Stochastic Models and Optimal Control of Epidemics under Partial Information

Ralf Wunderlich

Brandenburg University of Technology Cottbus-Senftenberg, Germany

Joint work with

Florent Ouabo Kamkumo, Ibrahim Mbouandi Njiasse (Cottbus)

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Introduction





- System of ODEs for $X = (S, I, R)^{\top}$: $\dot{X}(t) = F(X(t))$
- Basic reproduction number $\mathcal{R}_0 = \frac{\beta}{\gamma}$ Effective reproduction number $\mathcal{R}(t) = \frac{\beta}{\gamma} \frac{S(t)}{N}$

2

ODE Models: Properties and Limitations

- Description and prediction of relative subpopulation sizes and "average" absolute subpopulation sizes for large total populations size N
- No information about deviations from the average. Interesting for absolute subpopulation sizes and models with small and moderate total population size N, small compartments such as hospitals, intensive care units (ICU).



 ODE models do not address
 uncertain parameters and initial conditions, forecast uncertainties,

not directly observable subpopulation sizes

(partial information, statistical learning of dark figures, nowcast uncertainties).

COVID-19 Model with Partial Information

- I^- Infected, non-detected
- R^- Recovered, non-detected
- S Susceptible

I⁺ Infected, detected



Charpentier et al. (2020), Meyer-Hermann et al. (2021)

COVID-19 Model with Partial Information

 I^- Infected, non-detected I^+ Infected, detected R_1^-/R_2^- Recovered, non-detected/fading immunity R_1^+, \ldots, R_L^+ Recovered, detected S Susceptible



COVID-19 Model with Hospital







COVID-19 Model with Hospital and Vaccination



COVID-19 Model with Hospital and Vaccination

- I^- Infected, non-detected
- R_1^-/R_2^- Recovered, non-detected/fading immunity R_1^+, \ldots, R_1^+ Recovered detected
 - S Susceptible V^- Vaccinated
 - V^- Vaccinated, fading immunity





Parameters $\beta, \ \alpha, \ \mu$ may be time-dependent and controlled

Multi-Group Models

Models with several regions, age groups, vaccination states, ...



Microscopic Stochastic Epidemic Models

- Similar to models of chemical reaction networks (Anderson, Kurtz (2011))
- Divide population of size N into d compartments
- $X_i(t) \in \{0, \dots, N\}$ absolute size of subpopulation in compartment $i = 1, \dots, d$
- $\overline{X}_i(t) = \frac{1}{N}X_i(t) \in [0,1]$ relative size of subpopulation
- State $X = X(t) = (X_1, \dots, X_d)^\top$ (or $\overline{X} = (\overline{X}_1, \dots, \overline{X}_d)^\top$)
- Individuals may undergo $K \in \mathbb{N}$ transitions between compartments
- Transition vectors $\xi_k = \Delta X(t) = X(t) X(t-) \in \mathbb{Z}^d$ if the transition k occurs at time t, $k = 1, \dots, K$, typical entries of ξ_k are -1, 0, +1

• Counting processes $M_k(t)$: number of transition k in [0, t]

$$X(t) = X(0) + \sum_{k=1}^{K} \xi_k M_k(t)$$

Example: Stochastic SIRS Model



d = 3, $X = (S, I, R)^{\top}$, K = 3 transitions

k	Transition	Transition vectors ξ_k	intensity $\lambda_i(x)$
1	Infection of susceptible	$(-1, 1, 0)^ op$	$\beta S \frac{I}{N} = \beta x_1 \frac{x_2}{N}$
2	Recovering of infected	$(0, -1, 1)^ op$	$\gamma I = \gamma x_2$
3	Losing immunity	$(1, 0, -1)^{ op}$	$\rho R = \rho x_3$

Microscopic Stochastic Epidemic Models (cont.)

Recall: $X^{N}(t) = X^{N}(0) + \sum_{k=1}^{K} \xi_{k} M_{k}(t)$ state for population of size NAssume $\mathbb{P}(M_{k}(t + \Delta t) - M_{k}(t) = 1 | X^{N}(t)) = \lambda_{k}(X^{N}(t))\Delta t + o(\Delta t)$ Describe counting processes M_{k} by independent Poisson processes

Continuous–Time Markov Chain (CTMC)

$$X^{N}(t) = X^{N}(0) + \sum_{k=1}^{K} \xi_{k} \prod_{k} \left(\int_{0}^{t} \lambda_{k}(X^{N}(s)) ds \right)$$

where Π_1, \ldots, Π_K are independent standard Poisson processes

State-dependent intensities $\lambda_k = \lambda_k(X^N(s))$, for $k = 1, \dots, K$ Assume scaling property $\lambda_k(x) = \lambda_k^N(x) = N\nu_k(N^{-1}x)$ where $\nu_k(z)$ is the intensity in terms of relative subpopulation size $z = N^{-1}x$ and independent of NIntensities may depend on time: $\lambda_k = \lambda_k(t, x)$

Law of Large Numbers for Poisson Process $\left|\frac{1}{N}\Pi(Nu) - u\right| \xrightarrow[N \to \infty]{} 0 \quad \text{a.s., uniformly for all } u \le u_0$

implies $\overline{X}^{N}(t) \xrightarrow[N \to \infty]{} \overline{X}^{\infty}(t)$ uniformly for all $t \leq T$ \overline{X}^{∞} satisfies ODE Anderson & Kurtz (2011), Britton & Pardoux (2018)

$$rac{d}{dt}\overline{X}^{\infty}(t)=\overline{F}(t,\overline{X}^{\infty}(t)) \quad \textit{with} \quad \overline{F}(t,z)=\sum_{k=1}^{K}\xi_k
u_k(t,z)$$



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Central Limit Theorem for Poisson Process $\frac{1}{\sqrt{N}}(\Pi(Nu) - Nu) \xrightarrow[N \to \infty]{} W(u) \quad \text{Brownian motion}$

Scaling property $W(\int_0^t a(s)ds) \stackrel{d}{=} \int_0^t \sqrt{a(s)}dW(s)$

Diffusion Approximation of X^N and \overline{X}^N by SDEs Absolute $dX^D(t) = F(t, X^D(t))dt + \sigma(t, X^D(t))dW(t)$ Relative $d\overline{X}^D(t) = \overline{F}(t, \overline{X}^D(t))dt + \frac{1}{\sqrt{N}}\overline{\sigma}(t, \overline{X}^D(t))dW(t)$

with $F(t,x) = \sum_{k=1}^{n} \xi_k \lambda_k(t,x), \quad \sigma(t,x) = (\xi_1 \sqrt{\lambda_1(t,x)}, \dots, \xi_K \sqrt{\lambda_K(t,x)})$ $\overline{\sigma}(t,z) = (\xi_1 \sqrt{\nu_1(t,z)}, \dots, \xi_K \sqrt{\nu_K(t,z)})$ $\sqrt{N}(\overline{I}^N - \overline{I}^\infty)$ N=10 e 2 -0 $\overline{\nabla}$ Ŷ 200 400 ò 600 800 1000 Davs

Central Limit Theorem for Poisson Process $\frac{1}{\sqrt{N}}(\Pi(Nu) - Nu) \xrightarrow[N \to \infty]{} W(u) \text{ Brownian motion}$

Scaling property $W(\int_0^t a(s)ds) \stackrel{d}{=} \int_0^t \sqrt{a(s)}dW(s)$

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Central Limit Theorem for Poisson Process $\frac{1}{\sqrt{N}}(\Pi(Nu) - Nu) \xrightarrow[N \to \infty]{} W(u)$ Brownian motion

Scaling property $W(\int_0^t a(s)ds) \stackrel{d}{=} \int_0^t \sqrt{a(s)}dW(s)$

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Diffusion Approximation of COVID-19 Model



$$dY = \overline{f}(t, Y, Z)dt + \overline{\sigma}(t, Y, Z)dW^{1} + \overline{g}(t, Y, Z)dW^{2}$$
 hidden state

$$dZ = [\overline{h}_{0}(t, Z) + \overline{h}_{1}(t, Z)Y]dt + \overline{\ell}(t, Y, Z)dW^{2}$$
 observation
linear in Y

Coefficients \overline{f} , $\overline{\sigma}$, \overline{g} , $\overline{\ell}$ are non-linear in the hidden state Y Time discretization, $t_n = n\Delta t$, n = 0, 1, ...

$$\begin{aligned} Y_{n+1} &= Y_n + f(n, Y_n, Z_n) + \sigma(n, Y_n, Z_n) \mathcal{E}_{n+1}^1 + g(n, Y_n, Z_n) \mathcal{E}_{n+1}^2 \\ Z_{n+1} &= Z_n + [h_0(n, Z_n) + h_1(n, Z_n) Y_n] + \ell(n, Y_n, Z_n) \mathcal{E}_{n+1}^2 \end{aligned}$$

 $(\mathcal{E}_n^1), (\mathcal{E}_n^2)$ independent sequences of i.i.d. $\mathcal{N}(0, 1)$ random vectors Given the observations of Z_n we want to estimate hidden state Y_n

Filtering Problem

Decompose state vector $X = (Y, Z)^{\top}$ into

- Y: hidden (non-observable) state
- Z: observation
- Given observations Z_k for $k = 0, \ldots, n$ and

 \mathcal{F}_0^I initial information about distribution of Y_0

Mean-square optimal estimate of Y_n given $\mathcal{F}_n^Z = \sigma\{Z_k, k = 0, \dots, n\} \vee \mathcal{F}_0^I$ is

Conditional Mean

$$M_n = \mathbb{E}\left[Y_n | \mathcal{F}_n^Z\right]$$

Measure of estimation error

Conditional Covariance

$$Q_n := \operatorname{Var}(Y_n | \mathcal{F}_n^Z) = \mathbb{E}[(Y_n - M_n)(Y_n - M_n)^\top | \mathcal{F}_n^Z]$$

Initial estimates $M_0 = m_0 = \mathbb{E}[Y_0|\mathcal{F}_0^Z]$ and $Q_0 = q_0 = \operatorname{Var}(Y_0|\mathcal{F}_0^Z)$

Kalman Filter for Conditionally Gaussian Sequences

$$\begin{aligned} Y_{n+1} &= [f_0 + f_1 Y_n] + \sigma \mathcal{E}_{n+1}^1 + g \mathcal{E}_{n+1}^2 & \text{hidden state/signal} \\ Z_{n+1} &= [h_0 + h_1 Y_n] + \ell \mathcal{E}_{n+1}^2 & \text{observation} \end{aligned}$$

 $(\mathcal{E}_n^1), (\mathcal{E}_n^2)$ independent sequences of i.i.d. $\mathcal{N}(0, 1)$ random vectors Coefficients $a = f_0, f_1, h_0, h_1, \sigma, g, \ell$ are of the form $a = a(n, \mathcal{Z}_n)$ may depend on time nand also on whole observation path $\mathcal{Z}_n = (Z_k)_{k \leq n}$ up to time n

Theorem (Liptser & Shiryaev (2001), Theorem 13.4)

Under technical assumptions the conditional distribution of Y_n given \mathcal{F}_n^Z is $\mathcal{N}(M_n, Q_n)$ (Gaussian). M_n and Q_n are defined by the following recursions driven by the observations $M_{n+1} = [f_0 + f_1 M_n] + [g\ell^\top + f_1 Q_n h_1^\top] [\ell\ell^\top + h_1 Q_n h_1^\top]^+ [Z_{n+1} - (h_0 + h_1 M_n)]$ $Q_{n+1} = -[g\ell^\top + f_1 Q_n h_1^\top] [\ell\ell^\top + h_1 Q_n h_1^\top]^+ [g\ell^\top + f_1 Q_n h_1^\top]^\top + f_1 Q_n f_1^\top + \sigma\sigma^\intercal$ with initial values $M_0 = m_0$, $Q_0 = q_0$ and $Y_0 \sim \mathcal{N}(m_0, q_0)$. $([A]^+ denotes the pseudoinverse of A)$

Note that all coefficients may depend on time n and the observation path \mathcal{Z}_n .

Extended Kalman Filter

$$Y_{n+1} = Y_n + f(n, Y_n, Z_n) + \sigma(n, Y_n, Z_n) \mathcal{E}_{n+1}^1 + g(n, Y_n, Z_n) \mathcal{E}_{n+1}^2$$

$$Z_{n+1} = Z_n + [h_0(n, Z_n) + h_1(n, Z_n) Y_n] + \ell(n, Y_n, Z_n) \mathcal{E}_{n+1}^2$$

Drift coefficient f non-linear w.r.t. signal Y

Diffusion coefficients σ, g, ℓ may also depend on signal Y

Idea: Gelb (1974), PARDOUX (1991), BAIN, CRISAN (2009)

- **(**) Linearize drift coefficient f by Taylor expansion around a "suitable" \overline{Y}_n
- **2** Substitute signal Y by \overline{Y}_n in diffusion coefficients σ, g, ℓ

Approximation by Conditional Gaussian Sequences

$$\begin{split} \widetilde{Y}_{n+1} &= \widetilde{Y}_n + f(n, \overline{Y}_n, \widetilde{Z}_n) + \frac{\partial f}{\partial y}(n, \overline{Y}_n, \widetilde{Z}_n)(\widetilde{Y}_n - \overline{Y}_n) \\ &+ \sigma(n, \overline{Y}_n, \widetilde{Z}_n)\mathcal{E}_{n+1}^1 + g(n, \overline{Y}_n, \widetilde{Z}_n)\mathcal{E}_{n+1}^2 \\ \widetilde{Z}_{n+1} &= \widetilde{Z}_n + [h_0(n, \widetilde{Z}_n) + h_1(n, \widetilde{Z}_n)\widetilde{Y}_n] + \ell(n, \overline{Y}_n, \widetilde{Z}_n)\mathcal{E}_{n+1}^2 \end{split}$$

• Apply Kalman filter for conditional Gaussian sequences $\rightsquigarrow (M_n, Q_n)$ Extended Kalman filter linearizes around current filter estimate: $\overline{Y}_n = M_n$. For theoretical justification and error estimates see PICARD (1991)

Numerical Experiments

• COVID-19 model with partial information



- Calibrate model parameters to real-world data set for Germany Time-depending β and α match daily basic reproduction numbers, positive tests
- T = 3 years from March 2020 to February 2023, $\Delta t = 1$ day
- Population size N = 100.000
- Simulate hidden states and observations
- Compute filter estimates of hidden states based on observations
- Compare estimated and true values
 - \longrightarrow precision of the filter estimates

Observations: Detected Infected







Observations: Detected Infected & Recovered







Observations: Hospital











Observations: Vaccinated



Hidden Signal Simulation: Non-Detected Infected I⁻







Hidden Signal Estimation: Non-Detected Infected I⁻





Hidden Signal Estimation: Non-Detected Infected I⁻





Large initial uncertainty is reduced by learning from observations

Impact of Initial Estimate & Effect of Learning





RedLarge initial uncertainty is reduced by learning from observationsGreenSmall initial uncertainty is fading out by observation noise

Impact of Initial Estimate & Effect of Learning



RedLarge initial uncertainty is reduced by learning from observationsBlue"Wrong" initial uncertainty needs long time to be corrected

Optimal Control Problem

For containment of an epidemics decision makers (government) try to influence the course of the epidemics by

- Social distancing / lock-down with (relative) force u₁ ∈ [0, 1], reduces transmission rate from β to (1 − u₁)β
- **2** Tests/Diagnosis with intensity $u_2 \ge 0$
- Vaccination with intensity $u_3 \ge 0$,

These measures have financial or social costs.

Available capacities for testing and vaccination are limited.

Aim: cost-optimal containment of the epidemics through an appropriate mix of measures

Decision-making problem under uncertainty about

future course of epidemics (forecasts),

current state of epidemics (nowcasts, dark numbers)

Simplified Model

Model a disease with lifelong immunity after infection or vaccination Example: measles



Running and Terminal Cost

Running cost proportional to number x of "affected" individuals, Penalties if capacity threshold \overline{x} is exceeded $C_k: \mathbb{R}^2 \to \mathbb{R}_+, (x, \overline{x}) \mapsto C_k(x, \overline{x})$ $C_k(x,\overline{x})$ increasing and convex functions w.r.t. x_{i} Example: $C_k(x, \overline{x}) = \begin{cases} a_k x, & x \leq \overline{x} \\ a_k x + b_k (x - \overline{x})^2, & x > \overline{x} \end{cases}$ $a_{\iota x}$ \overline{x} \overline{x} $\overline{x} = 0$: quadratic, $\overline{x} \to \infty$: linear Vaccination $\mu = u_3$ Social distancing $C_1(u_1 X^{Work}, 0), \quad X^{Work} = N - I^+$ γ^- (Lockdown) CHARPENTIER ET AL. (2020) $S (1-u_1)\beta$ Social Distancing $C_2(u_2 X^{\text{Test}}, \overline{x}^{\text{Test}}), \quad X^{\text{Test}} = N - I^+ - R^+$ Tests $\alpha = u_2$ Vaccination $C_3(u_3 X^{\text{Test}}, \overline{X}^{\text{Vacc}})$ Test/Diagnosis $C_4^{\pm}(I_{N_4}^{\pm},0)$ for infected γ^+ Penalties

Running cost

$$\Psi(X_n, u_n)$$

) = $C_1 + C_2 + C_3 + C_4^+ + C_4^-$

Terminal cost

$$\Phi(X_{N_t}) = C_T^+(I_{N_t}^+, 0) + C_T^-(I_{N_t}^-, 0)$$

Penalties for infected at terminal time $T = N_t \Delta t$

Performance Criterion

Expected Aggregated Cost: Full Information, X = (Y, Z)

$$\mathcal{J}^{\mathcal{F}}(x; u) = \mathbb{E}\Big[\sum_{n=0}^{N_t-1} \Psi(X_n, u_n) + \Phi(X_{N_t})\Big|X_0 = x\Big]$$

Problem: X = (Y, Z) depends on hidden state Y Initial state $X_0 = x = (y, z)$ is not known Decisions (control u) have to based on observable quantities Z only

• Take conditional expectation w.r.t. \mathcal{F}_0^Z (initial information)

$$\mathbb{E}[\mathcal{J}^{F}(X_{0}; u) | \mathcal{F}_{0}^{Z}] = \mathbb{E}\left[\sum_{n=0}^{N_{t}-1} \Psi(\underbrace{(Y_{n}, Z_{n})}_{=X_{n}}, u_{n}) + \Phi(Y_{N_{t}}, Z_{N_{t}}) \middle| \mathcal{F}_{0}^{Z}\right]$$

tower law
Fubini
$$= \mathbb{E}\left[\sum_{n=0}^{N_{t}-1} \mathbb{E}\left[\Psi((Y_{n}, Z_{n}), u_{n}) \middle| \mathcal{F}_{n}^{Z}\right] + \mathbb{E}\left[\Phi(Y_{N_{t}}, Z_{N_{t}}) \middle| \mathcal{F}_{N_{t}}^{Z}\right] \middle| \mathcal{F}_{0}^{Z}\right]$$

For Ψ, Φ linear and quadratic in y conditional expectation E[... |F_n²] can be expressed in terms of Extended Kalman filter (M, Q) for hidden state Y. Recall: conditional distribution of Y_n is Gaussian N(M_n, Q_n)

Performance Criterion: Partial Information, $X^P = (M, Q, Z)$

$$\mathcal{J}(x^{P}; u) = \mathbb{E}\Big[\sum_{n=0}^{N_{t}-1} \Psi^{P}(X_{n}^{P}, u_{n}) + \Phi^{P}(X_{N_{t}}^{P}) \Big| X_{0}^{P} = x^{P}\Big]$$

Optimal Control Problem with Partial Information

Replace hidden state Y by filter (M, Q)

Rewrite dynamics of *M* and *Z* in terms of innovations process $(\overline{\mathcal{E}}_n)$

with
$$\overline{\mathcal{E}}_n = ([\ell\ell^\top + h_1Q_{n-1}h_1^\top]^+)^{1/2}(Z_n - (h_0 + h_1M_{n-1})),$$

 $(\overline{\mathcal{E}}_n)$ i.i.d. $\mathcal{N}(0, \mathbb{1})$ r.v.'s with $\mathcal{F}_n^Z = \mathcal{F}_n^{\overline{\mathcal{E}}} \vee \mathcal{F}_0^I$ (LIPTSER, SHIRYAEV (2001))

Treat control problem as Markov decision process (MDP) with

state process $X^P = (M, Q, Z)^{\top}$ taking values in state space \mathcal{X} dynamics $X^P_{n+1} = \mathcal{T}(n, X^P_n, u_n, \overline{\mathcal{E}}_{n+1})$ with transition operator \mathcal{T} and Gaussian transition kernel.

 $X^P = (M, Q, Z)$ is adapted to the observable filtration

$$\mathbb{F}^{Z} = (\mathcal{F}_{n}^{Z})_{n \geq 0} \quad \text{with} \quad \mathcal{F}_{n}^{Z} = \sigma\{Z_{k}, k \leq n\} \vee \mathcal{F}_{0}^{L}$$

Admissible controls

 $\mathcal{A} = \{(u_n)_{n=0,\dots,N_t-1} \mid \mathbb{F}^Z \text{-adapted}, \text{ integrability cond., Markov control } u_n = \widetilde{u}(n, X_n^P), \\ \text{control constraints } u_n \in \mathcal{U} = [0, 1] \times \mathbb{R}^2_+ \}$

Performance criterion for $n = 0, ..., N_t, x = (m, q, z)^{\top}$ and $u \in \mathcal{A}$ $J(n, x; u) = \mathbb{E}\left[\sum_{k=n}^{N_t-1} \Psi^P(X_k^P, u_k) + \Phi^P(X_{N_t}^P) \middle| X_n^P = x\right]$

Optimization problem

Find
$$u^* \in \mathcal{A}$$
 such that $J(n,x;u^*) = V(n,x) := \inf_{u \in \mathcal{A}} J(n,x;u)$

Solution Using Dynamic Programming

Bellman Equation / Dynamic Programming Equation $V(n,x) = \inf_{\nu \in \mathcal{U}} \left\{ \Psi^{P}(x,\nu) + \mathbb{E}_{n,x} \left[V(n+1, \underbrace{\mathcal{T}(n,x,\nu,\overline{\mathcal{E}}_{n+1})}_{=X_{n+1}^{P}} \right) \right] \right\}, \ n = 0, 1, \dots, N-1$ $V(N_{t},x) = \Phi^{P}(x) \qquad (\text{terminal condition})$

... can be solved by backward recursion

Challenge Compute $\mathbb{E}_{n,x}[V(n+1, \mathcal{T}(n, x, \nu, \overline{\mathcal{E}}_{n+1}))]$ at each time *n* for all $x \in \mathcal{X}$! No closed-form expressions of the expectation are available. For high-dimensional state this becomes computationally intractable. \rightarrow Curse of dimensionality Simplified model: dimension of state $X^P = (M, Q, Z)^T$ is 7. Remedies Apply quantization techniques as in PAGÈS (2015), CALLEGARO ET AL. (2017) Model order reduction: PCA for covariance matrix Q

Q-Learning

References



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