A practical introduction to Latent Gaussian Models with INLA

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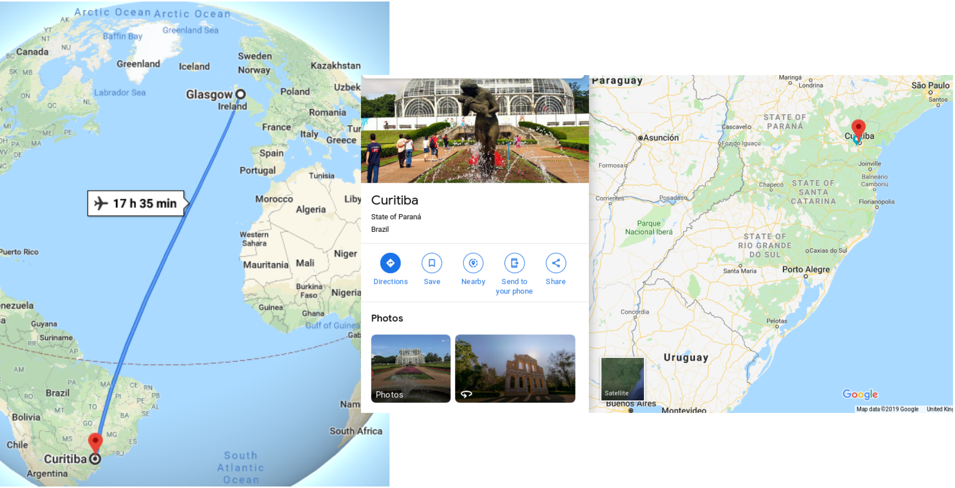
So, where is Curitiba?



What is INLA?

- **The short answer:** INLA is a fast method to do Bayesian inference with latent Gaussian models and `INLA` is an `R`-package that implements this method with a flexible and simple interface.

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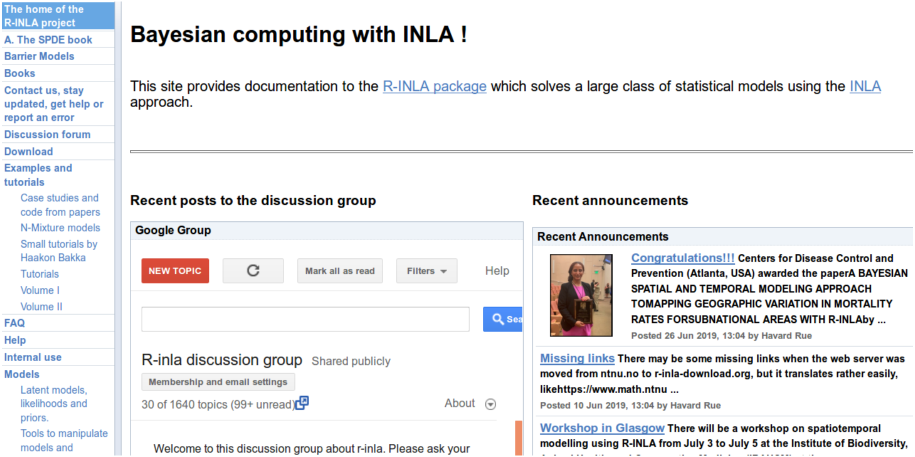
- **The short answer:** INLA is a fast method to do Bayesian inference with latent Gaussian models and `INLA` is an `R`-package that implements this method with a flexible and simple interface.

- **A much longer answer:**
  - Is in the paper H. Rue, Martino, and Chopin (2009) **Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations.** *Journal of the Royal Statistical Society: Series B*. 319–392
  - Or, first, read H. Rue et al. (2017) **Bayesian Computing with INLA: A Review.** *Annual Review of Statistics and Its Application* 4, 395–421.

Informations? `http://www.r-inla.org`



- There are some books around . . .

So... Why should you use R-INLA?

- What type of problems can we solve?
- What type of models can we use?
- When can we use it?

To have proper answers, we need to start at the very beginning

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- **The core**
  - We have questions
  - We observe/collect some data.
  - We want answers

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- **How do we find answers?**
- We need to make choices:
  - Bayesian or frequentist?
  - How do we model the data?
  - How do we compute the answer?
- **These questions are *not* independent.**

Sumário

Basic statistical model structure

- Observations of a phenomena may follow the model

$$\mathbf{y} = \mu(\mathrm{F}, \beta) + \mathbf{e}$$

  - **y** is the observation
  - $\mu(\mathrm{F}, \beta)$ is the explanation
    - if it is a linear model, then

$$\mu(\mathrm{F}_i, \beta) = \beta_0 + \beta_1 \mathrm{F}_{i,1} + ... + \beta_p \mathrm{F}_{i,p}$$

  - **e** is the unexplained part

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- The "explanation part" may not be the "truth"
  - choose $\mu(.,.)$ that reduces $\mathbf{e}$
  - there may be some options for $\mu(.,.)$
  - $\mu(.,.)$ is "a vision of the world"

Basic statistical model structure contd.

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- Statistics at this point (more to come):
  - **e** follows a probability distribution
  - $\mu(.,.)$ may be a simplification
  - *all the models are wrong, but some are useful*

The statistical modeling problem

- Propose $\mu(\mathrm{F}, \beta)$ that
  - sets *e* as completely random
    - i.e. no other information available to explain *e*

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  - estimate β

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- For a given $\mu(\mathrm{F}, \beta)$, β is unknown
  - estimate β
- Account for uncertainty

The linear predictor

Suppose $\mu(\mathrm{F}, \beta)$ is a linear function of β on F, the linear predictor is

$$\mu(\mathrm{F}_i, \beta) = \beta_0 + \beta_1 \mathrm{F}_{i,1} + \ldots + \beta_p \mathrm{F}_{i,p}$$

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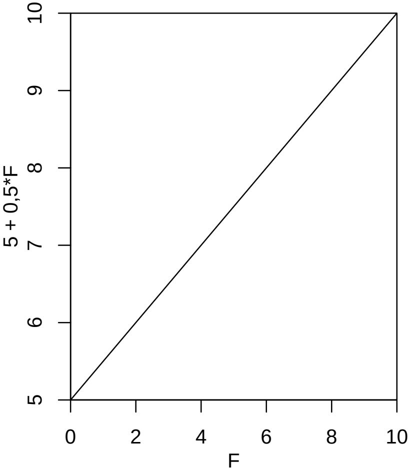
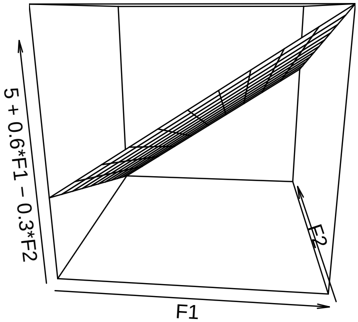
- this can be written as $\mathrm{E}(\mathbf{y}|\mathrm{F}, \beta)$, where we model the expected value of **y** conditional on F and β
- **F** includes the design matrix, factors, explanatory variables, covariates, independent variables, etc.
  - usually it is assumed to be fixed
- β is a vector of unknown *constants*
  - regression coefficients (measure the effect of the covariates)
  - usually are the parameters of main interest

About the coefficients

- the effect of F_j is constant (β_j) among the range of F_j values
- It is a hyper-plane on the p dimensional space



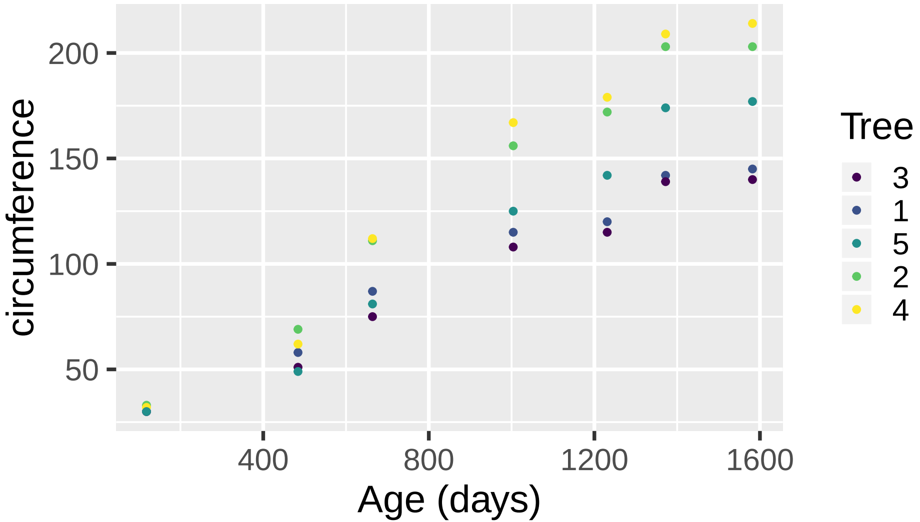


Orange data

```
##   Tree age circumference
## 1    1 118            30
## 2    1 484            58
## 3    1 664            87
```

```
##    Tree  age circumference
## 33    5 1231           142
## 34    5 1372           174
## 35    5 1582           177
```

Orange data (visualize)



Orange: model 1

- **model 1**: circumference increases as age increases

$$\text{circumference} = \beta_0 + \beta_1 \text{Age} + \text{error}$$

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$$\text{circumference} = \beta_0 + \beta_1 \text{Age} + \text{error}$$

- Outcome (circunference): $\mathbf{y} = (y_1, \ldots, y_n)$
- Covariate (age): $\mathbf{w} = (w_1, \ldots, w_n)$

$$\mathrm{E}(y_i) = \beta_0 + \beta_1 w_i, \quad \mathrm{Var}(y_i) = \tau^{-1}, \quad i = 1, \ldots, n$$

On the common linear model

- Observation model $\mathbf{y} \mid \underbrace{\beta_0, \beta_1}_{\mathbf{x}}, \underbrace{\tau}_{\theta}$:
  - Encodes information about observed data
- Latent model $\mathbf{x}$: The unobserved process
- Hyperprior for θ

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  - Encodes information about observed data
- Latent model $\mathbf{x}$: The unobserved process
- Hyperprior for θ

- From this we can compute the posterior distribution

$$\pi(\mathbf{x}, \theta \mid \mathbf{y}) \propto \pi(\mathbf{y} \mid \mathbf{x}, \theta)\pi(\mathbf{x})\pi(\theta)$$

and then the corresponding posterior marginal distributions.

  - each model parameter has its own posterior marginal distribution, which is the distribution after accounting for the other parameters

Fitting using INLA

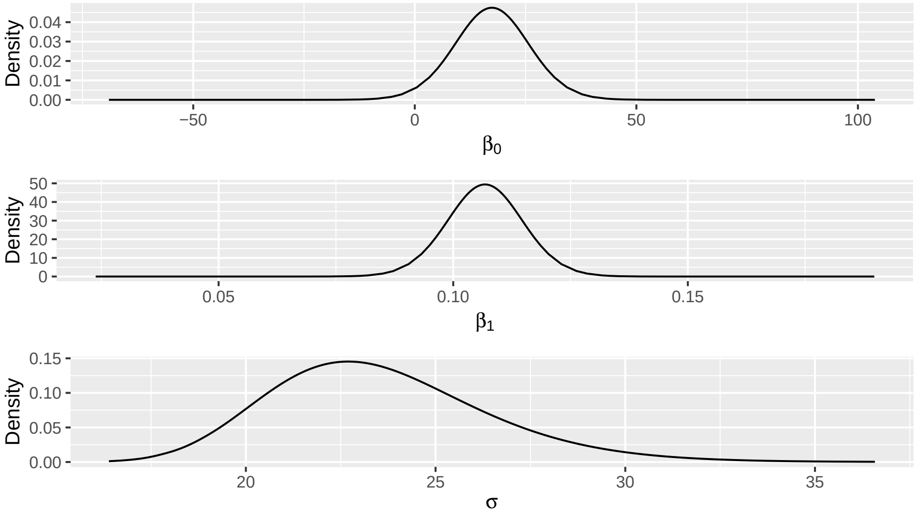
```
m1 <- inla(circumference ~ age, data=Orange,
           control.compute = list(cpo = TRUE))
m1$summary.fixed
```

```
##                 mean      sd 0.025quant 0.5quant 0.975quant
## (Intercept) 17.400 8.59090     0.4363   17.399     34.350 1
## age          0.107 0.00825     0.0905    0.107      0.123
```

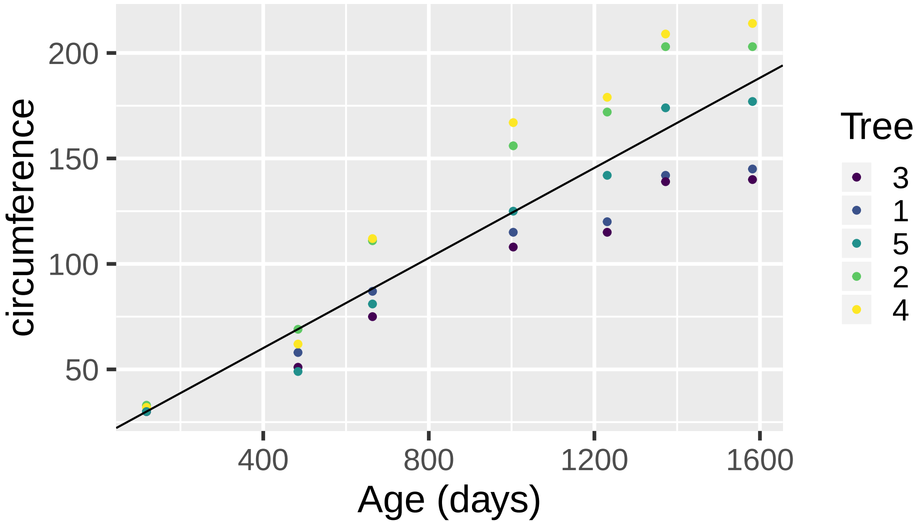
```
m1$summary.hyperpar[1,]
```

```
##                                            mean       sd 0.
## Precision for the Gaussian observations 0.00188 0.000449
##                                         0.5quant 0.975quant
## Precision for the Gaussian observations  0.00185    0.0028
```

Posterior marginals



Model 1 fit



200
150
100
50
circumference
400
800
1200
1600
Age (days)
Tree
3
1
5
2
4

Goodness-of-fit measures

- ***C**onditional **P**redictive **O**rdinate* - CPO:

$$P(y_i^{\mathrm{obs}}|\mathbf{y}_{-i})$$

$\mathbf{y}_{-i}$ is the $\mathbf{y}$ vector without the y_i element

  - useful for model comparison

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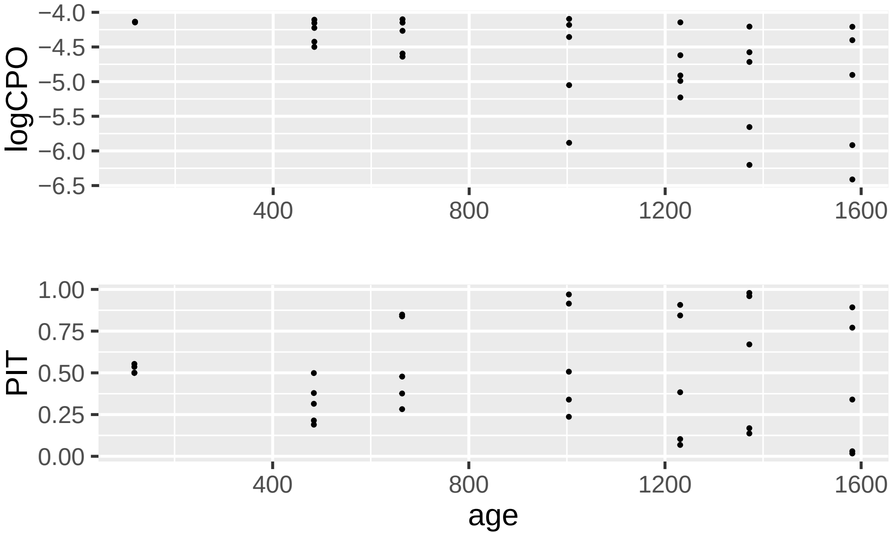
- ***P**robability **I**ntegral **T**ransform* - PIT:

$$P(Y_i \leq y_i^{\mathrm{obs}}|\mathbf{y}_{-i})$$

  - useful to detect lack of fit or outliers

Orange: model 1 check



Sumário

Orange example: effect for each tree

- **model 2** the increase in circumference with age is different for each tree

$$\text{circumference} = \beta_0 + \beta_{tree}\text{Age} + \text{error}$$

- β_0 and β_j, j for each tree, are unknown
- Now we have: $\mathbf{y} \mid \underbrace{\beta_0, \beta_1, \ldots, \beta_5}_{\mathbf{x}}, \underbrace{\tau}_{\theta}$

About the coefficients

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- Usually it is assumed that β_j is
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- It is **very common** to consider $\beta_j \sim N(0, \tau_\beta^{-1})$
  - even non Bayesian does this
- Being Bayesian:
  - It is **also common** to consider $\beta_0 \sim N(m_0, \tau_0^{-1})$, m_0 and τ_0 fixed
  - $\beta = \{\beta_0, \beta_1, \ldots, \beta_5\}$ is a Gaussian with precision

$$\begin{bmatrix} \tau_0 & & & & & \\ & \tau_\beta & & & & \\ & & \tau_\beta & & & \\ & & & \tau_\beta & & \\ & & & & \tau_\beta & \\ & & & & & \tau_\beta \end{bmatrix}$$

A small point to think about

- From a Bayesian point of view fixed effects and random effects are all the same (unobservable and unknown)
- Fixed effects are also random
- They only differ in the prior we put on them

Orange example, model 2

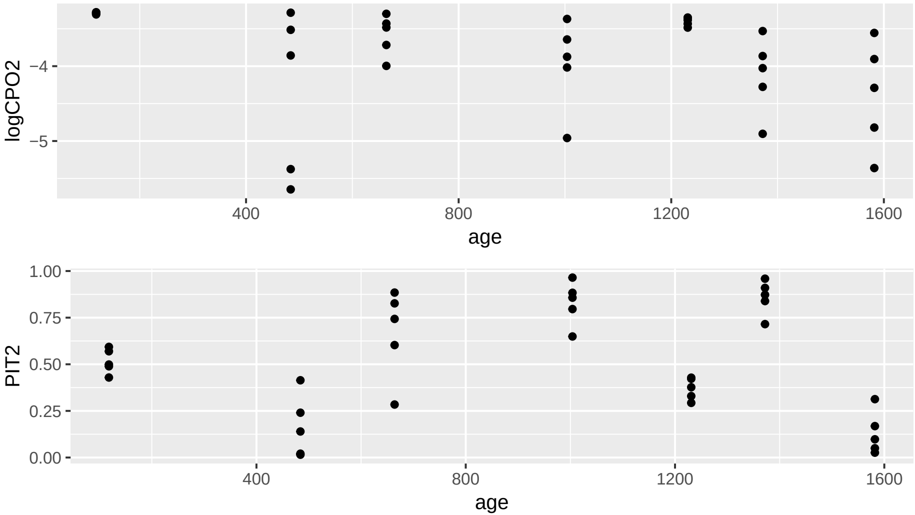
```r
f2 <- circumference ~ 1 + f(Tree, age, model='iid')
m2 <- inla(f2, data=Orange, control.compute=list(cpo=TRUE))
m2$summary.fixed
```

```
##              mean    sd 0.025quant 0.5quant 0.975quant  mod
## (Intercept) 18.11 3.674      10.91    18.08      25.43 18.0
```

```r
m2$summary.random$Tree
```

```
##   ID    mean       sd 0.025quant 0.5quant 0.975quant     mod
## 1  3 0.08192 0.004807    0.07234  0.08194    0.09134 0.0819
## 2  1 0.08672 0.004808    0.07715  0.08675    0.09615 0.0867
## 3  5 0.10293 0.004809    0.09335  0.10295    0.11235 0.1030
## 4  2 0.12644 0.004812    0.11685  0.12647    0.13587 0.1265
## 5  4 0.13202 0.004812    0.12243  0.13205    0.14145 0.1321
```

Orange example, model 2 check



Extending the model framework

- So far the basic (linear) model

$$\begin{aligned} \mathbf{y} &= X\beta + \mathbf{e} \\ &= \eta + \mathbf{e} \end{aligned}$$

does not solves all the problems

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- random effects

$$\eta = \mu(F, \beta) + Z\mathbf{b}$$

- non-linear effects
  - work more on $\mu(F, \beta)$
- non-Gaussian outcomes
  - $p(\mathbf{y}|...)$ may be non-Gaussian

Salmonella example

Breslow (1984) analyses some mutagenicity assay data (shown below) on salmonella in which three plates have been processed at each dose *i* of quinoline and the number of revertant colonies of TA98 Salmonella measured. A certain dose-response curve is suggested by theory.

dose of quinoline (μg per plate)

0	10	33	100	333	1000
15	16	16	27	33	20
21	18	26	41	38	27
29	21	33	69	41	42

Figure 1: Salmonella data

Salmonella model

This is assumed to be a random effects Poisson model allowing for over-dispersion. Let x_i be the dose on the plates *i* 1, *i* 2 and *i* 3. Then we assume

$$y_{ij} \sim \text{Poisson}(m_{ij})$$

$$\log(m_{ij}) = a + b \log(x_i + 10) + g\, x_i + l_{ij}$$

$$l_{ij} \sim \text{Normal}(0, t)$$

a , b , g , t are given independent ``noninformative'' priors. The appropriate

Figure 2: Salmonella model

Salmonella model fit

```r
data(Salm)
head(Salm)
```

```
##    y dose rand
## 1 15    0    1
## 2 21    0    2
## 3 29    0    3
## 4 16   10    4
## 5 18   10    5
## 6 21   10    6
```

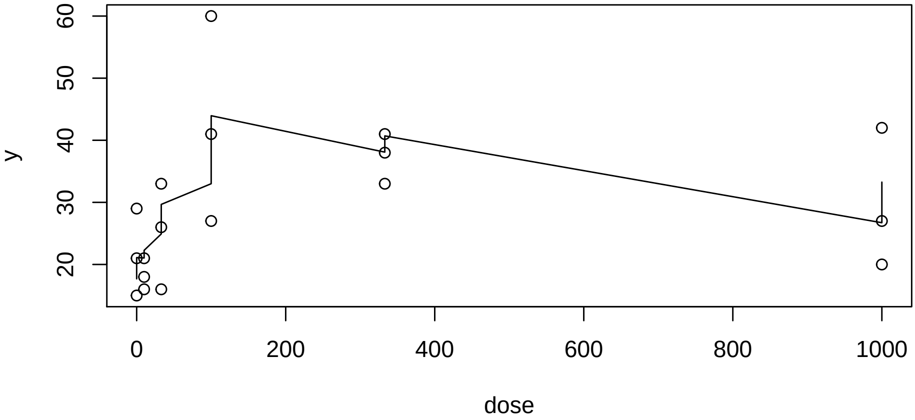
```r
salmm <- inla(y ~ log(dose+10) + dose + f(rand, model='iid'),
              family='Poisson', data=Salm,
              control.compute=list(cpo=TRUE))
```

Salmonella model results

```
##                  mean   sd 0.025quant 0.5quant 0.975quant mod
## (Intercept)      2.17 0.28       1.61     2.17       2.72 2.1
## log(dose + 10) 0.32 0.07       0.16     0.32       0.46 0.3
## dose             0.00 0.00       0.00     0.00       0.00 0.0

##                       mean    sd 0.025quant 0.5quant 0.975quar
## Precision for rand 8205 15938          9       71       5553
```

Salmonella model fit result



Epilepsia example

Breslow and Clayton (1993) analyse data initially provided by Thall and Vail (1990) concerning seizure counts in a randomised trial of anti-convulsant therpay in epilepsy. The table below shows the successive seizure counts for 59 patients. Covariates are treatment (0,1), 8-week baseline seizure counts, and age in years. The structure of this data is shown below

Patient	y_1	y_2	y_3	y_4	Trt	Base	Age
1	5	3	3	3	0	11	31
2	3	5	3	3	0	11	30
3	2	4	0	5	0	6	25
4	4	4	1	4	0	8	36
....							
8	40	20	21	12	0	52	42
9	5	6	6	5	0	12	37
....							
59	1	4	3	2	1	12	37

Figure 3: Epilepsia data

Epilepsia data

```
data(Epil)
head(Epil)
```

```
##   y Trt Base Age V4 rand Ind
## 1 5   0   11  31  0    1   1
## 2 3   0   11  31  0    2   1
## 3 3   0   11  31  0    3   1
## 4 3   0   11  31  1    4   1
## 5 3   0   11  30  0    5   2
## 6 5   0   11  30  0    6   2
```

Sumário

Hierarchical models, level 1

- **Likelihood**, the conditional model for the outcome, **y**

$$\mathbf{y}|\mathbf{x}, \theta_1 \sim \pi(\mathbf{y}|\mathbf{x}, \theta_1) \quad = \quad \prod_{i=1}^{n} \pi(y_i|x_i, \theta_{\mathbf{1}})$$

(conditional independence)

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(conditional independence)

- $\mathbf{x}$, see H. Rue et al. (2017) for an example
  - x_i, for $i = 1, ..., n$ is the linear predictor
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- **x**, see H. Rue et al. (2017) for an example
  - x_i, for $i = 1, ..., n$ is the linear predictor
  - x_j, $j > n$ includes fixed and random effects

- θ_1: likelihood extra parameter
  - example: variance (dispersion), zero inflation

Likelihood:

The likelihood, $\pi(\mathbf{y}|\mathbf{x}, \theta)$ depends on

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Likelihood:

The likelihood, $\pi(\mathbf{y}|\mathbf{x}, \theta)$ depends on

- the kind of response
  - binary, counts, continuous, censored
- how is it collected
  - *usually* each individual has only one observation
  - *possible* for more than one
  - *Unusual example:* point process (point pattern) where we only have the locations of a set of events Can you explain in the course what you mean by having only the locations of a set of events?

Hierarchical model, level 2

- the model for the random effect
  - not observable, latent
  - assumed to have a probability distribution
    - usually Gaussian $\rightarrow$ INLA

$$\mathbf{x}|\theta_2 \sim \pi(\mathbf{x}|\theta_2) \quad = \quad N(\mathbf{0}, \mathbf{Q}(\theta_2)^{-1})$$

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- the model for the random effect
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$$\mathbf{x}|\theta_2 \sim \pi(\mathbf{x}|\theta_2) \quad = \quad N(\mathbf{0}, \mathbf{Q}(\theta_2)^{-1})$$

- this distribution has its own parameters, θ_2, the hyper-parameters

Random effect distribution:

- The random effect distribution, $\pi(\mathbf{x}|\mathbf{Q}(\theta))$ is
  - Non-observable (thus latent)
  - if Gaussian $\rightarrow$ latent Gaussian
  - Markovian $\rightarrow$ $\mathbf{Q}(.)$ sparse $\rightarrow$ computational benefits

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  - covariate effects (coefficients or smoothed effects)
  - random effects (individuals, temporal, spatial)
    - unstructured or structured

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- It represents
  - covariate effects (coefficients or smoothed effects)
  - random effects (individuals, temporal, spatial)
    - unstructured or structured
- It can be
  - unstructured (independent, non-correlated individuals)
  - structured (dependent, correlated, similar neighbour effects)
  - more than one structure (or level) combined

Hierarchical model, level 3

- if Bayesian
  - assumed a distribution for the hyper-parameters

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- if Bayesian
  - assumed a distribution for the hyper-parameters
- have $\theta = \{\theta_1, \theta_2\}$

$$\theta \sim \pi(\theta)$$

Prior distribution for the hyper-parameters θ : $\pi(\theta)$

- likelihood examples
  - precision parameter
    - Normal, gamma, beta, binomial negative
  - zero inflation probability
- random effect examples
  - random effect precision parameter
  - correlation parameter
  - range parameter

Hierarchical Model Summary

What are the

1. distribution of the responses?
2. distribution of the underlying unobserved (latent) components?

Hierarchical Model Summary

What are the

1. distribution of the responses?
2. distribution of the underlying unobserved (latent) components?

. . . *if Bayesian*

3. prior beliefs about the parameters (distribution) on the hyper-parameters in the model?

Latent Gaussian models

- Assume a Gaussian distribution for the
  - regression coefficients
  - smoothed effects
  - random effects

Latent Gaussian models

- Assume a Gaussian distribution for the
  - regression coefficients
  - smoothed effects
  - random effects
- Latent Gaussian Model - **LGM**
  - Basically, if you have Gaussian distribution for each of the unknowns in the linear predictor you have a LGM

Sumário

What is INLA?

- Integrated Nested Laplace Approximations
- Short answer: **fast** method for Bayesian inference on **LGM**
- More details: see H. Rue, Martino, and Chopin (2009)
  - Recommended to start with the review in H. Rue et al. (2017)

INLA overview

- Integrated Nested Laplace Approximations for $p(\theta_j|y)$ and $p(x_i|y)$

INLA overview

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- Step 1: approach $p(\theta|y) \approx \tilde{p}(\theta|y)$
  - Laplace approximation at its mode $\tilde{\theta}$, $\tilde{p}(\tilde{\theta}|y)$
  - select a **good** set of values for θ around $\tilde{\theta}$
    - *eb*: just the mode (empirical Bayes)
    - *grid*: grid around the mode
    - *ccd*: central composite design

INLA overview contd

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- Step 2: approach $p(x_i|y,\theta) \approx \tilde{p}(x_i|y,\theta)$
  - for **a** set of values of θ
  - Gaussian, adaptive, simplified Lapplace or (full) Laplace approximation

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- Step 2: approach $p(x_i|y,\theta) \approx \tilde{p}(x_i|y,\theta)$
  - for **a** set of values of θ
  - Gaussian, adaptive, simplified Lapplace or (full) Laplace approximation
- Step 3: approach $p(x_i|y)$ and $p(\theta_j|y)$
  - numerical integration over θ

INLA overview contd

- Integrated Nested Laplace Approximations for $p(\theta_j|y)$ and $p(x_i|y)$
- Step 2: approach $p(x_i|y,\theta) \approx \tilde{p}(x_i|y,\theta)$
  - for **a** set of values of θ
  - Gaussian, adaptive, simplified Lapplace or (full) Laplace approximation
- Step 3: approach $p(x_i|y)$ and $p(\theta_j|y)$
  - numerical integration over θ
- **IF** $p(\mathbf{y}|...)$ is Gaussian, there are **no approximations** in steps 1 and 2

Several models under this framework

- Generalized (mixed) models
- Generalized additive (mixed) models
- Survival models
- Dynamic models
- Stochastic volatility models
- Smoothing spline
- Semi-parametric regression
- Disease mapping
- Model based geostatistics*
- Log-Gaussian Cox processes
- Space-time models
- Semi-parametric regression with spatial (space-time) varying coefficients
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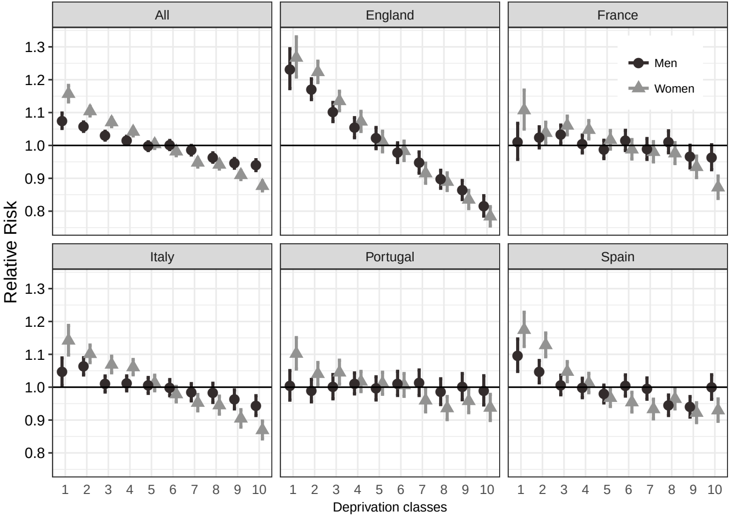
→ GLMM, GAM, GAMM, ... different names for a similar thing

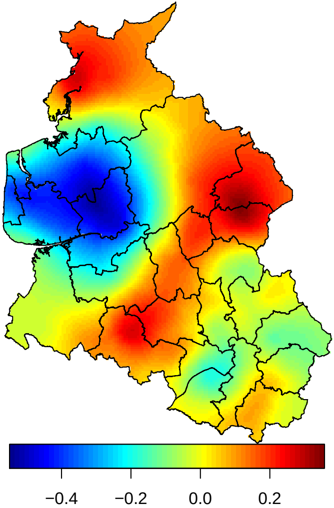
Some applications cited in H. Rue et al. (2017)

Recent examples of applications using the R-INLA package for statistical analysis include disease mapping (Schrödle & Held 2011a , b ; Ugarte et al. 2014 , 2016 ; Papoila et al. 2014 ; Goicoa et al. 2016 ; Riebler et al. 2016); age-period-cohort models (Riebler & Held 2016); a study of the evolution of the Ebola virus (Santermans et al. 2016); the relationships between access to housing, health, and well-being in cities (Kandt et al. 2016); the prevalence and correlates of intimate partner violence against men in Africa (Tsiko 2016); a search for evidence of gene expression heterosis (Niemi et al. 2015); analysis of traffic pollution and hospital admissions in London (Halonen et al. 2016); early transcriptome changes in maize primary root tissues in response to moderate water deficit conditions by RNA sequencing (Opitz et al. 2016); performance of inbred and hybrid genotypes in plant breeding and genetics (Lithio & Nettleton 2015); a study of Norwegian emergency wards (Goth et al. 2014); effects of measurement errors (Muff et al. 2015 , Muff & Keller 2015 , Kröger et al. 2016); network meta-analysis (Sauter & Held 2015); time-series analysis of genotyped human campylobacteriosis cases from the Manawatu region of New Zealand (Friedrich et al. 2016); modeling of parrotfish habitats (NC Roos et al. 2015); Bayesian outbreak detection (Salmon et al. 2015); long-term trends in the number of Monarch butterflies (Crewe & Mccracken 2015); long-term effects on hospital admission and mortality of road traffic noise (Halonen et al. 2015); spatio-temporal dynamics of brain tumors (Iulian et al. 2015); ovarian cancer mortality (García-Pérez et al. 2015); the effect of preferential sampling on phylodynamic inference (Karcher et al. 2016); analysis of the impact of climate change on abundance trends in central Europe (Bowler et al. 2015); investigation of drinking patterns in US counties from 2002 to 2012 (Dwyer-Lindgren et al. 2015); resistance and resilience of terrestrial birds in drying climates (Selwood et al. 2015); cluster analysis of population amyotrophic lateral sclerosis risk (Rooney et al. 2015); malaria infection in Africa (Noor et al. 2014); effects of fragmentation on infectious disease dynamics (Jousimo et al. 2014); soil-transmitted helminth infection in sub-Saharan Africa (Karagiannis-Voules et al. 2015); analysis of the effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015 (Bhatt et al. 2015); adaptive prior weighting in generalized regression (Held & Sauter 2016); analysis of hand, foot, and mouth disease surveillance data in China (Bauer et al. 2016); estimation of the biomass of anchovies in the coast of Perú (Quiroz et al. 2015); and many others.

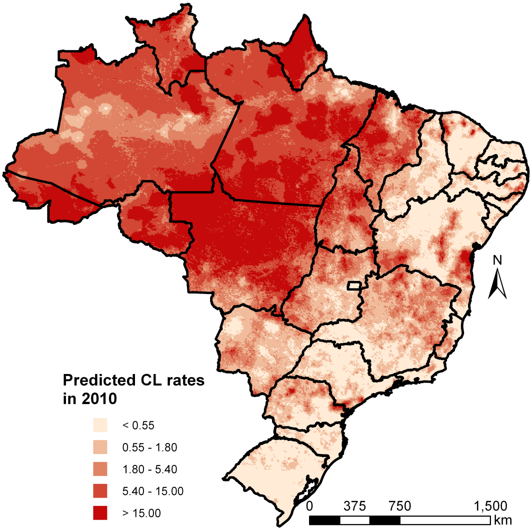
Deprivation effect, Ribeiro et al. (2018)



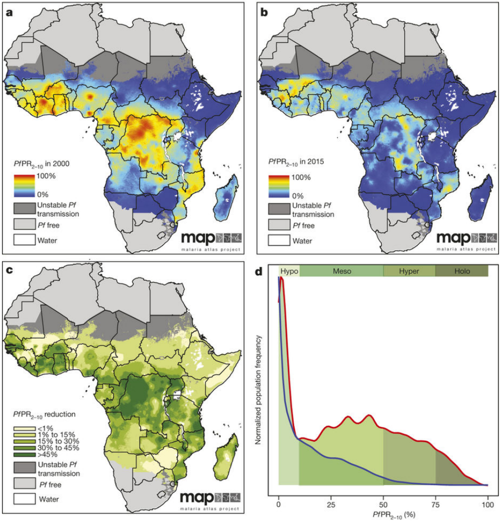
Survival: frailty map



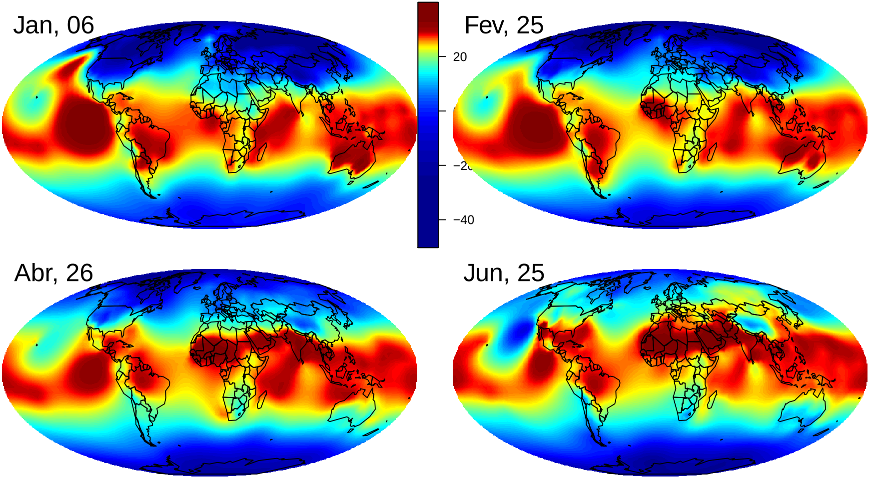
Leishmaniasis in Brazil, Karagiannis-Voules et al. (2013)



Malaria in Africa, Gething (2015)



Non-separable space-time modeling in the globe



Flexibility must come with responsability

- PC-prior ***P****enalized* ***C****omplexity* prior
  - Simpson et al. (2016)
  - Fuglstad et al. (2019)

Sumário

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