

# QSP-Copilot: An AI-Powered Multi-Agent System for Accelerating Model Development

Ali Farnoud<sup>1</sup>, Anuraag Saini<sup>1</sup>

<sup>1</sup>.Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany

## Highlights

**Pain point:** QSP model development is an iterative resource intensive process which demands tight cross-disciplinary effort

**Solution:** QSP-Copilot, a cloud based, AI-driven multi-agent platform to automate QSP workflows

**Core tech:** Integrates large-language models + retrieval-augmented generation under human-in-the-loop oversight

**Impact:** Accelerates end-to-end QSP project time by at least 40 %

## Introduction

**Quantitative Systems Pharmacology (QSP)** combines systems biology, mechanistic modelling, and pharmacology to simulate disease progression and therapeutic effects.

QSP model development requires significant manual effort, including literature review, building biologically relevant mathematical framework, hypothesis generation, model calibration, and validation [1]. The process is often time-consuming, iterative requiring close collaboration between biologists, pharmacologists, and mathematical modelers.

To improve these aspects, we introduce **QSP-Copilot**, a cloud-based, AI-powered multi-agent system designed to streamline QSP workflows.

QSP-Copilot integrates multiple large language models (LLMs), retrieval-augmented generation (RAG), and AI-driven multi-agent orchestration [2] to accelerate model building, calibration, and validation, while maintaining human oversight for final decision making, compliance and interpretability.

### Challenges in QSP model development

#### Complex Biological Systems

- **Multi-scale complexity:** Diseases involve interactions across molecular, cellular, tissue, and organism levels
- **Biological uncertainty:** Gaps in pathway knowledge require evidence-based assumptions
- **Interaction diagram:** Translating biological mechanisms into coherent interaction networks
- **Data prioritization:** Weighing human vs. animal vs. in vitro data with appropriate confidence levels
- **Parameter identification:** Determining biologically relevant values from literature or proprietary datasets

#### Mathematical & Computational Hurdles

- **Mathematical representation:** Translating biological networks into appropriate coupled ODE systems
- **Technology stack:** Choosing optimal programming environments (MATLAB, R, Julia, Python)
- **Calibration complexity:** Parameter estimation with limited data and multiple constraints
- **Model identifiability:** Ensuring unique solutions and addressing parameter interdependence
- **Computational efficiency:** Optimizing simulation performance for parameter sweeps, virtual population generation, etc

## Methods

Modular multi-agent AI framework, specialized agents handle distinct modelling tasks; AI accelerates retrieval and reasoning while scientists stay in control.

### Multi-Agent System for QSP Modelling

- **Literature Review Agent:** reviews PDFs, extracts mechanisms/components/interactions, retrieves supporting references, and proposes a list of interactions for user approval.
- **Model Building Agent:** converts the diagram into mathematical framework, performs parameter estimation, calibration, sensitivity analysis, and virtual cohort generation.
- **Orchestration Layer:** coordinates other agents so they collaborate seamlessly by keeping user in the loop.

### Dynamic LLM Selection for Optimized Performance

- Users can switch between economic LLMs (Claude 3 Haiku, GPT-4o-mini) for rapid look-ups and high-reasoning LLMs (GPT-4o, Claude 3 Sonnet) for complex tasks such as parameter value search, generate valid assumption and implementation in the model.

### Human-in-the-Loop (HITL) Oversight

- At every step, modellers review AI-generated citations, assumptions, and parameters before acceptance, ensuring scientific rigor, interpretability, and compliance.

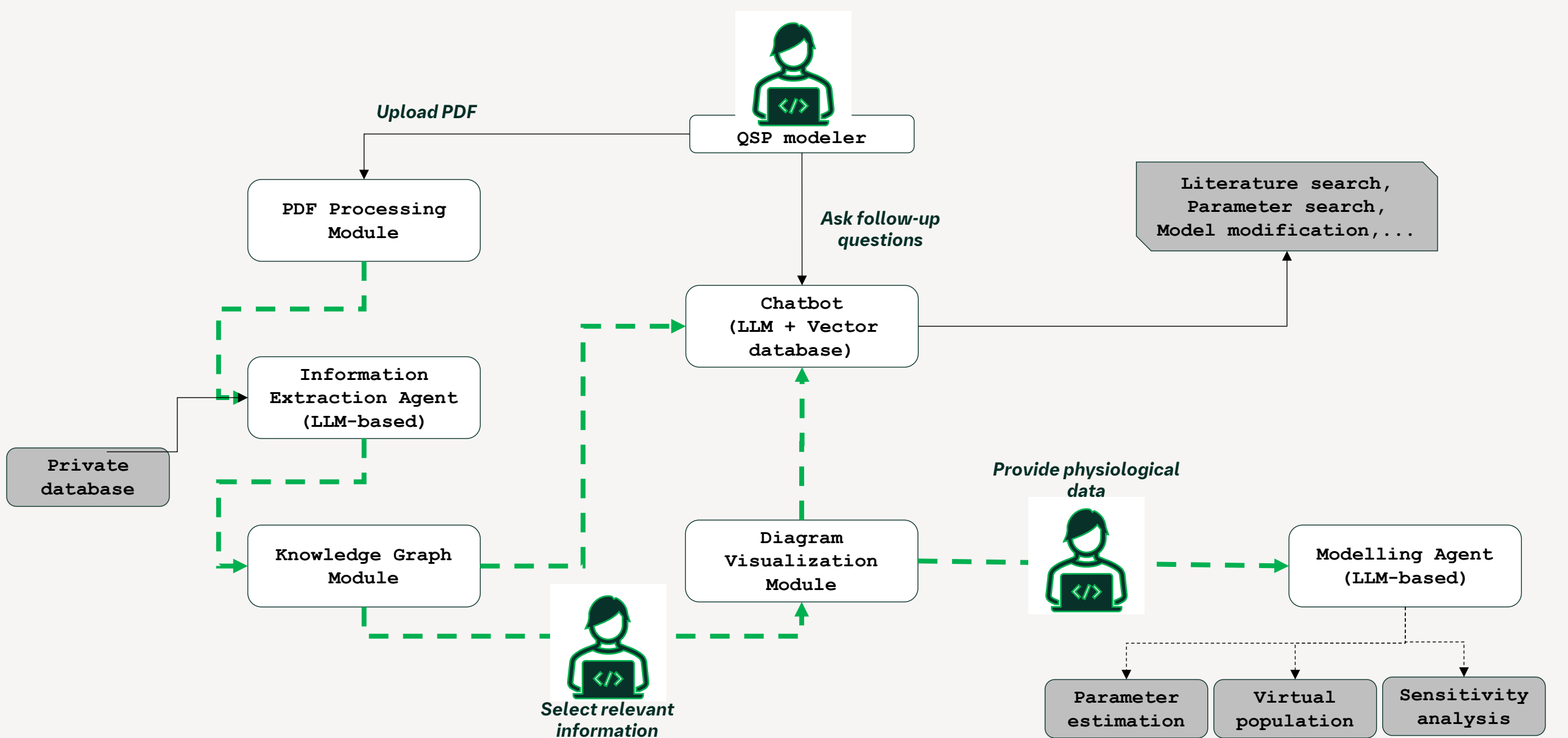
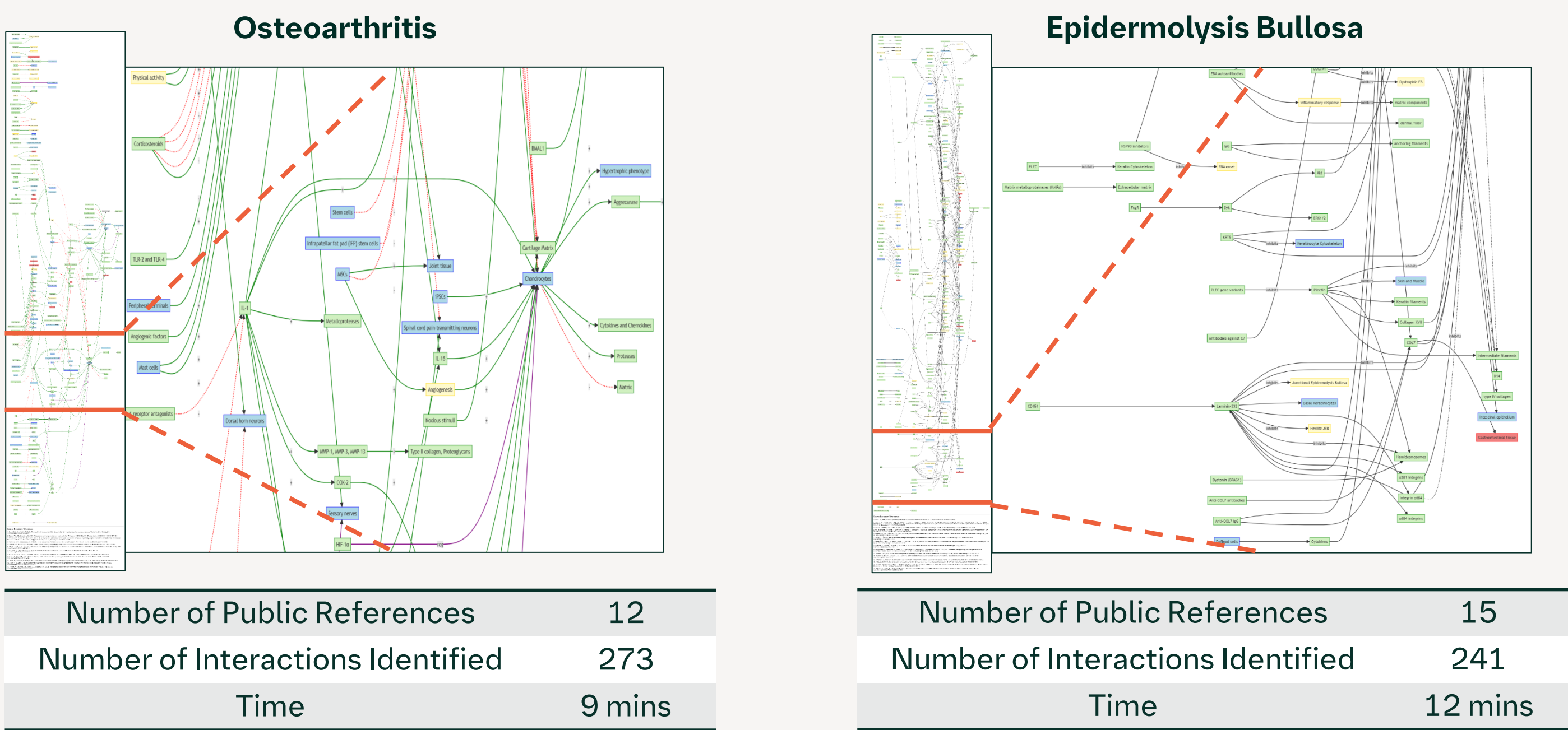


Figure 2. System architecture of QSP-Copilot

## QSP-Copilot showcase for Diseases

### Biological Interactions Extraction Using Public Literature



### Proposed Solution

#### Current Approach

- Knowledge Gaps**
- Limited cross-therapeutic expertise
  - Siloed information across disciplines
- Process Challenges**
- Lengthy development cycles
  - Manual data integration
  - Slow iterative refinement
- Communication**
- Terminology gaps between experts
  - Inefficient knowledge transfer

#### With QSP-Copilot

- Knowledge Integration**
- Comprehensive knowledge base
  - Intelligent extraction from literature
- Accelerated Development**
- **40% faster** model development
  - Automated diagram to ODE translation and faster literature/parameter search
  - Rapid hypothesis testing cycles
- Enhanced Collaboration**
- Streamlined expert communication
  - Interactive model visualization

## Conclusion

- **Faster turn-around time:** Across three internal test projects, QSP-Copilot shortened full model-development cycles by 40 % through automated literature mining, code generation, and structural model update.
- **Enhanced collaboration & traceability:** A shared workspace with built-in citation tracking and versioned artifacts boosted cross-disciplinary transparency and reproducibility.
- **Human-in-the-loop rigor:** Expert review checkpoints preserved scientific validity; users reported a brief learning curve but high trust after two to three iterations.
- **Scalable & extensible:** The modular architecture readily integrates new agents and external solvers (R, python, Julia), supporting applications across multiple therapeutic areas.

### References

1. Gadkar, Kapil, et al. "A six-stage workflow for robust application of systems pharmacology." CPT: pharmacometrics & systems pharmacology 5.5 (2016): 235-249.
2. Wu, G., Bansal, G., Zhang, J., Wu, Y., Li, B., Zhu, E., ... & Wang, C. (2023). Autogen: Enabling next-gen llm applications via multi-agent conversation. arXiv preprint arXiv:2308.08155.

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