

Structural identifiability analysis of epidemic models based on differential equations

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Today's Agenda

1. Overview of structural identifiability
2. Methods for structural identifiability analysis
3. Differential algebra approach
4. Case Studies and Examples
5. Summary

Parameter identifiability analysis

Identifiability analysis: Describes whether it is possible to uniquely estimate model parameters from a given set of data.

- **Structural Identifiability:** Determines if the model is structured to uniquely reveal its parameters from perfect, noise-free observational data. If structurally unidentifiable, different parameter sets can produce the same output.
- **Practical Identifiability:** Considers the actual data, including noise, to determine if parameters can be reliably estimated in practice.

Let the model and observations be represented in the following compact form

$$x'(t) = f(x, p)$$

$$y(t) = g(x, p)$$

$$x(0) = x_0$$

Structural Identifiability Analysis

Structural Identifiability: The model is structured to uniquely reveal its parameters from perfect, noise-free observational data. Therefore,

Property of Structural Identifiability

$$y(t; p) = y(t; \hat{p}) \text{ implying } p = \hat{p}$$

$y(t)$: Noise-free and continuous observations

p & \hat{p} : Two distinct sets of model parameters

- It is an inherent attribute of the model (i.e., depends on model structure) and DOES NOT depend on the data.

Methods for Structural Identifiability Analysis

Differential Algebra Method

Uses differential algebra to derive input-output equations, eliminating unobserved variables; handles complex models, requires symbolic computation software (e.g., DAISY, Mathematica).

Taylor Series Method

Expands model equations into a Taylor series; simple for small models, computationally intensive for large ones.

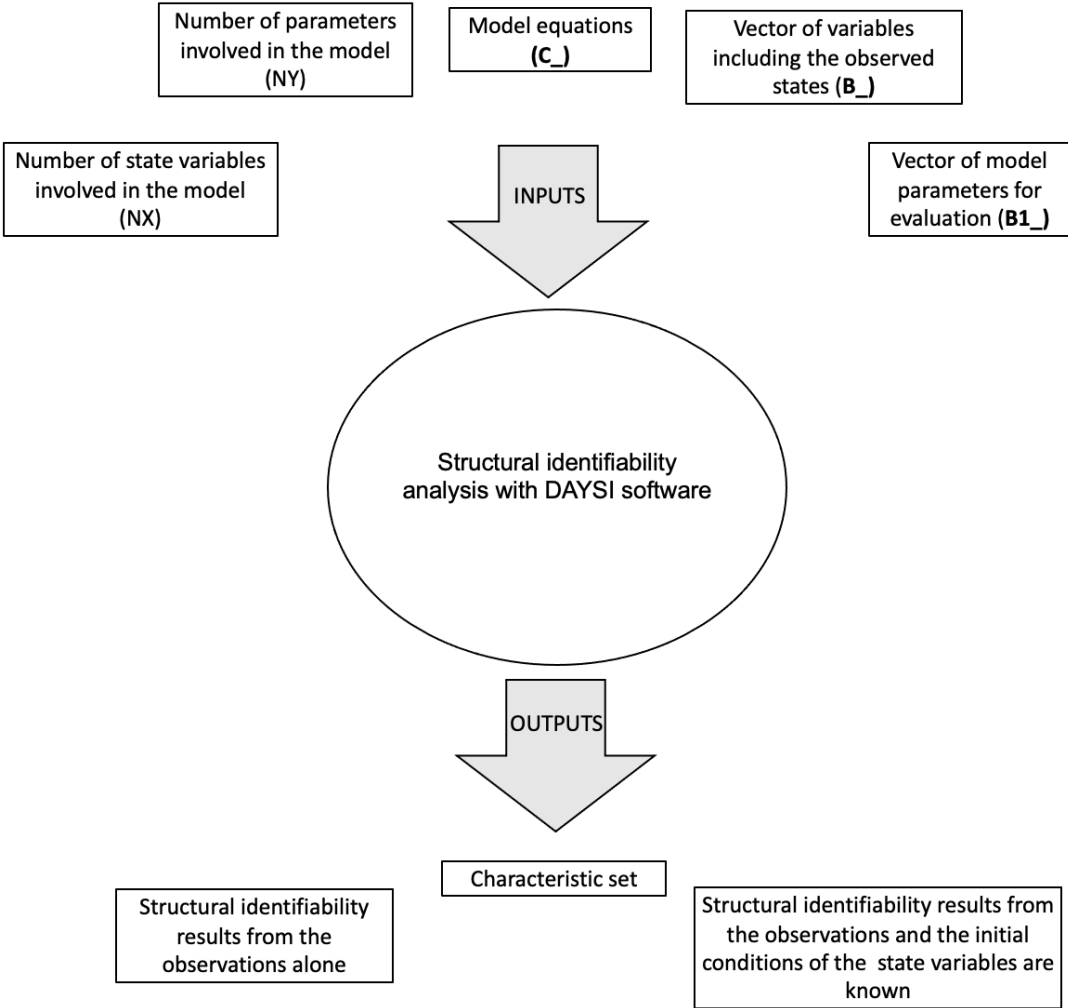
Direct Test Method

Tests uniqueness of parameter values by solving model equations for different parameter sets; straightforward, impractical for models with many parameters.

Symbolic computation

- Differential algebra
- Generating series
- Lie derivatives
- Input-output relationship analysis
- Observability and Controllability (e.g., StructuralIdentifiability.jl)

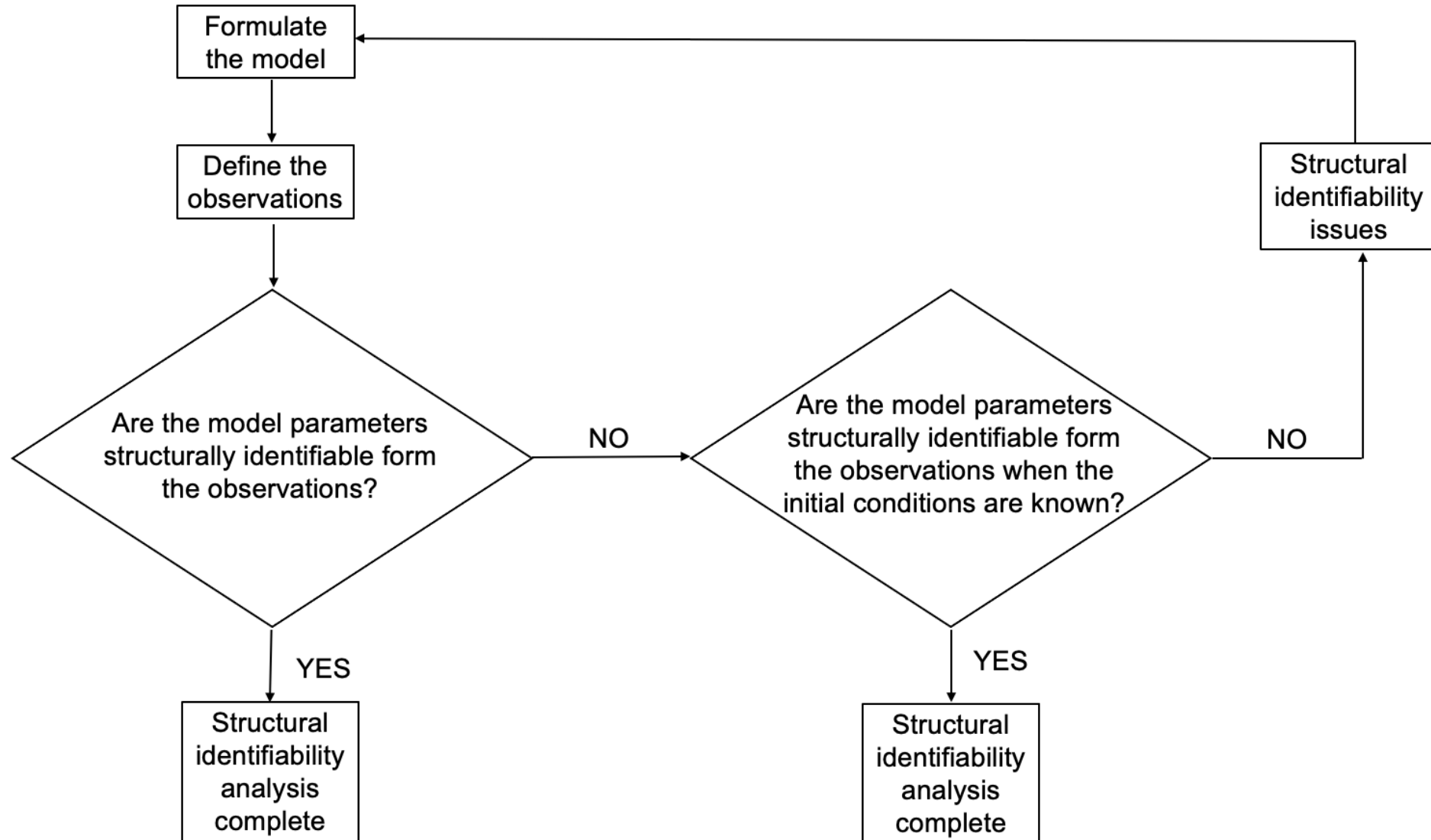
Structural identifiability components



Schematic diagram that shows the input and output components associated with structural identifiability analyses conducted using differential algebra with DAISY software. *Chowell et al. Journal of Mathematical Biology*

Chowell et al. *Journal of Mathematical Biology*. 2023

Workflow for conducting structural identifiability



Example 1: Susceptible-Exposed-Infectious Recovered (SEIR) Model

- Describes the spread of infectious diseases in a closed population.

$$\begin{cases} \frac{dS}{dt} = -\beta \frac{SI}{N}, S(0) = S_0 \\ \frac{dE}{dt} = \beta \frac{SI}{N} - \kappa E, E(0) = E_0 \\ \frac{dI}{dt} = \kappa E - \gamma I, I(0) = I_0 \\ \frac{dR}{dt} = \gamma I, R(0) = R_0 \end{cases}$$

β : Transmission rate

κ : Rate at which exposed individuals become infectious

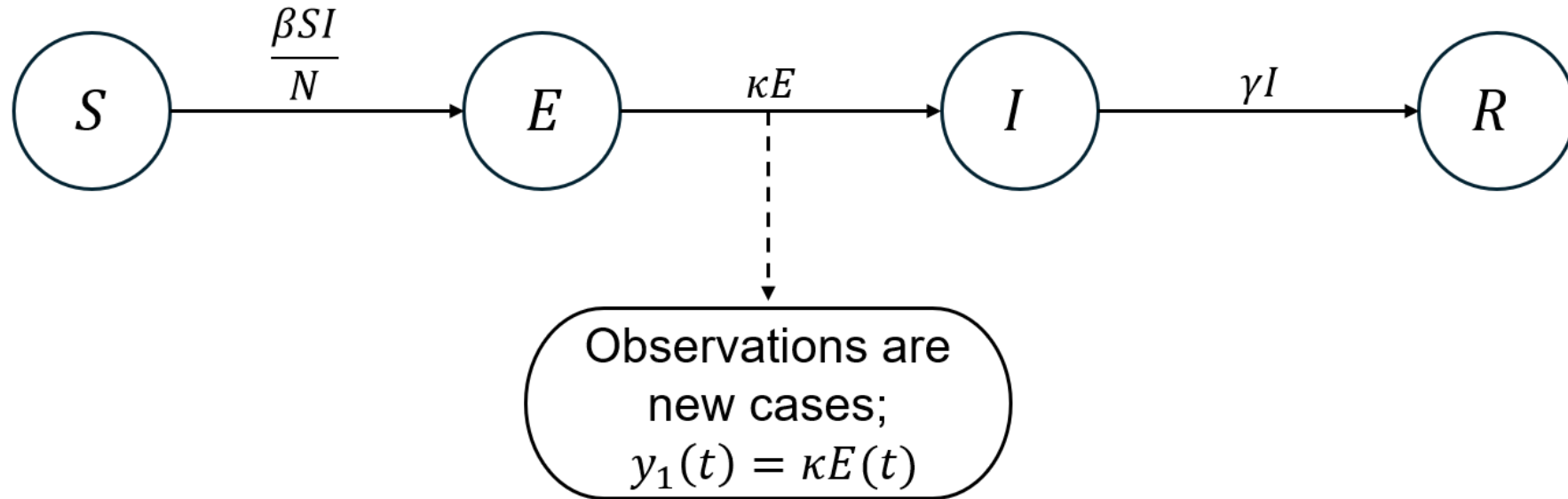
γ : Recovery rate

N : Total Population size

The primary observation is the number of new infected cases over time given by:

$$y_1 = \kappa E(t)$$

Example 1: Structural identifiability results



Identifiability Results: Without Initial Conditions

- (1) Identifiable parameters: κ, γ
- (2) Unidentifiable parameters: β, N
- (3) Parameter correlations: $\frac{\beta}{N} = \frac{\hat{\beta}}{\hat{N}}$

Identifiability Results: With Initial Conditions

- (1) Identifiable parameters: κ, γ, β, N

Example 2: SEIR model with symptomatic and asymptomatic infections

- Extends the traditional SEIR model to incorporate symptomatic and asymptomatic infections providing a more detailed representation of disease transmission dynamics

$$\begin{cases} \frac{dS}{dt} = -\beta \frac{SI}{N}, S(0) = S_0 \\ \frac{dE}{dt} = \beta \frac{SI}{N} - \kappa E, E(0) = E_0 \\ \frac{dI}{dt} = \kappa \rho E - \gamma I, I(0) = I_0 \\ \frac{dA}{dt} = \kappa(1 - \rho)E - \gamma A, A(0) = A_0 \\ \frac{dR}{dt} = \gamma I + \gamma A, R(0) = R_0 \end{cases}$$

β : Transmission rate

κ : Rate at which exposed individuals become infectious

ρ : Fraction of exposed individuals who become symptomatic

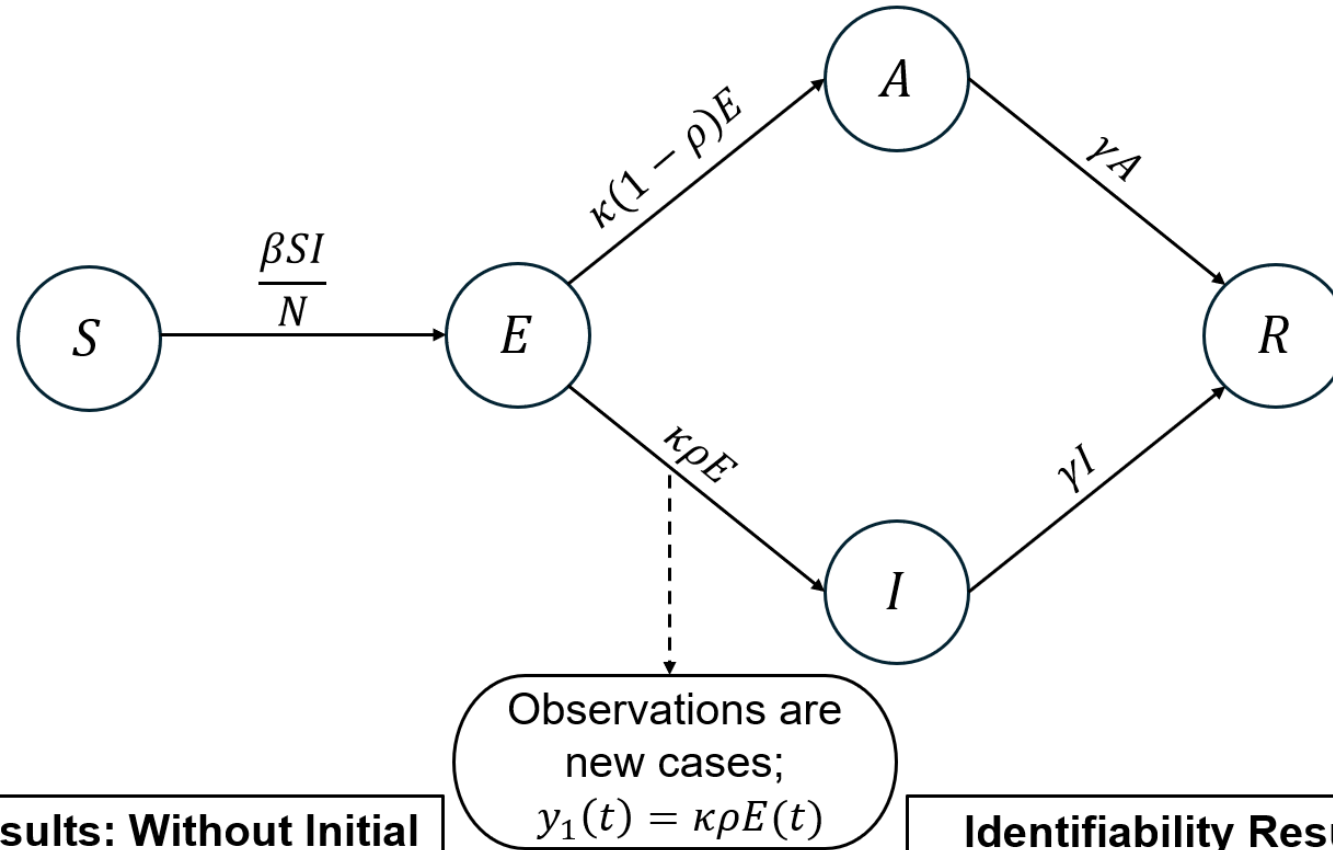
γ : Recovery rate

N : Total Population size

The primary observation is the number of new infected cases over time given by:

$$y_1 = \kappa \rho E(t)$$

Example 2: Structural identifiability results



Identifiability Results: Without Initial Conditions

- (1) Identifiable parameters: κ, γ
- (2) Unidentifiable parameters: β, N, ρ
- (3) Parameter correlations: $\frac{\beta}{N} = \frac{\hat{\beta}}{\hat{N}}$

Identifiability Results: With Initial Conditions

- (1) Identifiable parameters: $\kappa, \gamma, \beta, N, \rho$

Example 3: SEIR model with infectious asymptomatic individuals

- Extends the traditional SEIR model to incorporate symptomatic and asymptomatic infections where both groups are considered infectious and have different transmission rates

$$\begin{cases} \frac{dS}{dt} = -\frac{(\beta_A A + \beta_I I)S}{N}, S(0) = S_0 \\ \frac{dE}{dt} = \frac{(\beta_A A + \beta_I I)S}{N} - \kappa E, E(0) = E_0 \\ \frac{dI}{dt} = \kappa \rho E - \gamma I, I(0) = I_0 \\ \frac{dA}{dt} = \kappa(1 - \rho)E - \gamma A, A(0) = A_0 \\ \frac{dR}{dt} = \gamma I + \gamma A, R(0) = R_0 \end{cases}$$

β_I : Transmission rate - Symptomatic

β_A : Transmission rate - Asymptomatic

κ : Rate at which exposed individuals become infectious

ρ : Fraction of exposed individuals who become symptomatic

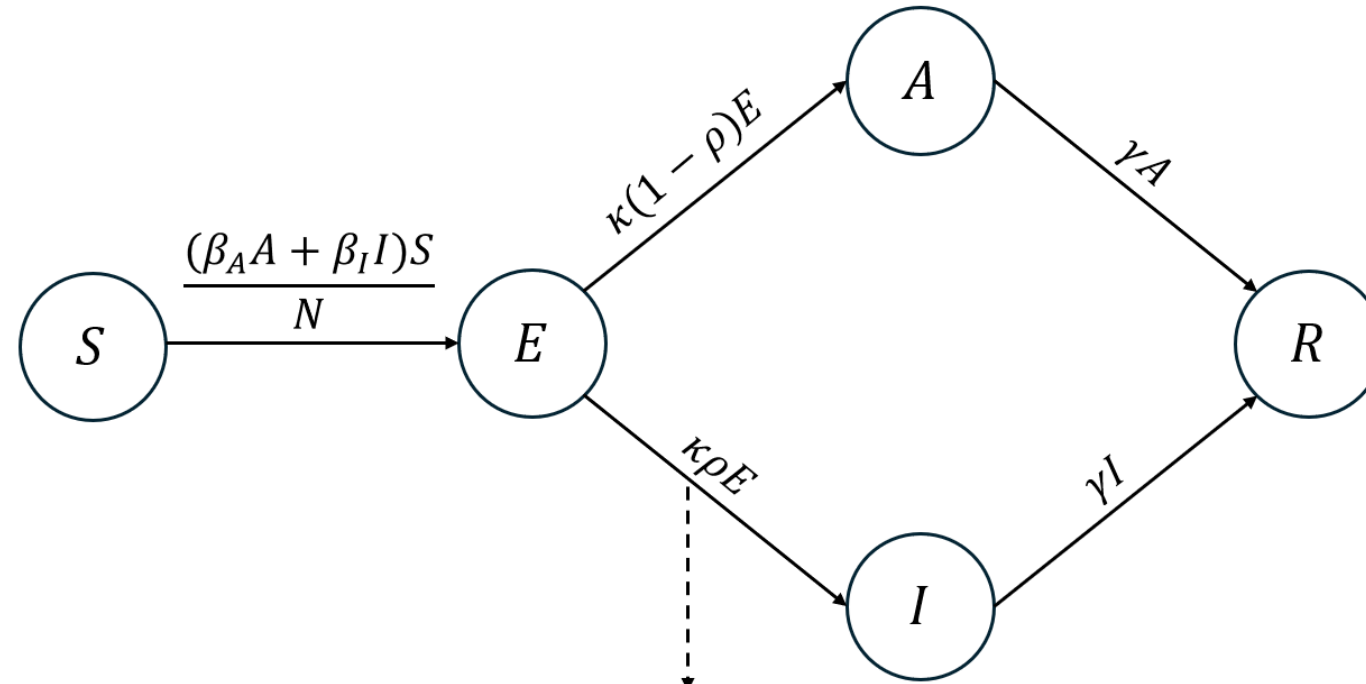
γ : Recovery rate

N : Total Population size

The primary observation is the number of new infected cases over time given by:

$$y_1 = \kappa \rho E(t)$$

Example 3: Structural identifiability results



Identifiability Results: Without Initial Conditions

- (1) Identifiable parameters: κ, γ
- (2) Unidentifiable parameters: $\beta_A, \beta_I, N, \rho$
- (3) Parameter correlations:
$$\beta_I \rho + \beta_A(1 - \rho) = \hat{\beta}_I \hat{\rho} + \hat{\beta}_A(1 - \hat{\rho}),$$
$$N\rho = \hat{N}\hat{\rho}$$

Observations are new cases;
 $y_1(t) = \kappa\rho E(t)$

Identifiability Results: With Initial Conditions

- (1) Identifiable parameters:
 $\kappa, \gamma, \beta_A, \beta_I, N, \rho$

Example 4: SEIR model with disease-induced deaths

- Extends the traditional SEIR model to account for disease-induced deaths by adding an additional compartment to represent the deceased population.

$$\begin{cases} \frac{dS}{dt} = -\beta \frac{SI}{N(t)}, S(0) = S_0 \\ \frac{dE}{dt} = \beta \frac{SI}{N(t)} - \kappa E, E(0) = E_0 \\ \frac{dI}{dt} = \kappa E - (\gamma + \delta)I, I(0) = I_0 \\ \frac{dR}{dt} = \gamma I, R(0) = R_0 \\ \frac{dD}{dt} = \delta I, D(0) = D_0 \end{cases}$$

β : Transmission rate

κ : Rate at which exposed individuals become infectious

γ : Recovery rate

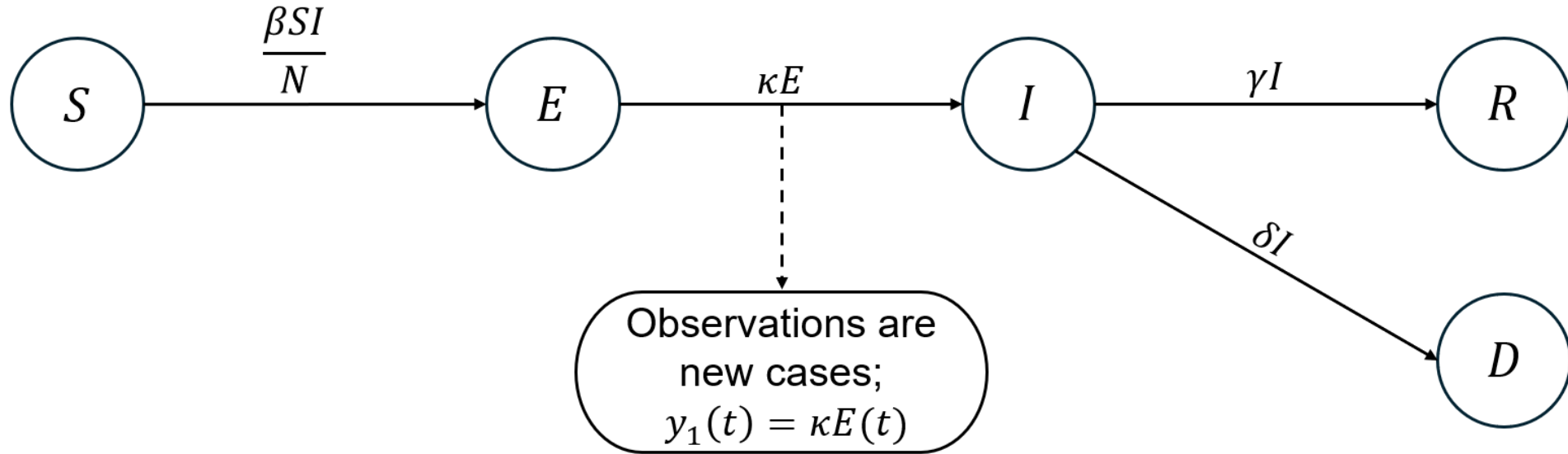
δ : Death rate due to the disease

N : Total Population size

The primary observation is the number of new infected cases over time given by:

$$y_1 = \kappa E(t)$$

Example 4: Structural identifiability results



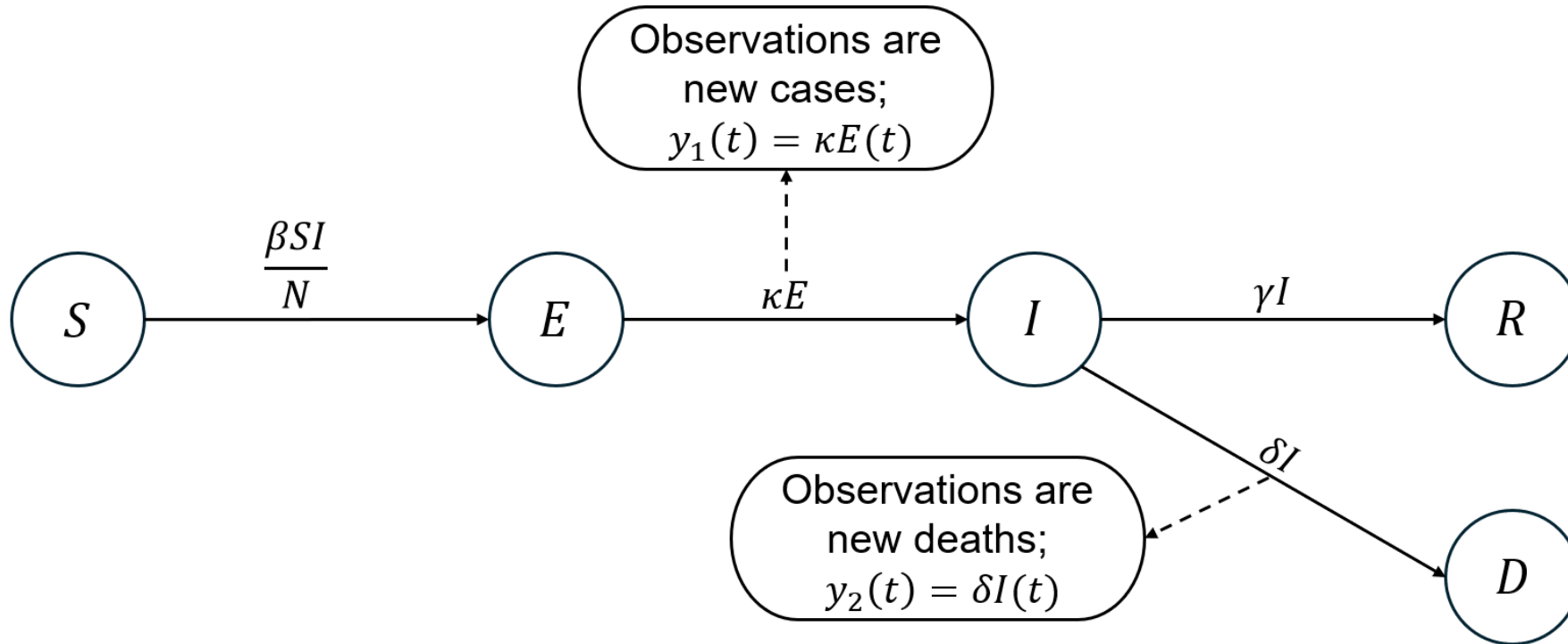
Identifiability Results: Without Initial Conditions

- (1) Identifiable parameters: κ
- (2) Unidentifiable parameters: β, γ, δ
- (3) Parameter correlations:
$$\frac{\beta}{\delta} = \frac{\hat{\beta}}{\hat{\delta}}$$
$$\gamma + \delta = \hat{\gamma} + \hat{\delta}$$

Identifiability Results: With Initial Conditions

- (1) Identifiable parameters: $\kappa, \beta, \gamma, \delta$

Structural identifiability results based on additional observations



The primary observation are:

- (1) Number of new infected cases over time: $y_1(t) = \kappa E(t)$
- (2) Number of new deaths due to disease over time: $y_2(t) = \delta I(t)$

Identifiability Results: Without Initial Conditions

- (1) Identifiable parameters: $\kappa, \beta, \gamma, \delta$
- (2) Unidentifiable parameters: None

Summary

Ensuring structural identifiability is crucial before estimating model parameters from observational data.

Identifiability guarantees that each parameter can be uniquely estimated from perfect, noise-free data.

Including multiple types of observations can help resolve identifiability issues.

When only a limited subset of the system's states is observed, identifiability issues are more likely to occur.

Some parameters may be unidentifiable due to correlations with other parameters.

Knowing the initial conditions can make previously unidentifiable parameters identifiable.

A structurally identifiable model may still face practical identifiability challenges if the data quality is poor.

Incorporating prior knowledge or fixing certain parameters can help achieve structural identifiability.