IC08 Leveraging LLM and RAG for Advanced Pharmaceutical Statistical Programming

A Novel Chatbot Framework Approach

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Biography

Jaime Yan:

Jaime Yan is a statistical programmer with Merck Sharp & Dohme. He has seven years of experience working as a statistical programmer in the oncology and cardiovascular therapy area in the pharmaceutical industry. He has used SAS and R and Python for seven years to handle clinical trial data and prepare clinical reports.

Chao Su:

Chao Su has 14-year experience as statistical programmer. He has worked at different pharmaceutical companies and CROs. He is an expert in SAS and R, Currently, he is working in Merck Sharp & Dhome, based in new Jersey.

Changhong Shi:

Changhong Shi been a statistical programmer for 21 years. Before that, she worked as a software developer using Oracle, VB script and Java. Recently she acquired knowledge on R.

Currently, Changhong is a director in statistical programming in Merck Sharp & Dhome, based in new Jersey.

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Agenda

- Introduction
- Proposed framework
- Future work

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Abstract the three main tasks

As a statistical programmer, we:

1. *Review the document*
2. *Data explore(check the ADaM data)*
3. *Output the report*

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Target

Use LLM with Framework like LangChain/llamaIndex to optimize:

1. ***Documents review***
2. ***Data explore(check the ADaM data)***
3. ***Report generate***

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Former Process

Review the documents:

Contains:

- *CDISC standard(SDTM, ADaM IG)*
- *SAP & Protocol*
- *Company training material*

Self learning or workshop

Data explore(check the ADaM data):

- *Edit check(data quality)*
- *Request from custom(Stat/Clinical etc.)*

Based on requirement to prepare sas/r code. Take 1-2 days

Prepare code&Output the report:

- *Based on analysis data(ADaM datasets) and mock(ICH E3 guidance)*
- *Use company macro(most), user defined sas code*

Taken most of the time of the process

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Former Work to simplify the process

Data explore(check the ADaM data):

- *Edit check: P21 report*
- *Develop R shiny app*

Review the document:

- *Prepare training material*

Output the report:

- *Transfer from user defined code to standard macro.*
- *Provide interface to select the condition for macro(R shiny etc.)*
- *Make data machine readable(CDISC 360 project)*

Gaps in Using Pre-Trained LLM Directly

***Domain Knowledge**: Pre-trained LLMs often lack the nuanced understanding necessary for pharmaceutical tasks, such as interpreting complex regulatory standards.*

***Security Concerns**: Processing confidential data with LLMs poses risks, necessitating strict adherence to data protection laws like HIPAA.*

***Industry Optimization**: General-purpose LLMs may not meet the specific needs of pharmaceutical statistical programming, affecting performance and compliance.*

Exploring Potential Solutions

Helpful method:

Prompt engineering, let LLM better know user's request, not give extra info beside the LLM original training data.

Feasible method:

- *Advanced Retrieval-Augmented Generation (RAG): Improves LLM's contextual understanding, enabling precise information retrieval and response generation.(Doc and analysis)*
- *Open source LLM, deploy in server/cloud or run in local(security concern)*
- *SAS Macro Integration: Fine-tuning LLMs for seamless interaction with SAS macro libraries, streamlining the TLF generation process.(reporting)*

Why LLM + RAG + Fine tunning + Code interpreter could work

LLM:

- *LLM naturally good at process/organize and do summary for text.*
- *LLM has the ability to abstract the feature/rule/relationship by fine tuning.*

RAG:

- *Provide domain knowledge based on user prepared document to LLM.*
- *Would work as 'RAG code Model' by prepareing the train data to LLM.*

Fine tuning:

- *Link the private sas mcro library to LLM, go further, make anlysis and report process automation.*

Code interpreter:

- *Deal/run with the LLM provided code in desired local environment.*

Potential LLM solution

One Chatbot empowered by LLM:

Review the document:

- *RAG(optimized for pdf and support the other format)*

Outcome: Search key point and get summary by communicating with file

Data explore(check the ADaM data):

- *RAG + SAS kernel*

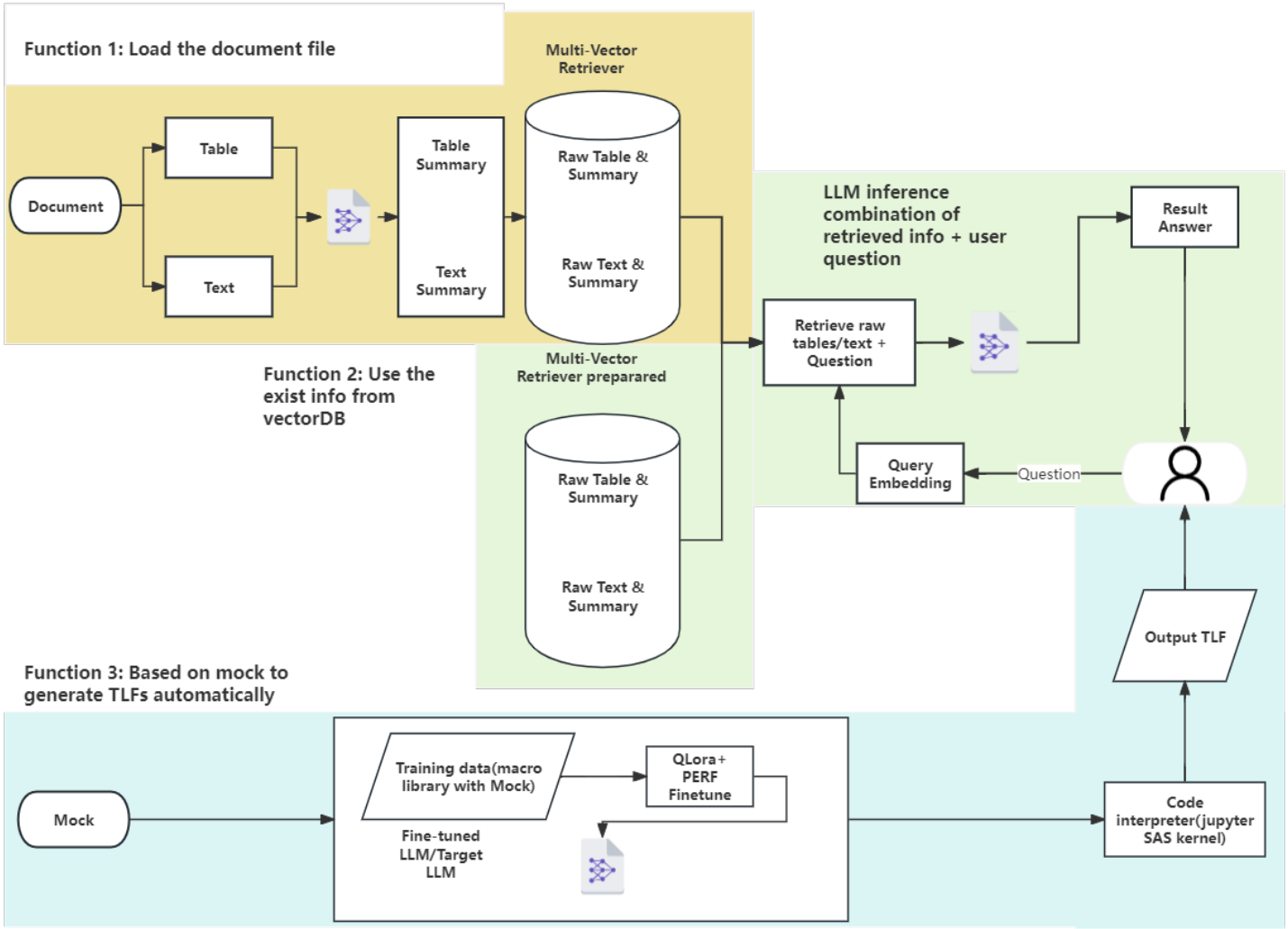
Outcome: Deal with most of the task immediately by ask question(chat using nature language)

Output the report:

- *Well-designed SAS reporting macro system + Fine-tuned LLM*

Outcome: End to end automation report generator (from mock to report immediately)

Proposed Framework for the Chatbot



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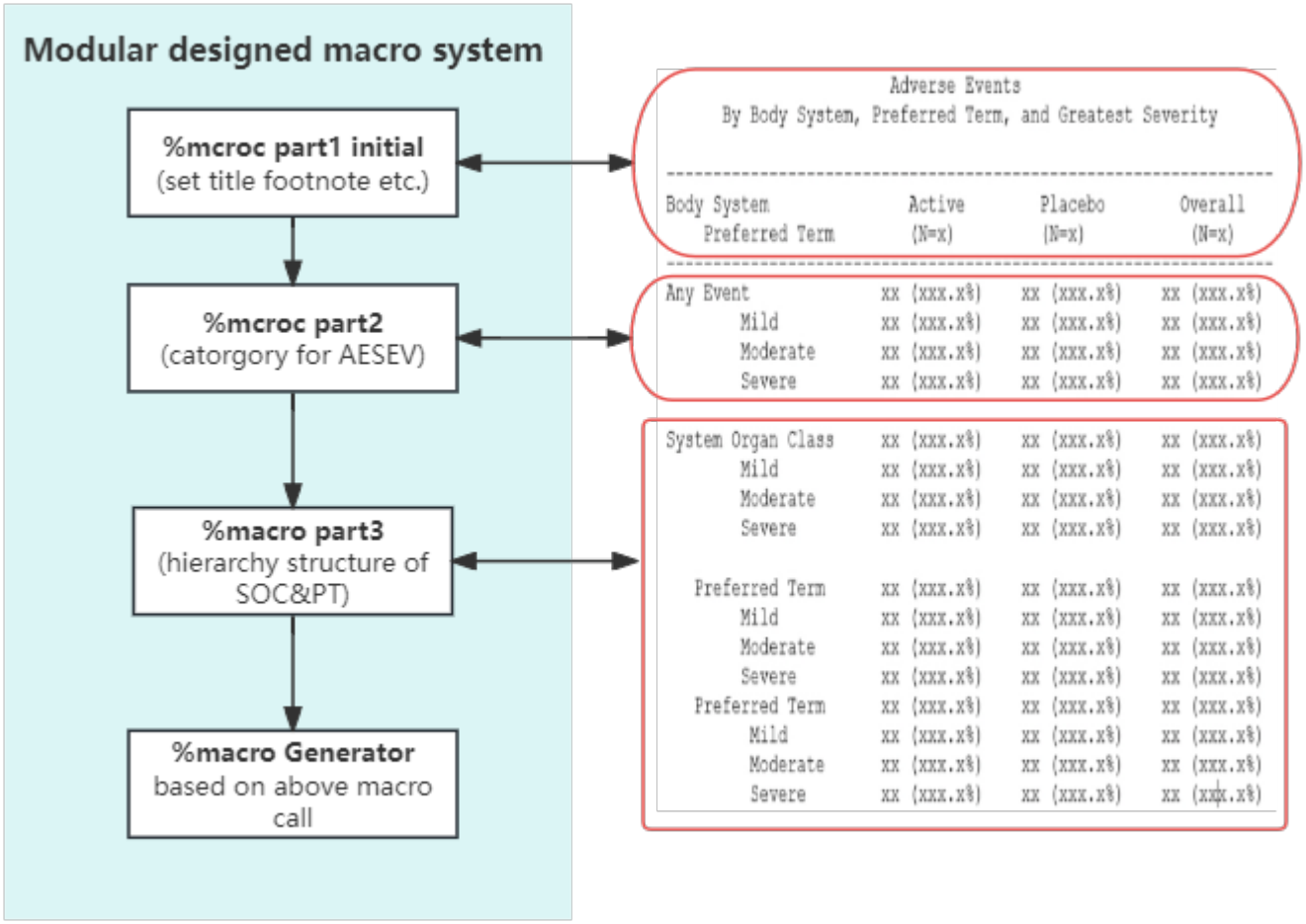
Design the reporting macro fit to LLM

Macro Library Compatibility: Adjusts macro libraries to be more compatible with LLM architectures, facilitating dynamic report generation.



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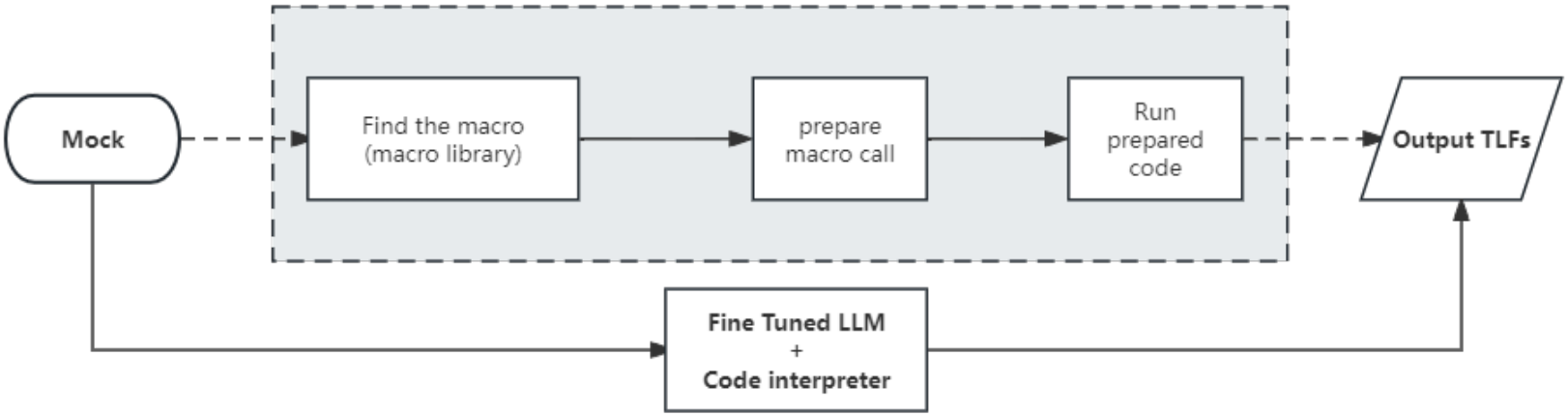
End to end TLFs generator process

Fine-Tuning Process: Focuses on teaching LLM to recognize and replicate patterns between mock templates and SAS macro calls, improving TLF generation accuracy.

Fine-Tuned LLM give ready to use macro call based on input mock, then code interpreter(SAS kernel) will run the code and generate the report.



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Innovation point

Integrate the framework and technic in LLM filed for statistical programming usage.

Give the solution to solve the three main task in statistical programming:

1. *Use RAG for statistical programming related documents, optimize the pdf embedding.*
2. *'Train' RAG by providing the dataset using CDISC standard and SDTM/ADaM data structure/scheme.*
3. *Test and indicate which kind of SAS report macro library would fit to LLM and achieve end to end report generating automatically.*

In summary, the proposed framework and solution is cost efficient and would cover most of routine daily work of statistical programming.

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Future Work

- *Automation the validation process by combine well designed qc sas macro system with LLM and check the result with human involve.*
- *Implement new advanced technic and framework in LLM area from latest paper.*
- *Adopt in local environment by using distillation model.*
- *Cover some task in early phase(PK/PD, simulation etc.).*
- *Seeks to foster further development of these solutions in an open, collaborative environment across the industry, ultimately enhancing the efficacy and reliability of statistical programming in clinical research*

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Q&A

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