Modelling power-law spread of infectious diseases

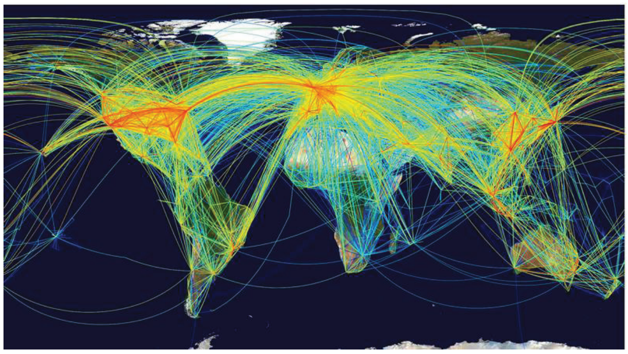
Sebastian Meyer   Leonhard Held

Financially supported by the Swiss National Science Foundation
(project 137919: *Statistical methods for spatio-temporal modelling and prediction of infectious diseases*)

Epidemic Modelling

- Prospective surveillance: outbreak detection (Farrington).
- This talk is concerned with retrospective surveillance:
  - Explain the spread of epidemics through statistical modelling
  - Assess influential factors, e.g., seasonality, climate, concurrent epidemics of related pathogens, contact networks
- Data basis: routine public health surveillance including temporal *as well as spatial* information
- This talk deals with two types of surveillance data:
  - individual case reports
  - aggregated counts by week and administrative district

Mobility networks determine the spread of epidemics



Source: Max Planck Institute for Dynamics and Self-Organization
(http://www.mpg.de/4406928/)

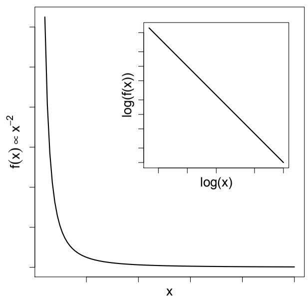
How to quantify spatial interaction between regions or individuals in the absence of network data?

Power law? Eh?

$$f(x) \propto x^{-d} \quad \text{with positive decay parameter } d$$

Widely appearing, for instance:

- Pareto, 1896: distribution of income
- Zipf, 1949: city sizes and word frequencies in texts
- Gutenberg and Richter, 1944: magnitudes of earthquakes



Power law? Why?

Brockmann et al., 2006:

- Analysed trajectories of 464 670 dollar bills in the USA
- Short-time travel behaviour follows a power law wrt distance

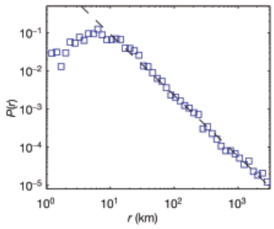


Fig. 1c: Histogram of the distance r traversed within 4 days.
Dashed line: $P(r) \propto r^{-1.59}$

- "Starting point for the development of a new class of models for the spread of infectious diseases"

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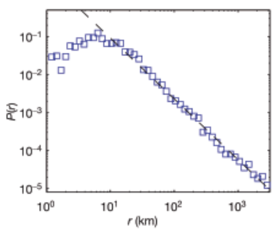

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- "Starting point for the development of a new class of models for the spread of infectious diseases"

Let's do it! We use this finding to improve upon two previously established model frameworks for infectious disease spread.

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"`twinstim`" (Meyer, Elias, and Höhle, 2012)

- Spatio-temporal point process model for individual case reports
- Models the conditional intensity $\lambda^*(t, \mathbf{s})$ of infections at time point t and location $\mathbf{s}$
- The intensity $\lambda^*(t, \mathbf{s})$ is additively decomposed into two components:
  - endemic: population, seasonality, climate, ...
  - epidemic: dependency on previously infected individuals

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Formally:

$$\lambda^*(t, \mathbf{s}) = \nu_{[t][\mathbf{s}]}\, \rho_{[t][\mathbf{s}]} + \sum_{j : t_j < t} \eta_j \cdot g(t - t_j) \cdot f(\|\mathbf{s} - \mathbf{s}_j\|)$$

$$\log(\nu_{[t][\mathbf{s}]}) = \beta_0 + \boldsymbol{\beta}^\top \mathbf{z}_{[t][\mathbf{s}]} \,, \qquad \log(\eta_j) = \gamma_0 + \boldsymbol{\gamma}^\top \mathbf{m}_j$$

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"`hhh4`" (Held and Paul, 2012, and previous work)

- Multivariate time-series model for aggregated surveillance counts
- Models the number of cases $Y_{it} | \mathbf{Y}_{\cdot,t-1} \sim \text{NegBin}(\mu_{it}, \psi)$ by region i and period t, where ψ is the overdispersion parameter
- The mean μ_{it} is additively decomposed into three components:
  - endemic: population, seasonality, climate, ...
  - auto-regressive: dependency on previous cases $Y_{i,t-1}$
  - spatio-temporal: dependency on neighbouring regions $Y_{j,t-1}$

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Formally:

$$\mu_{it} = \nu_{it} \, e_{it} + \lambda_{it} \, Y_{i,t-1} + \phi_{it} \sum_{j \neq i} w_{ji} \, Y_{j,t-1}$$

$$\log(\cdot_{it}) = \beta_0^{(\cdot)} + b_i^{(\cdot)} + \boldsymbol{\beta}^{(\cdot)\top} \mathbf{z}_{it}^{(\cdot)} \qquad \cdot \in \{\nu, \lambda, \phi\}$$

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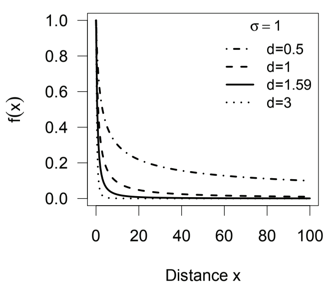
Kernel of the density of the shifted Pareto distribution ("Lomax"):

$$f(x) = (x + \sigma)^{-d}$$



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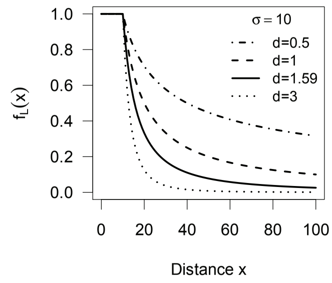
Alternative "lagged" power law with uniform short-range dispersal:

$$f_L(x) = \begin{cases} 1 & \text{for } x < \sigma, \\ \left(\frac{x}{\sigma}\right)^{-d} & \text{otherwise.} \end{cases}$$



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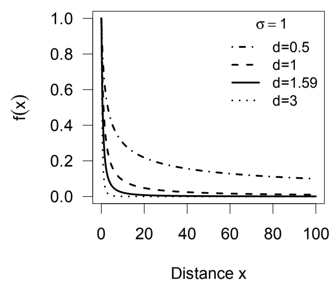
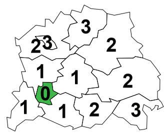


- Joint ML-inference for all model parameters
- Numerical cubature of $f_{2D}(\mathbf{s}) = f(\|\mathbf{s}\|)$ over polygonal domains in likelihood via product-Gauss cubature (Sommariva and Vianello, 2007)

Power-law weights in hhh4

- On which distance measure between regions should the power law act?
  $\longrightarrow$ Order of neighbourhood o_{ji}!



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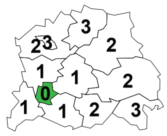
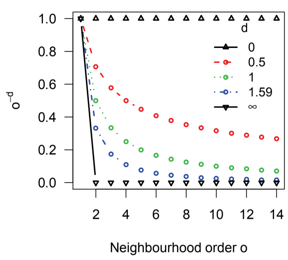


- Generalisation of previously used first-order weight matrix:

w_{ji} $(j \neq i)$	first-order	power law
raw	$\mathbb{1}(j \sim i)$	o_{ji}^{-d}
normalised	$\mathbb{1}(j \sim i)/n_j$	$o_{ji}^{-d} / \sum_{k=1}^{I} o_{jk}^{-d}$



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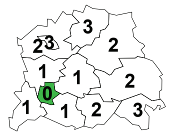

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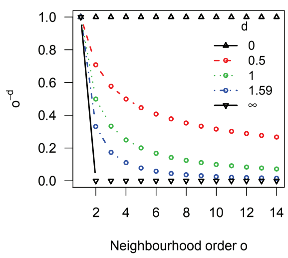
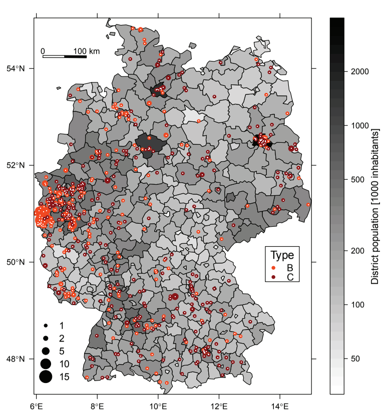
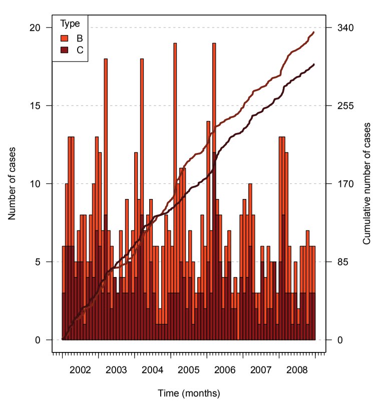


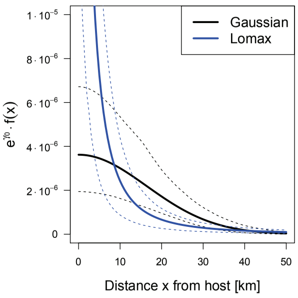
- Estimate d within the penalised likelihood framework simultaneously with all other model parameters.

Example of individual-level surveillance data: Invasive meningococcal disease in Germany (2002–8)





▷ Estimated power law



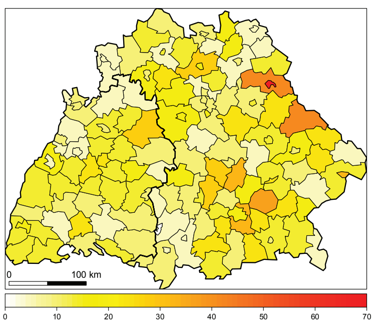
Endemic: seasonality, trend, population density as offset

Epidemic: type, age group

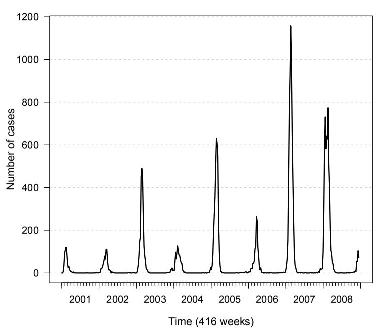
Decay parameter: $\hat{d} = 2.3$ (95% CI: $[1.74, 3.03]$)

	AIC	$\hat{R}(B)$	$\hat{R}(C)$
Gaussian	18972.04	0.22 [0.17,0.31]	0.10 [0.06,0.15]
Power law	18944.25	0.26 [0.14,0.35]	0.13 [0.06,0.19]

Example of aggregated surveillance data: Influenza in Southern Germany (2001–8)



Mean yearly incidence per 100 000 inhabitants in the 140 districts of Baden-Württemberg and Bavaria



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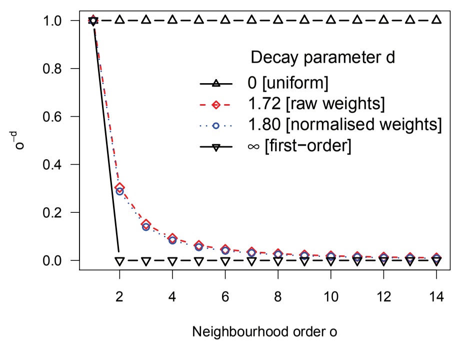


- population fractions as endemic offset
- seasonality, region-specific random intercepts in all three components

▷ Predictive performance

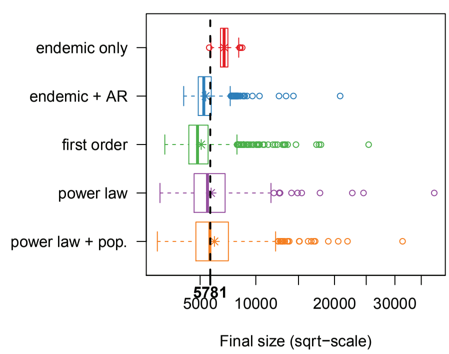
- Use strictly proper scoring rules to evaluate consistency of predictive distribution with later observed value: logarithmic score (logS) and ranked probability score (RPS) (Czado et al., 2009)
- Based on one-week-ahead predictions in the last two years
- Calculate mean scores and p-values via permutation tests

	raw weights		normalised weights	
	logS	RPS	logS	RPS
first order	0.5522	0.4205	0.5511	0.4194
power law	0.5453	0.4174	0.5448	0.4168
p-value	0.00005	0.11	0.0001	0.19

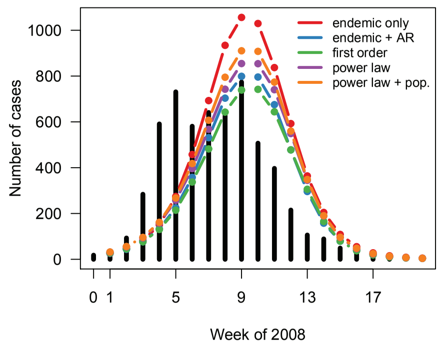
▷ Long-term predictive performance

- Simulate the 2008 wave of influenza
- Based on models fitted on 2001–2007
- Initialised by the 18 cases of the last week of 2007
- Run 1000 simulations for each model and evaluate by
  - the final size distribution
  - proper scoring rules on the empirical distribution of the simulations compared to the later reported counts
- Additional benchmark against
  - endemic-only model
  - model without neighbourhood effects
  - model with additional population effect in spatio-temporal component

▷ Long-term predictive performance
└ final size

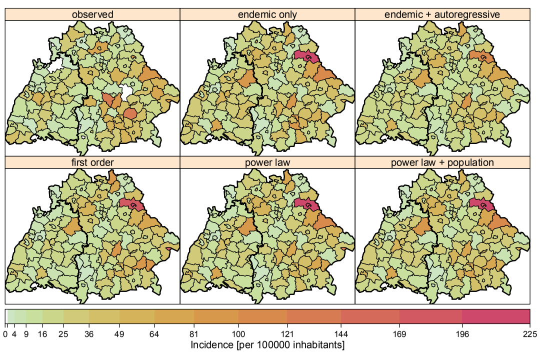


▷ Long-term predictive performance
└ time domain



DSS	RPS
27.03	149.77
31.36	112.15
26.46	**108.61**
16.41	110.2
15.49	111.86

▷ Long-term predictive performance
└ space domain



	DSS	RPS
endemic only	7.85	15.39
endemic + AR	7.59	15.04
first order	7.51	15.63
power law	7.36	14.75
power law + pop.	**7.24**	**14.3**

▷ Long-term predictive performance
└ space-time domain

	DSS	RPS
endemic only	2.91	1.31
endemic + AR	2.58	1.26
first order	2.5	1.26
power law	2.29	1.25
power law + pop.	**2.29**	**1.24**

[animation]

Discussion

- Human mobility
  - is an important driver of epidemic spread
  - follows a power law with respect to distance
- Predictive performance improves when using a power law for spatial interaction of cases
- Population effects:
  - infectivity tends to increase with population density
  - infectious imports increase with population size
- Edge effects:
  - random intercepts account for unobserved heterogeneity
  - incorporate region-specific incoming traffic from abroad

Outlook

- Semiparametric estimate of weight function to confirm power law
- Estimate impact of traffic data on neighbourhood weights w_{ji} (Geilhufe et al., 2013)
- Use model for outbreak detection: alarm if observed count above high quantile of predictive distribution

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- Further reading: arXiv:1308.5115
- Further application: all methods are implemented in the open-source R package `surveillance` for visualisation, modelling and monitoring of epidemic phenomena.

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Thanks for your attention!

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Appendix

IMD — parameter estimates

	Estimate	95% CI		
β_0	-20.53	-20.62	to	-20.44
β_{trend}	-0.05	-0.09	to	-0.00
β_{sin}	0.26	0.14	to	0.39
β_{cos}	0.26	0.14	to	0.39
γ_0	-12.53	-13.15	to	-11.91
γ_C	-0.91	-1.44	to	-0.39
$\gamma_{3\text{-}18}$	0.67	0.04	to	1.31
$\gamma_{\geq 19}$	-0.29	-1.19	to	0.61
σ	16.37	13.95	to	19.21

(a) Gaussian kernel.

	Estimate	95% CI		
β_0	-20.58	-20.68	to	-20.47
β_{trend}	-0.04	-0.09	to	0.00
β_{sin}	0.26	0.12	to	0.39
β_{cos}	0.27	0.14	to	0.40
γ_0	-7.01	-9.47	to	-4.54
γ_C	-0.79	-1.31	to	-0.28
$\gamma_{3\text{-}18}$	0.80	0.12	to	1.48
$\gamma_{\geq 19}$	-0.17	-1.13	to	0.78
σ	3.17	1.25	to	8.06
d	2.30	1.74	to	3.03

(b) Power-law kernel.

IMD — parameter estimates (RR)

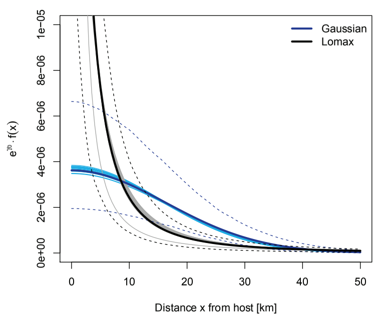
	RR	95% CI	p-value
β_{trend}	0.953	0.91–1.00	0.03
β_{sin}	1.302	1.15–1.48	<0.0001
β_{cos}	1.300	1.15–1.47	<0.0001
γ_{C}	0.401	0.24–0.68	0.0006
$\gamma_{3\text{-}18}$	1.964	1.04–3.69	0.036
$\gamma_{\geq 19}$	0.751	0.31–1.85	0.53

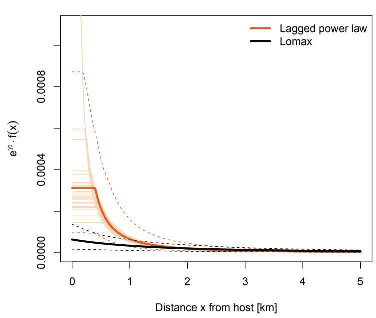
(a) Gaussian kernel.

	RR	95% CI	p-value
β_{trend}	0.956	0.91–1.00	0.052
β_{sin}	1.291	1.13–1.47	0.0002
β_{cos}	1.308	1.15–1.49	<0.0001
γ_{C}	0.452	0.27–0.75	0.0024
$\gamma_{3\text{-}18}$	2.231	1.13–4.41	0.021
$\gamma_{\geq 19}$	0.840	0.32–2.17	0.72

(b) Power-law kernel.

▷ Estimated power laws (with sensitivity analysis)

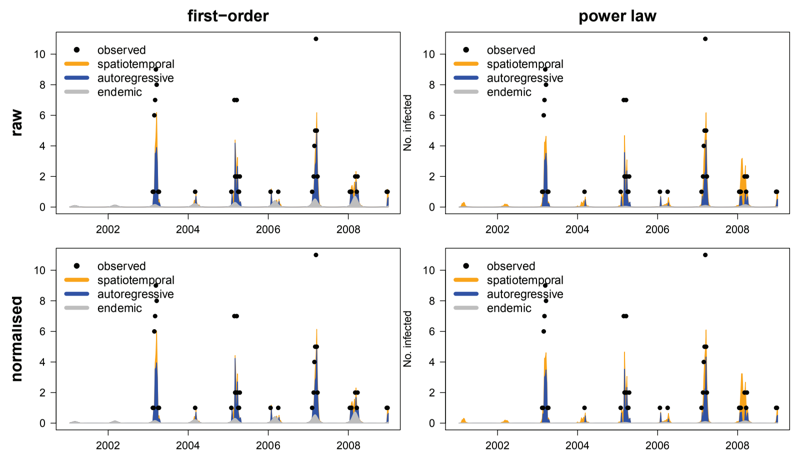




Influenza — parameter estimates (w/o seasonal coefficients)

	raw weights		normalised weights		
	first order	power law	first order	power law	PL + pop.
$\beta^{(\phi)}_{\log(\text{pop})}$	—	—	—	—	0.76 (0.13)
d	—	1.72 (0.10)	—	1.80 (0.10)	1.65 (0.10)
ψ	0.93 (0.03)	0.86 (0.03)	0.92 (0.03)	0.86 (0.03)	0.86 (0.03)
σ^2_λ	0.14	0.17	0.13	0.17	0.16
σ^2_ϕ	0.94	0.92	0.98	0.89	0.71
σ^2_ν	0.5	0.67	0.51	0.67	0.66
$\rho_{\lambda\phi}$	0.02	0.2	0.03	0.21	0.13
$\rho_{\lambda\nu}$	0.11	0.31	0.12	0.31	0.27
$\rho_{\phi\nu}$	0.56	0.29	0.55	0.3	0.39
$l_{\text{pen}}(l_{\text{mar}})$	-18400 (-433)	-18129 (-456)	-18387 (-436)	-18124 (-453)	-18124 (-439)

▷ Fitted values for Regensburg



▷ Estimated seasonal variation