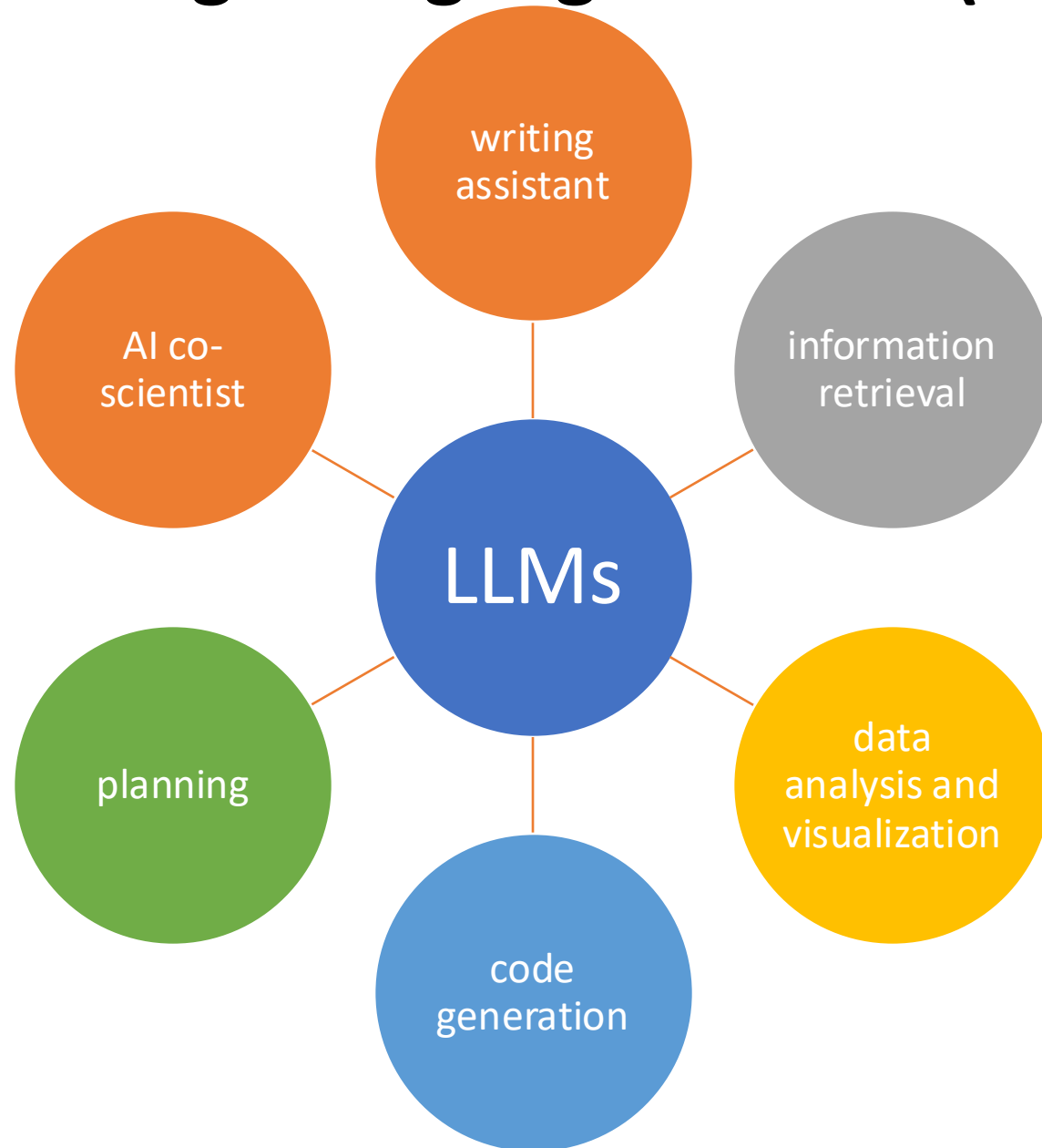


[1] Omer Shahab, *Therap Adv Gastroenterol*, 2024

[2] Ashish Vaswani, *NeurIPS*, 2017

[3] [medium.com](https://medium.com) post by Ignacio de Gregorio, 2024

# Large Language Models (LLMs)



ChatGPT 4o Share

Can you summarize recent findings on the crystal structure of the hypothetical protein 'Protein XYZ', involved in cellular regeneration

**hallucinations**

Searched 3 sites

Recent studies have unveiled fascinating details about the crystal structure of the protein AT2, a member of the G protein-coupled receptors (GPCRs) superfamily, which has implications for cellular regeneration and other physiological processes. This protein is significant in its involvement with nerve growth, pain control, and heart tissue regeneration [dornsife.usc.edu](#).

Researchers have discovered that AT2 behaves differently from typical GPCRs. It doesn't activate through the usual pathways involving G proteins or arrestins. Instead, it employs alternative, currently unidentified mechanisms for signal transduction within cells. This unique action suggests that AT2 might propagate signals through other proteins, which has not been clearly defined yet [today.usc.edu](#).

[1] Ziwei Ji, *ACM Comput. Surv.*, **2023**

[2] Dritjon Gruda, *Nature*, **2024**

# LLM Hallucinations

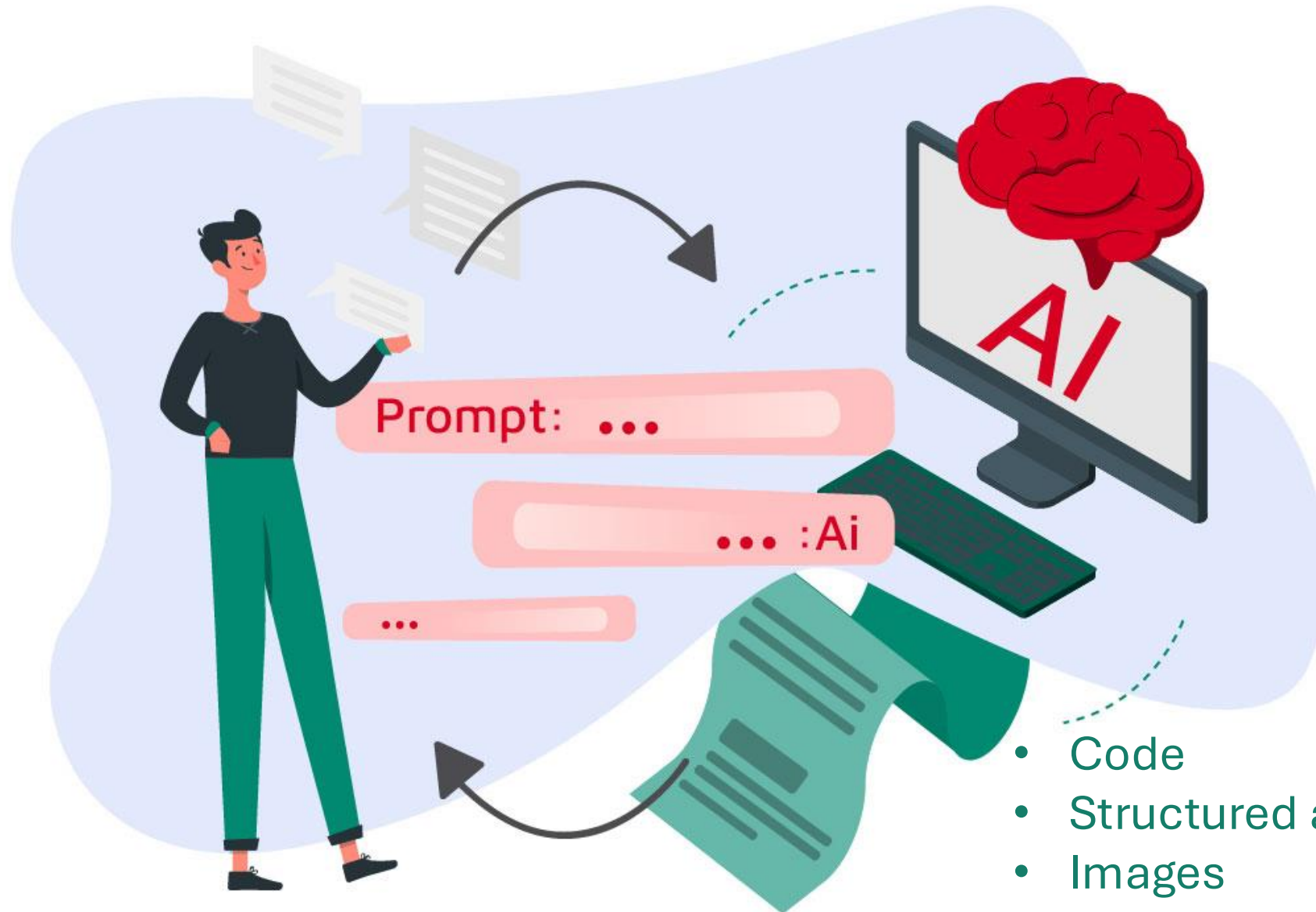
- Definition: the generation of content that is nonsensical or unfaithful to the provided source;
- Types:
  - In-context hallucination: input != output
  - Extrinsic hallucination: unverifiable content, can be wrong or correct
- Techniques to mitigate hallucination
  - Higher quality pre-training data
  - Fine-tune with domain-specific knowledge/data
  - Retrieval Augmented Generation (RAG)
  - **Advanced prompting techniques**

[1] Ziwei Ji, *ACM Comput. Surv.*, 2023

[2] <https://www.redhat.com/en/blog/when-llms-day-dream-hallucinations-how-prevent-them>

# Prompt Engineering

Think of prompting in the same way you would assigning a task to a person.



- Code
- Structured and unstructured texts
- Images
- ...

# Prompt Engineering

## ■ Components

- Expectation/Task
- Constraints (optional)
- Context (optional)

➤ Tell me about the protein dynamics.

**Protein dynamics** refers to the movements and conformational changes that proteins undergo over time. These dynamics are essential for their biological function, structure, and interaction with other molecules. Proteins are not rigid structures—they fluctuate between different conformational states due to thermal energy, even at equilibrium.

### Key Aspects of Protein Dynamics

#### 1. Timescales of Motion:

- ...

#### 2. Types of Motions:

- Local motions: Side chain rotations, backbone fluctuations.
- Domain motions: Movement of entire segments or domains of the protein.
- Allosteric transitions: Long-range conformational changes upon ligand binding that affect activity at another site.

#### 3. Biological Relevance:

- ...

#### 4. Experimental Methods to Study Dynamics:

- ...

ChatGPT 4o

# Prompt Engineering

## ■ Components

- Expectation/Task
- Constraints (optional)
- Context (optional)

➤ Tell me about the protein dynamics of G protein-coupled receptors (GPCRs).

The protein dynamics of **G protein-coupled receptors (GPCRs)** are central to their function as versatile signal transducers. GPCRs are membrane proteins that respond to a wide range of extracellular signals ... Here's a structured overview of their dynamics:

### 1. Basic Structural Features

GPCRs share a common architecture:

- Seven transmembrane (7TM)  $\alpha$ -helices.
- An extracellular N-terminus and intracellular C-terminus.
- Flexible extracellular and intracellular loops connecting the helices.

### 2. Conformational Dynamics

GPCRs are **highly dynamic** proteins and do not exist in just "active" or "inactive" forms. Instead, they sample a **spectrum of conformational states**, which include:

#### Inactive state

- Stabilized in the absence of ligand or bound to inverse agonists.
- G protein-binding site is occluded.

#### Active state(s)

- Triggered by agonist binding.

...



# Prompt Engineering

## ■ Components

- Expectation/Task
- Constraints (optional)
- Context (optional)

➤ I am working on a drug discovery project. Tell me about the protein dynamics of G protein-coupled receptors (GPCRs) so that it can help with the computational drug design.



## Computational Techniques to Study GPCR Dynamics

### 1. Molecular Dynamics (MD) Simulations:

- Capture atomic motions over time.
- Reveal **ligand-induced conformational changes**, water channel formation, and allosteric modulations.

### 2. Metadynamics / Accelerated MD / Gaussian Accelerated MD:

- Sample **rare events** like activation transitions.
- Useful for estimating **free energy landscapes** of conformational states.

### 3. Markov State Models (MSMs):

- Extract long-timescale dynamics from multiple short MD simulations.
- Identify metastable states useful for **structure-based virtual screening**.

### 4. Ensemble Docking:

- Dock ligands against an **ensemble of receptor conformations** (from MD or NMR).
- Accounts for receptor flexibility.

### 5. Dynamic Network Analysis:

- Identifies **communication pathways** and **allosteric sites**.

# Principles & Strategies of Prompt Engineering

- Clarity and conciseness
- Context and constraints
- Use examples
- Iterative refinement

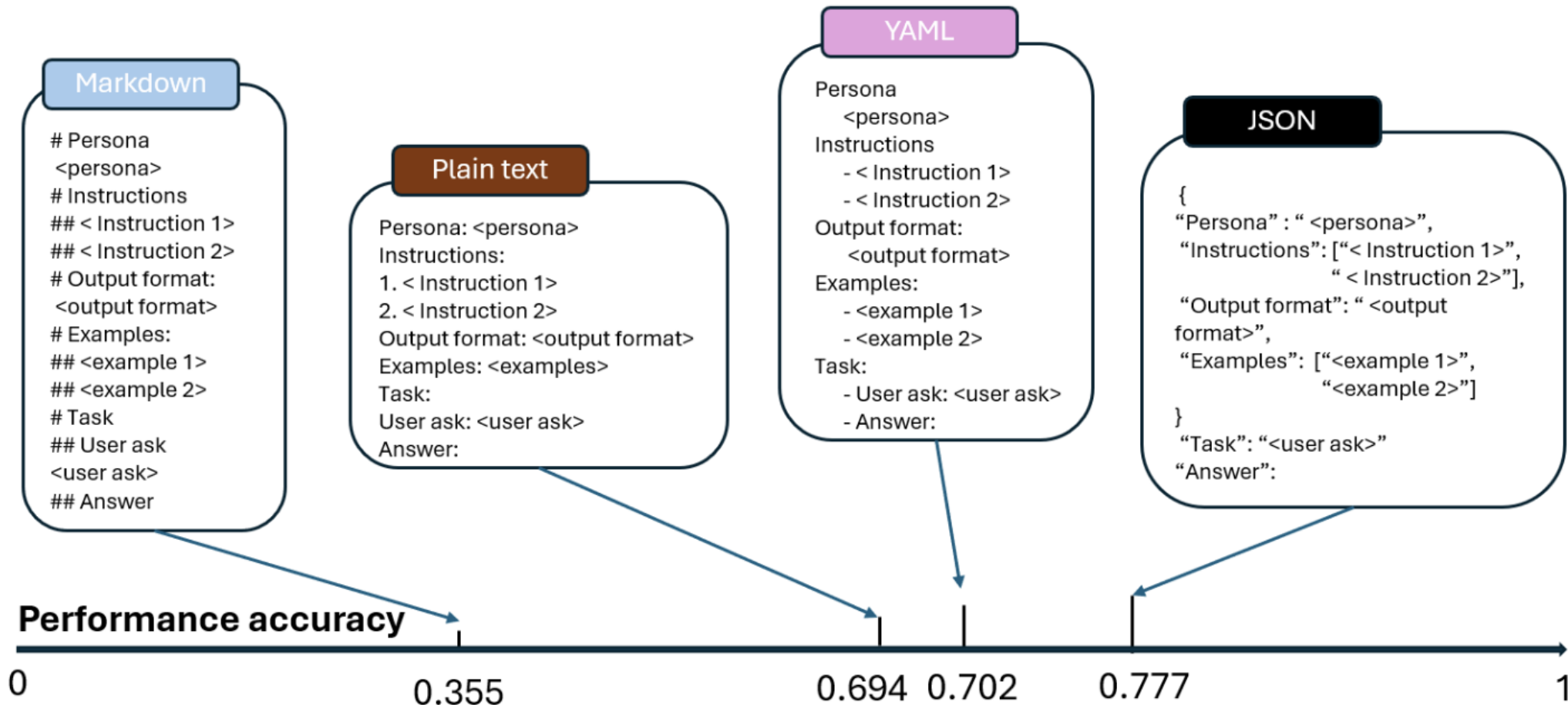
W's	Reasons
Who	do you want ChatGPT to role-play: an engineer, an editor, a teacher, or a student?
What	is the specific context of your prompts?
When	is the specific time period of interest? Specify if so.
Where	is the geographic region or conceptual area?
In what way	do you want ChatGPT to respond: in a programming language, code, text-to-image?

# Prompt Engineering Tricks with examples

- Write clear instructions with clear goals and objectives
  - Use delimiters: triple quotes ("""), triple backticks (`` `), angle brackets (< >), XML tags (<tag> </tag>)
- Summarize the text below about chemical kinetics as a bullet point list of the most important points. The output should be less than 500 words.

```
Text: """
{text input here}
"""
```

# Prompt Engineering Tricks: Formatting



GPT-35-turbo-16k-0613 model for MMLU multi-choice benchmark dataset

# Prompt Engineering Tricks: Role Playing

- Assign a specific role to LLMs, providing contextual information through a role and enhancing the query comprehension
- You are a renowned researcher specialized in computational drug discovery. Help me rewrite the cover letter for an industrial postdoc job for GPCR drug discovery in a pharm company. You write with clarity and conviction, the texts are concise and precise, you maintain an objective, detached tone. When you receive text samples you must summarize and rewrite these, while improving the style of the text. The output should be less than 500 words.

```
Text: ""  
{text input here}  
""
```

# Prompt Engineering Tricks: CoT

- Chain of thoughts/Split complex tasks into simpler subtasks

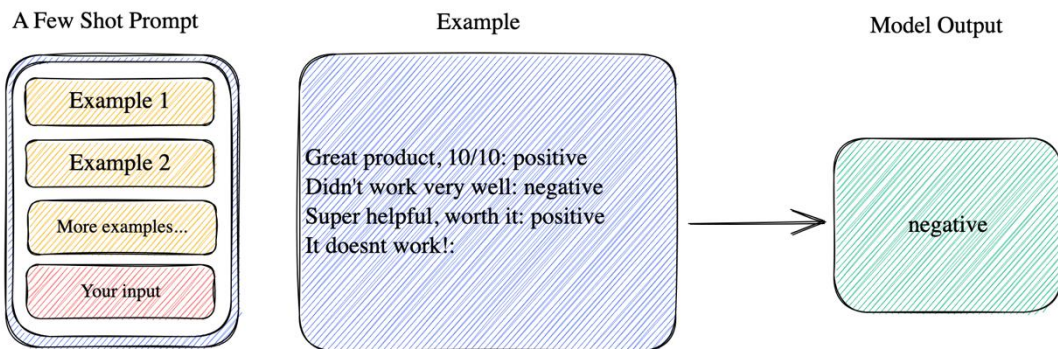
## **Problem:**

A 5.00 g sample of calcium carbonate ( $\text{CaCO}_3$ ) is heated until it completely decomposes into calcium oxide ( $\text{CaO}$ ) and carbon dioxide ( $\text{CO}_2$ ). What mass of  $\text{CaO}$  remains after decomposition?

- Help me get the solution to this problem.
- Help me get the solution to this problem by applying the mass conservation principle.
- You are an undergraduate student taking the general chemistry course. Solve the solution to this problem by applying the mass conservation principle. Explain your thought process step by step, explaining each calculation and assumption made.

# Prompt Engineering Trick:

- Few-shot prompts
  - Input-output pairs
  - Format consistency
  - Task relevance

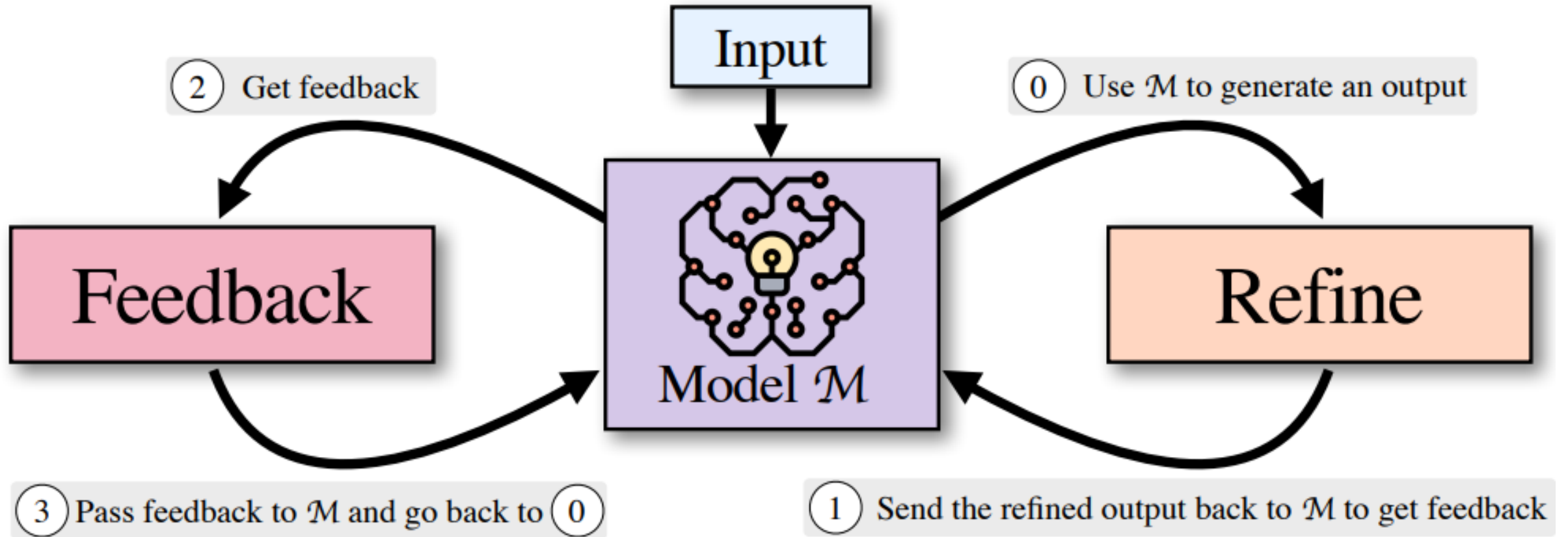


```
1 # Identity
2
3 You are a helpful assistant that labels short product reviews as
4 Positive, Negative, or Neutral.
5
6 # Instructions
7
8 * Only output a single word in your response with no additional fo
9 or commentary.
10 * Your response should only be one of the words "Positive", "Negat
11 "Neutral" depending on the sentiment of the product review you a
12
13 # Examples
14
15 <product_review id="example-1">
16 I absolutely love this headphones – sound quality is amazing!
17 </product_review>
18
19 <assistant_response id="example-1">
20 Positive
21 </assistant_response>
22
23 <product_review id="example-2">
24 Battery life is okay, but the ear pads feel cheap.
25 </product_review>
26
27 <assistant_response id="example-2">
28 Neutral
29 </assistant_response>
```

[1] Tom B. Brown, Language Models are Few-Shot Learners, *NeurIPS*, 2020

[2] Robert L Logan IV, *Cutting Down on Prompts and Parameters: Simple Few-Shot Learning with Language Models*, *ACL*, 2021

# Prompt Engineering Trick: Iterative Refinement





# Prompting Structure for GPT-4.1



# Role and Objective

# Instructions

## Sub-categories for more detailed instructions

# Reasoning Steps

# Output Format

# Examples

## Example 1

## Example 2

# Context

# Final instructions and prompt to think step by step

# Ethical Use of LLMs

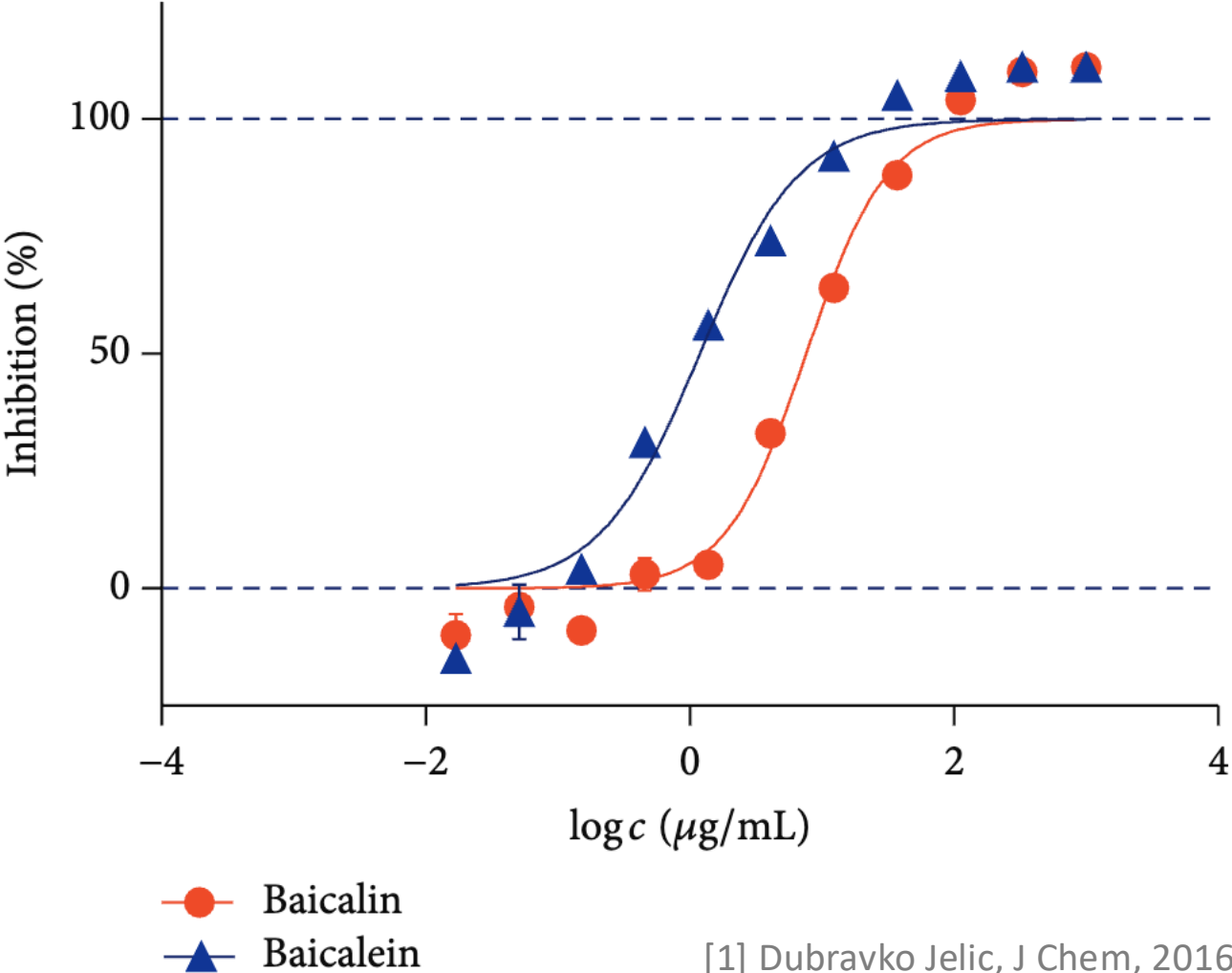


Privacy and Data Security



Bias and Fairness

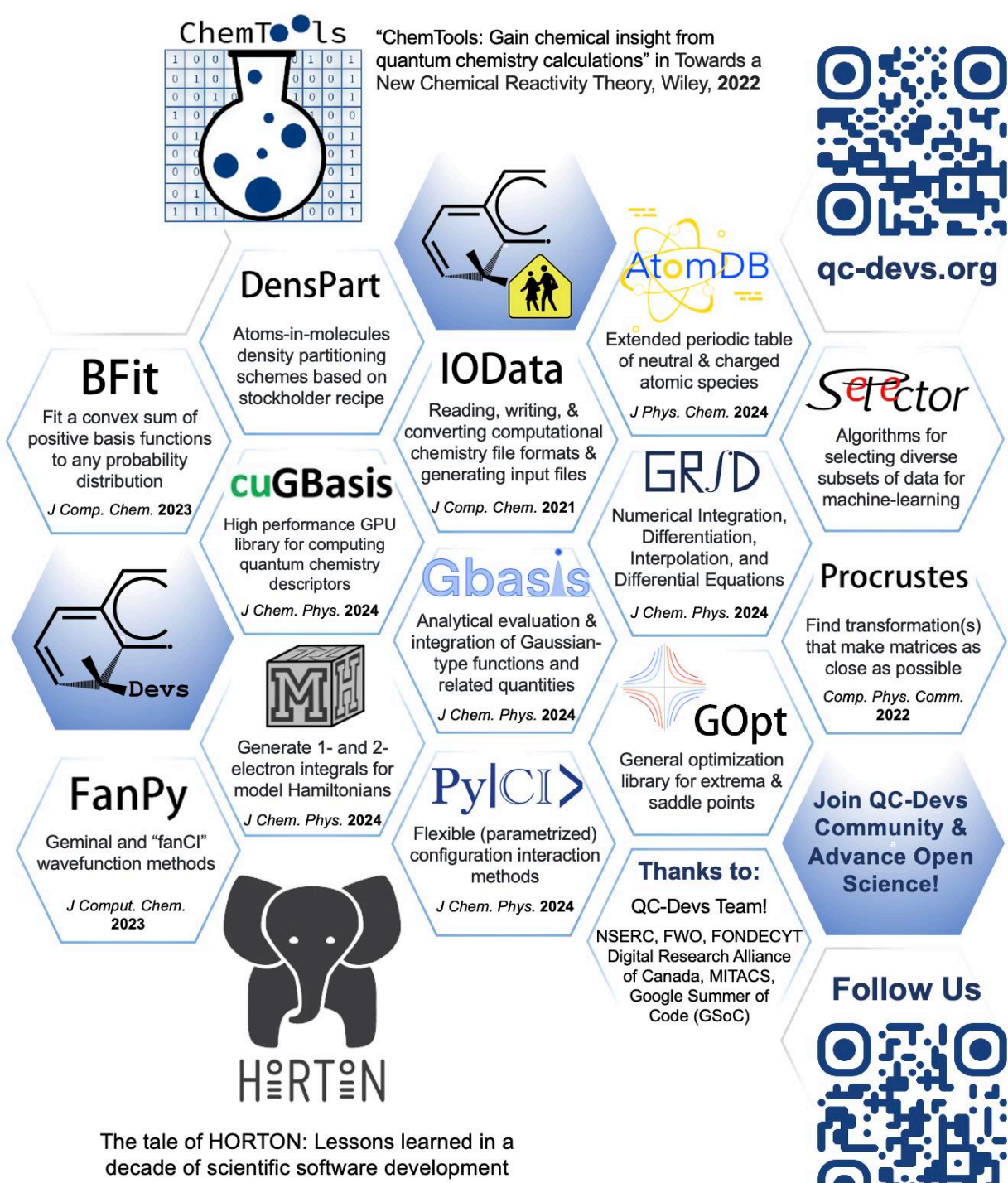
# Plotting Scientific Figures



1	[cNMP](M)	ligand	activity	activity	activity
2	0.0005	Lig_A	89.44276227	93.47812001	91.93199227
3	0.000143	Lig_A	87.54377039	89.91751024	89.61915311
4	0.0000408	Lig_A	80.42255085	87.30639641	84.90631433
5	0.0000117	Lig_A	59.77101417	62.61950199	61.59755516
6	0.00000333	Lig_A	39.83159945	43.8669572	43.76740606
7	0.000000952	Lig_A	18.70531481	28.2002742	23.59909084
8	0.000000272	Lig_A	10.87197331	14.1952091	12.88528639
9	7.77E-08	Lig_A	5.174997678	6.836615571	6.749057335
10	2.22E-08	Lig_A	0.664891967	-0.759351942	0.53903106
11	1E-13	Lig_A	3.038631815	4.700249708	3.688417708
12	0.0005	Lig_B	24.23134409	24.23134409	24.23134409
13	0.0002	Lig_B	22.14122611	21.22679949	21.50888185
14	0.00008	Lig_B	18.87541676	18.61415202	18.82876825
15	0.000032	Lig_B	16.65466641	15.74023979	15.78777996
16	0.0000128	Lig_B	10.64557722	10.90684196	10.80516063
17	0.00000512	Lig_B	6.726606005	6.595973631	6.696211886
18	0.00000205	Lig_B	4.244590903	3.330164287	3.918417287

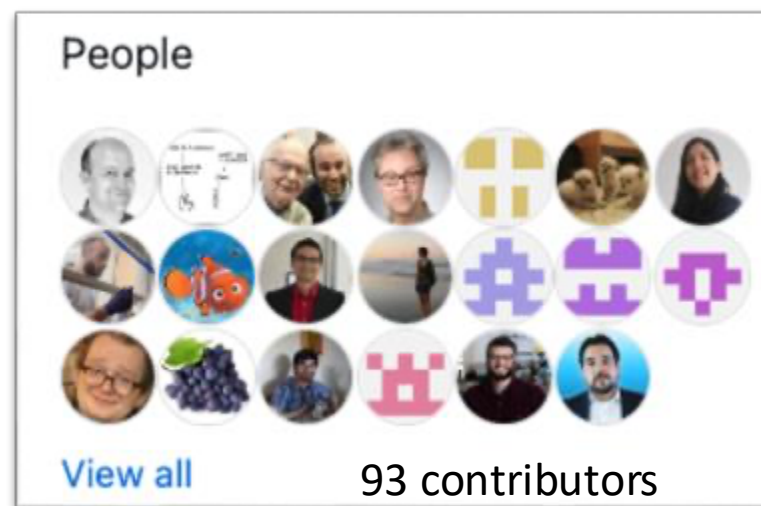
# Resources for Prompt Engineering

1. <https://learn.deeplearning.ai/courses/chatgpt-prompt-eng>
2. <https://www.coursera.org/learn/prompt-engineering>
3. <https://github.com/dair-ai/Prompt-Engineering-Guide>
4. <https://cloud.google.com/blog/products/application-development/five-best-practices-for-prompt-engineering>
5. <https://cloud.google.com/discover/what-is-prompt-engineering?hl=en>
6. <https://platform.openai.com/docs/guides/prompt-engineering>
7. <https://docs.anthropic.com/en/docs/build-with-claude/prompt-engineering/overview>



# QC-Devs Software Consortium

<https://github.com/theochem/qcdevs@gmail.com>



Thanks to NSERC, FWO, FONDECYT, Digital Research Alliance of Canada, MITACS, and Google Summer of Code (GSoC).