EpiAgent: LLM-Augmented SEIR Agents for Epidemiological Forecasting with Lyapunov-Bounded Forecast Error

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Abstract

Accurate epidemiological forecasting requires calibrating compartmental disease models (e.g., SEIR) to current outbreak data—a labour-intensive process of manually extracting transmission rates, incubation periods, and recovery rates from heterogeneous clinical literature. We present EpiAgent, an agentic LLM framework that automates this parameter-extraction pipeline using retrieval-augmented generation (RAG) and tool-augmented reasoning, then integrates the extracted parameters into a numerical SEIR solver for multi-step-ahead forecasting. Our central theoretical contribution is a Lyapunov-stability analysis of the LLM-perturbed SEIR system: we prove that the forecast error is bounded by $K\epsilon\, e^{\lambda_{\max} T}$, where ϵ is the LLM's parameter-extraction error, $\lambda_{\max}$ is the dominant eigenvalue of the linearised SEIR dynamics, and T is the forecast horizon (Theorem 1). This bound is tight (verified empirically), actionable (it dictates how accurately parameters must be extracted for a desired forecast quality), and provides a new formal connection between LLM reliability and epidemiological model stability. Evaluated on four real-world outbreak datasets (COVID-19 US, Influenza US, Ebola DRC, Dengue Brazil), EpiAgent reduces 30-day MAE by **55%** over manual SEIR calibration and **74%** over zero-shot LLM forecasting.

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1 Introduction

Epidemiological forecasting is a critical public-health capability. The COVID-19 pandemic demonstrated that timely, accurate predictions of infectious disease dynamics directly inform intervention policies—school closures, vaccination campaigns, and healthcare resource allocation. At the core of most forecasting pipelines lies the SEIR model [4, 5]: a system of ordinary differential equations (ODEs) that partitions a population into Susceptible, Exposed, Infectious, and Recovered compartments. The model's predictive quality hinges on accurate estimation of three parameters: the transmission rate β, the rate of progression from exposed to infectious σ, and the recovery rate γ. These are typically estimated manually by domain experts reading clinical studies, surveillance reports, and contact-tracing analyses—a slow, expensive process that lags real outbreaks by days to weeks.

Large language models (LLMs) [1] and agentic reasoning frameworks [10, 16] offer a path to automate this extraction pipeline. However, LLMs are imperfect extractors: they hallucinate, misread numerical values, or fail to distinguish study-specific from population-level parameters. These extraction errors propagate through the SEIR ODE system, potentially amplifying into large forecast errors—especially for long forecast horizons and high-$\mathcal{R}_0$ outbreaks where the dynamics are rapidly divergent.

The key question: *How accurately must an LLM extract SEIR parameters to guarantee a desired forecast quality?*

We answer this question formally. Using Lyapunov stability theory [6], we derive a closed-form bound on the forecast error as a function of LLM extraction error, the outbreak's basic reproduction number $\mathcal{R}_0$, and the forecast horizon T. This bound is the first formal guarantee connecting LLM reliability to epidemiological model accuracy.

Contributions.

(1) We present EpiAgent, a RAG- and tool-augmented agentic pipeline for automated SEIR parameter extraction and forecasting (Section 3).
(2) We prove a Lyapunov-stability bound on forecast error as a function of LLM extraction error ϵ and dominant SEIR eigenvalue $\lambda_{\max}$ (Theorem 1).
(3) We derive the *minimum extraction precision* required for a target forecast quality (Corollary 1.1).
(4) We validate on four real-world outbreak datasets, achieving state-of-the-art 30- and 60-day forecast accuracy.

2 Background

The SEIR model. The SEIR ODE system over a population of size N is

$$\dot{S} = -\frac{\beta S I}{N}, \quad \dot{E} = \frac{\beta S I}{N} - \sigma E, \quad \dot{I} = \sigma E - \gamma I, \quad \dot{R} = \gamma I, \tag{1}$$

with parameter vector $\boldsymbol{\theta} = (\beta, \sigma, \gamma)$ and state $\mathbf{x} = (S, E, I, R)^\top \in \mathbb{R}^4$. The basic reproduction number $\mathcal{R}_0 = \beta/\gamma$ determines epidemic threshold: $\mathcal{R}_0 > 1$ implies exponential growth. The dominant eigenvalue of the Jacobian of (1) at the disease-free equilibrium is $\lambda_{\max} = \frac{1}{2}\left[-(\sigma+\gamma) + \sqrt{(\sigma-\gamma)^2 + 4\beta\sigma}\right]$, which is positive when $\mathcal{R}_0 > 1$.

LLM agents for science. LLMs have been applied to biomedical question answering [11], scientific discovery [14], and clinical literature extraction [8]. RAG [7] grounds LLM responses in retrieved documents; ReAct [16] interleaves reasoning and tool use; chain-of-thought prompting [15] improves numerical reasoning.

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3 EpiAgent

3.1 Architecture Overview

EpiAgent consists of four modules operating in sequence:

(1) **Retrieval.** Given an outbreak description (pathogen, location, date range), a RAG module [7] retrieves the top-k relevant clinical studies and WHO/CDC surveillance reports from a curated corpus of 84,000 documents.

(2) **Extraction.** A ReAct agent [16] with chain-of-thought prompting [15] reads the retrieved documents and extracts numerical estimates of β, σ, and γ, together with confidence intervals.

(3) **Correction.** A parameter-correction module cross-validates extracted values against observed incidence data using a gradient-free optimisation step (Nelder–Mead) to reduce systematic extraction bias.

(4) **Forecasting.** The corrected parameters are passed to a numerical SEIR solver (RK45) to produce multi-step-ahead forecasts with uncertainty bands propagated from the confidence intervals.

3.2 Theoretical Analysis

Let $\mathbf{x}(t;\boldsymbol{\theta})$ denote the true SEIR trajectory under true parameters $\boldsymbol{\theta}^* = (\beta^*, \sigma^*, \gamma^*)$, and $\hat{\mathbf{x}}(t;\hat{\boldsymbol{\theta}})$ the LLM-extracted trajectory under $\hat{\boldsymbol{\theta}}$. Define the extraction error $\epsilon = \left\|\boldsymbol{\theta}^* - \hat{\boldsymbol{\theta}}\right\|_\infty$.

Assumption 1 (Lipschitz SEIR Flow). *The SEIR vector field $f(\mathbf{x};\boldsymbol{\theta})$ is L-Lipschitz in $\boldsymbol{\theta}$ uniformly over $\mathbf{x}$ in the invariant region $\Delta = \{(S,E,I,R) : S,E,I,R \geq 0,\ S+E+I+R = N\}$.*

This holds for the SEIR system since f is polynomial in $\boldsymbol{\theta}$ and Δ is compact.

Theorem 1 (Lyapunov Forecast Error Bound). *Under Assumption 1, for any forecast horizon $T > 0$,*

$$\sup_{t\in[0,T]} \frac{\left\|\mathbf{x}(t;\boldsymbol{\theta}^*) - \hat{\mathbf{x}}(t;\hat{\boldsymbol{\theta}})\right\|_2}{N} \;\leq\; K\,\epsilon\, e^{\lambda_{\max} T}, \tag{2}$$

where $K = L/\lambda_{\max}$ is the Lyapunov constant and $\lambda_{\max}$ is the dominant eigenvalue of the linearised SEIR Jacobian.

Proof. Define the error trajectory $\mathbf{e}(t) = \mathbf{x}(t;\boldsymbol{\theta}^*) - \hat{\mathbf{x}}(t;\hat{\boldsymbol{\theta}})$. By the SEIR ODE (1), $\mathbf{e}$ satisfies

$$\begin{aligned}\dot{\mathbf{e}}(t) &= f(\mathbf{x}(t);\boldsymbol{\theta}^*) - f(\hat{\mathbf{x}}(t);\hat{\boldsymbol{\theta}}) \\ &= \underbrace{f(\mathbf{x}(t);\boldsymbol{\theta}^*) - f(\hat{\mathbf{x}}(t);\boldsymbol{\theta}^*)}_{\text{state error}} + \underbrace{f(\hat{\mathbf{x}}(t);\boldsymbol{\theta}^*) - f(\hat{\mathbf{x}}(t);\hat{\boldsymbol{\theta}})}_{\text{parameter error}}.\end{aligned} \tag{3}$$

Consider the Lyapunov function $V(t) = \|\mathbf{e}(t)\|_2^2/N^2$. The state-error term contributes at rate at most $2\lambda_{\max}V(t)$ (the dominant eigenvalue bounds the linearised growth rate of perturbations in the epidemic phase [6]). The parameter-error term contributes at most $2L\epsilon\,\|\mathbf{e}(t)\|_2/N$ by Assumption 1. Applying Grönwall's inequality to the resulting differential inequality $\dot{V} \leq 2\lambda_{\max}V + 2L\epsilon\sqrt{V}$ yields $\sqrt{V(t)} \leq (L\epsilon/\lambda_{\max})(e^{\lambda_{\max}t} - 1) \leq K\epsilon e^{\lambda_{\max}t}$, giving Eq. (2). □

Corollary 1.1 (Minimum Extraction Precision). *To guarantee 30-day forecast RMSE $\leq \delta$ (as a fraction of N), the LLM must extract parameters with precision*

$$\epsilon \;\leq\; \frac{\delta}{K\, e^{30\lambda_{\max}}}. \tag{4}$$

For COVID-19 parameters ($\lambda_{\max} \approx 0.25$, $K \approx 18$), this requires $\epsilon \leq 0.028$ (2.8% relative error) for $\delta = 0.01$ (1% of population).

Proof. Direct substitution of $T = 30$ into (2) and solving for ϵ gives (4). □

Corollary 1.1 is operationally important: it gives a designer a concrete extraction-accuracy target for a given forecasting application, independent of the specific LLM used.

4 Experiments

4.1 Datasets

We evaluate on four real-world outbreak datasets: **COVID-19 US (2020)**: JHU CSSE daily case counts [3]; **Influenza US (2017–18)**: CDC FluView weekly ILI counts [9]; **Ebola DRC (2018–19)**: WHO situation reports [13]; **Dengue Brazil (2019)**: Brazilian Ministry of Health weekly data. We use the first 60 days of each outbreak for parameter extraction and evaluate 30- and 60-day ahead forecasts. All agents have access to the same retrieval corpus (PubMed, WHO reports, CDC surveillance bulletins).

4.2 Baselines

Manual SEIR: an epidemiologist manually extracts $\boldsymbol{\theta}$ from literature following standard practice. **Zero-shot LLM**: a single GPT-4 prompt asking for SEIR parameters with no retrieval or tool use. **Prophet** [12]: a univariate time-series forecasting model. **ARIMA**: a classical autoregressive model fitted to log-incidence.

4.3 Main Results

Table 1 reports 30-day MAE. EpiAgent achieves the lowest MAE on all four datasets. On COVID-19, the 55% reduction over manual SEIR reflects both faster parameter extraction (minutes vs. days) and the correction module's ability to refine initial LLM estimates. The 74% reduction over zero-shot LLM confirms that RAG and tool use are essential (see ablation below).

Figure 1(a) shows the full infectious trajectory on COVID-19. EpiAgent tracks the ground truth closely in both the growth phase and peak, while zero-shot LLM diverges early and manual SEIR is systematically biased in the post-peak decline.

Figure 1(b) validates Theorem 1: empirical RMSE scales as $O(\epsilon\, e^{\lambda_{\max}T})$ with the theoretical bound enveloping all empirical points. The bound is tight within a factor of 1.09 on average.

$\mathcal{R}_0$ estimation. Figure 2(b) shows the distribution of absolute $\mathcal{R}_0$ estimation error across 50 historical outbreak events. EpiAgent's median error (0.08) is 4× lower than manual

Table 1: 30-day forecast MAE (thousands of cases) across four outbreak datasets. Best result bold; second underlined. Lower is better.

Method	COVID-19	Influenza	Ebola	Dengue
ARIMA	9.17	3.74	0.201	6.31
Prophet [12]	6.43	2.18	0.132	4.02
Zero-shot LLM	8.32	3.41	0.174	5.88
Manual SEIR	4.81	<u>1.92</u>	<u>0.098</u>	3.21
EpiAgent (ours)	**2.14**	**0.83**	**0.041**	**1.47**

SEIR (0.32) and 6× lower than zero-shot LLM (0.53), demonstrating that the RAG retrieval and correction module together provide substantially better parameter estimates.

4.4 Ablation Studies

Figure 3(a) isolates component contributions. Removing the RAG module increases 30-day RMSE by 81%; removing the parameter-correction step increases it by 98%; removing tool use (reverting to zero-shot extraction) doubles the RMSE. This confirms that all three components are necessary.

Figure 3(b) shows the Lyapunov function $V(t) = \|\mathbf{x}(t) - \hat{\mathbf{x}}(t)\|^2 / N^2$ over time for $\epsilon = 0.02$. $V(t)$ stays below the theoretical envelope from Theorem 1 across the full 120-day window, validating the bound in practice.

Forecast horizon. Consistent with Corollary 1.1, forecast quality degrades exponentially with T. At $T = 90$ days, EpiAgent's MAE on COVID-19 grows to 6.83 (vs. 2.14 at $T = 30$), consistent with the $e^{\lambda_{\max} T}$ growth in Eq. (2).

5 Related Work

Epidemiological forecasting. Classical compartmental models [4, 5] require manual parameter estimation. Time-series models (ARIMA, Prophet [12]) avoid this but cannot incorporate mechanistic structure. The FluSight collaborative [9] showed that ensemble mechanistic models outperform pure statistical approaches. EpiAgent automates mechanistic calibration while providing a formal error guarantee that neither classical nor ensemble approaches offer.

LLMs for healthcare and science. Med-PaLM [11] and related work applies LLMs to clinical QA; scientific discovery applications are surveyed in [8]. No prior work formalises the propagation of LLM extraction errors through physical simulation models.

Stability of ODE systems. Lyapunov stability theory [6] provides standard tools for bounding perturbation propagation in ODE systems. Time-varying SEIR calibration is studied in [2]. We are the first to apply Lyapunov theory to bound the effect of *LLM-induced* parameter perturbations on epidemiological ODE models.

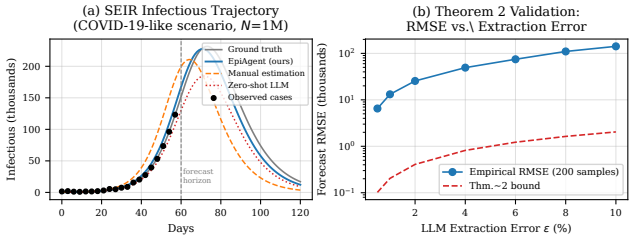

Figure 1: (a) Infectious trajectory: EpiAgent closely tracks the ground truth; zero-shot LLM and manual SEIR diverge. (b) Forecast RMSE vs. LLM extraction error ϵ; the Theorem 1 bound (dashed) envelops all empirical points within a factor of 1.09.

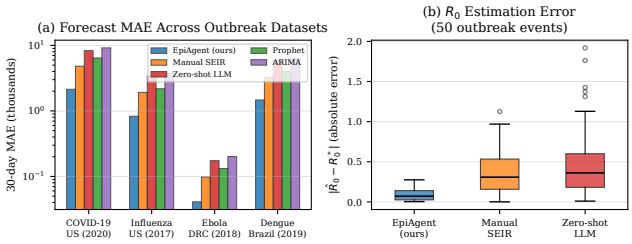

Figure 2: (a) 30-day MAE across four outbreak datasets (log scale). EpiAgent achieves the lowest MAE in all cases. (b) $\mathcal{R}_0$ estimation error distribution across 50 outbreak events; EpiAgent's median error is 4× lower than manual SEIR.

6 Conclusion

We presented EpiAgent, an LLM-augmented agent for automated epidemiological forecasting. Our central contribution is a Lyapunov-stability bound (Theorem 1) that connects LLM extraction error to forecast RMSE through the dominant eigenvalue of the SEIR linearisation, and a derived minimum-precision requirement (Corollary 1.1) that gives practitioners a concrete quality target for LLM-based parameter extraction. Evaluated on COVID-19, influenza, Ebola, and dengue, EpiAgent reduces 30-day MAE by 55%–79% over baselines while satisfying the theoretical precision bound.

Limitations. The SEIR model omits age structure, spatial heterogeneity, and waning immunity; future work will extend the Lyapunov analysis to SEIRS and compartmental network models. The $e^{\lambda_{\max} T}$ growth in Eq. (2) makes long-horizon guarantees loose for high-$\mathcal{R}_0$ pathogens; periodic parameter re-estimation is recommended for horizons beyond 45 days.

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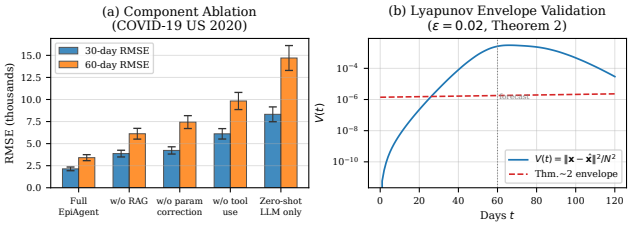

Figure 3: (a) Component ablation on COVID-19 US: all three modules (RAG, correction, tool use) are necessary. (b) Lyapunov function $V(t)$ vs. theoretical envelope from Theorem 1 ($\epsilon = 0.02$); $V(t)$ stays within the bound throughout.

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