Distributional regression for fitting heterogeneous longitudinal response

Statistiques au sommet de Rochebrune 2026

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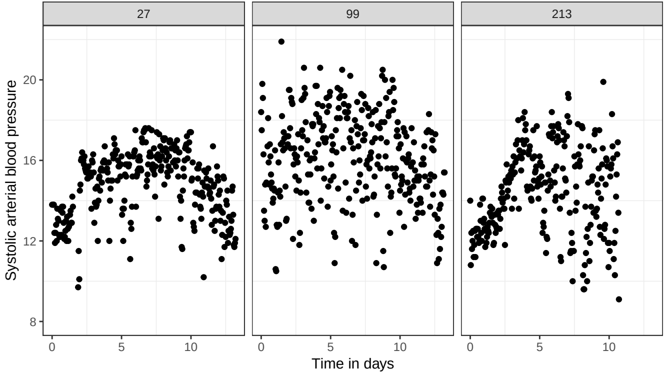
Clinical motivation

- Explain and predict a cardio and cerebro-vascular events
  - Joint modeling for longitudinal and time-to-event data
- Focus on blood pressure
  - A modifiable and known risk factor
  - Recent risk factor hypotheses
    - Individual variability of measurements
    - Probability of being in a given interval (e.g. under a specific threshold)
  - Fit individual conditional distribution over time
- Data collected from 201 patients hospitalized in the intensive care unit in Bordeaux Hospital after a subarachnoid hemorrhage
  - Time-independent covariates (e.g. sex, age...)
  - Intensive biomarker measures (e.g. blood pressure)

Blood pressure measurements

- Heterogeneous longitudinal response
  - Presence of heteroskedasticity, asymmetry, *outliers*



GAMLSS approach

Generalized Additive Models for Location Scale and Shape (Kneib et al. 2023)

- Fit the conditional distribution of a response variable
  - Assume a probability distribution for the response variable
  - Each distribution parameter is modeled by a function of covariates, time and subject-specific random effect
  - Find the best balance between flexibility and interpretation

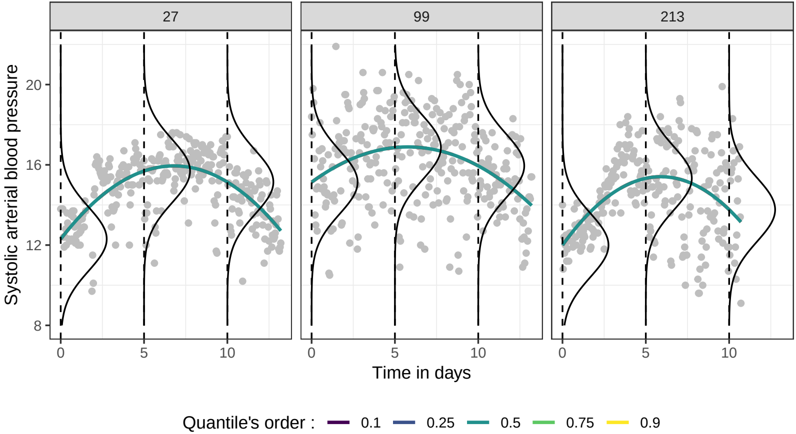
- Location-scale mixed model (LSMM) for dealing with heteroskedasticity (Courcoul et al. 2025)
  - For individual $i = 1, \ldots, n$ and its measurement $j = 1, \ldots, n_i$

$$Y_{ij} | \mathbf{r}_i \sim \mathcal{N}(\mu_{ij}, \sigma_{ij}) \quad \text{with} \quad \begin{cases} \mu_{ij} & = \mathbf{x}_{ij,\mu}^\top \boldsymbol{\beta} + \mathbf{z}_{ij,\mu}^\top \mathbf{b}_i \\ log(\sigma_{ij}) & = \mathbf{x}_{ij,\sigma}^\top \boldsymbol{\xi} + \mathbf{z}_{ij,\sigma}^\top \mathbf{u}_i \end{cases}$$

  - ⋆ $\boldsymbol{\beta}$ and $\boldsymbol{\xi}$ the fixed parameter vectors
  - ⋆ With vector of random effects $\mathbf{r}_i = \left(\mathbf{b}_i^\top, \mathbf{u}_i^\top\right)^\top \sim \mathcal{N}(\mathbf{0}, \Sigma_r)$

Illustration of LSMM

Individual conditional distributions over time



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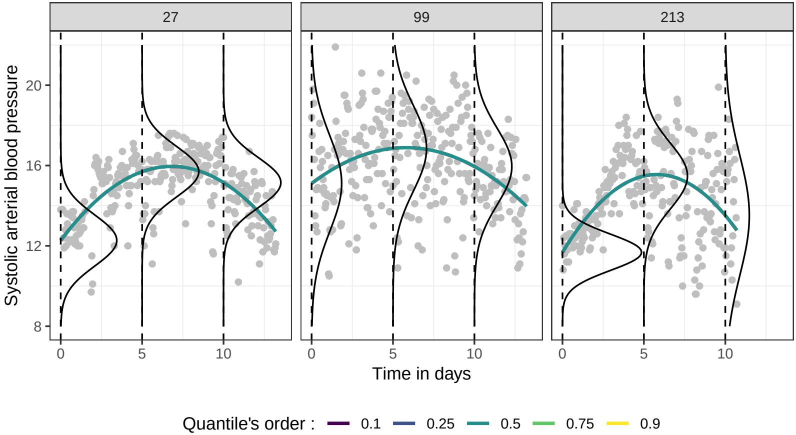

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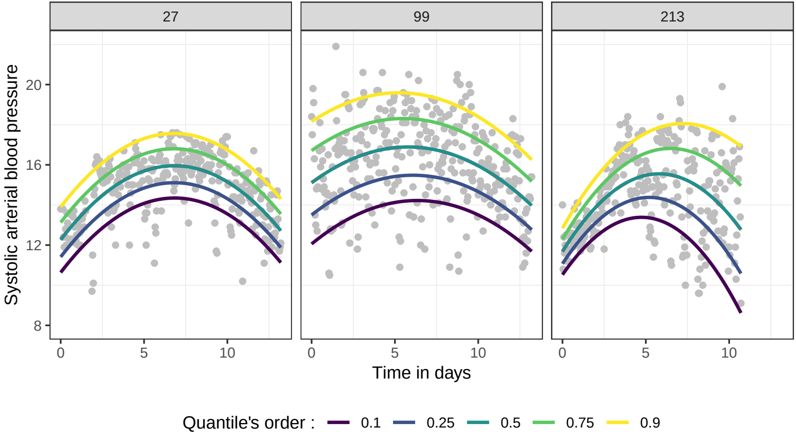

Quantile regression approach

(Koenker, 2005; Geraci, 2014)

- Focus on conditional quantiles the distribution of interest
  - A model for each fitted quantile
  - Explore the entire conditional distribution (asymmetry, heteroskedasticity)
  - Robust to outliers and flexible fit
- Linear quantile mixed model (LQMM)
  - Inference naturally based on Asymmetric Laplace ($\mathcal{AL}$) distribution

$$Y_{ij}|\mathbf{b}_i \sim \mathcal{AL}\left(\mu_{ij}, \sigma, \tau\right) \quad \text{with} \quad \mu_{ij} = \mathbf{x}_{ij,\mu}^\top \boldsymbol{\beta} + \mathbf{z}_{ij,\mu}^\top \mathbf{b}_i,$$

  - μ_{ij} the location parameter and the conditional quantile of order τ
  - $\sigma \in \mathbb{R}^+$ the scale parameter
  - $\tau \in]0, 1[$ a skewness parameter
    - Pre-fixed by user to the order of the quantile of interest

Illustration of LQMM

Conditional quantile trajectories over time

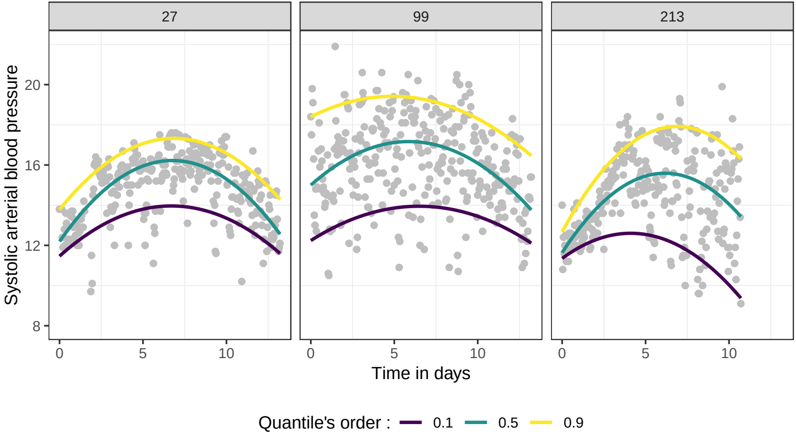

Illustration of LQMM

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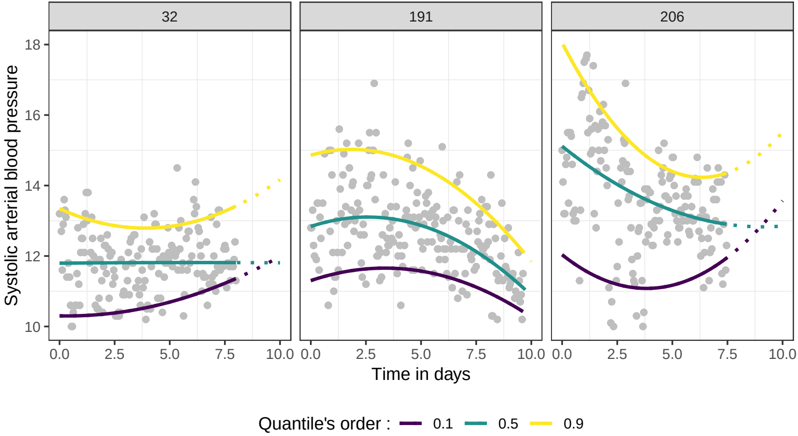


$\mathcal{AL}$ distribution regression model (ALDRM)

- GAMLSS approach using $\mathcal{AL}$ distribution
  - Each distribution parameter is modeled by a function of covariates, time and subject-specific random effects
  - Distribution driven by data
  - For individual $i = 1, \ldots, n$ and its measurement $j = 1, \ldots, n_i$

$$Y_{ij}|\mathbf{r}_i \sim \mathcal{AL}(\mu_{ij}, \sigma_{ij}, \tau_{ij}) \quad \text{with} \quad \begin{cases} \mu_{ij} & = \mathbf{x}_{ij,\mu}^{\top}\boldsymbol{\beta} + \mathbf{z}_{ij,\mu}^{\top}\mathbf{b}_i \\ log(\sigma_{ij}) & = \mathbf{x}_{ij,\sigma}^{\top}\boldsymbol{\xi} + \mathbf{z}_{ij,\sigma}^{\top}\mathbf{u}_i \\ logit(\tau_{ij}) & = \mathbf{x}_{ij,\tau}^{\top}\boldsymbol{\alpha} + \mathbf{z}_{ij,\tau}^{\top}\mathbf{a}_i \end{cases}$$

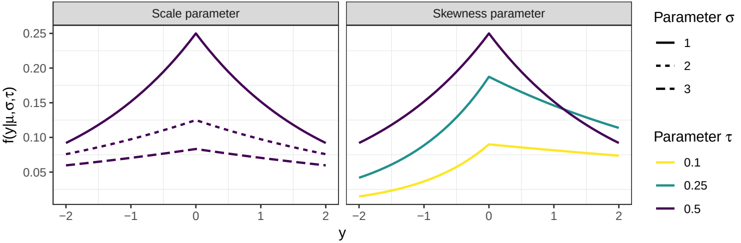
  - ⋆ $\boldsymbol{\beta}$, $\boldsymbol{\xi}$ and $\boldsymbol{\alpha}$ the fixed parameter vectors
  - ⋆ $\mathbf{r}_i$ vector of subject-specific random effects

$$\mathbf{r}_i = \begin{pmatrix} \mathbf{b}_i \\ \mathbf{u}_i \\ \mathbf{a}_i \end{pmatrix} \sim \mathcal{N}\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{pmatrix}, \Sigma_r = \begin{pmatrix} \Sigma_b & 0 & 0 \\ 0 & \Sigma_u & 0 \\ 0 & 0 & \Sigma_a \end{pmatrix}\right).$$

Why $\mathcal{AL}$ distribution?

Denoted by $Y \sim \mathcal{AL}(\mu, \sigma, \tau)$ (Yu et al. 2005)

- Flexible distribution and intuitive interpretation of parameters
  - $\mu \in \mathbb{R}$ is the mode
  - $\sigma \in \mathbb{R}^+$ is the dispersion around the mode
  - $\tau \in]0, 1[$ is the skewness around the mode



- Explicit features given the distributional parameters
  - Cumulative distribution function $F_{Y_{ij}|\mathbf{r}_i}(y)$
  - Inverse cumulative distribution function $\mathcal{Q}_{Y_{ij}|\mathbf{r}_i}(\gamma)$ with $\gamma \in]0, 1[$
  - Expectation and variance

Estimation procedure

Some details

- Bayesian estimation

$$\pi\left(\boldsymbol{\theta}, \mathbf{r}, \boldsymbol{w} | \boldsymbol{y}\right) \quad \propto \quad \prod_{i=1}^{n} \prod_{j=1}^{n_i} f\left(y_{ij} | \mathbf{r}_i, w_{ij}, \boldsymbol{\theta}\right) f\left(w_{ij} | \boldsymbol{\theta}\right) \phi\left(\mathbf{r}_i | \Sigma_r\right) \pi\left(\boldsymbol{\theta}\right)$$

  - Use the rewriting of the asymmetrical Laplace distribution
  - θ the vector of all parameters and prior distribution $\pi\left(\boldsymbol{\theta}\right)$
    - Vague priors
    - Gaussian distributions for fixed effects
    - Inverse-Wishart distribution for covariance matrices of random effects (or Inverse-Gamma for variance parameter)
  - Use the JAGS software to generate posterior samples of parameters
  - Convergence assessed using Gelman-Rubin criterion and parameter trace plots

Application - ALDRM

- Data collected from 201 patients hospitalized in the intensive care unit in Bordeaux Hospital
  - Time-independent covariates (e.g. sex, age...)
  - Intensive biomarker measures (e.g. blood pressure)
    - Total of 42,450 observations
    - Number of measurements per patient ranges from 10 to 322 (median: 224)

- Model specification with $Y_{ij}|\mathbf{b}_i, \mathbf{u}_i, \mathbf{a}_i \sim \mathcal{AL}(\mu_{ij}, \sigma_{ij}, \tau_{ij})$
  - $\mathbf{b}_i \sim \mathcal{N}(\mathbf{0}, \Sigma_b)$, $\mathbf{u}_i \sim \mathcal{N}(\mathbf{0}, \Sigma_u)$ and $\mathbf{a}_i \sim \mathcal{N}(\mathbf{0}, \Sigma_a)$

$$
\begin{aligned}
\mu_{ij} &= \beta_0 + \beta_1 t_{ij} + \beta_2 t_{ij}^2 + \beta_3 Age_i + \beta_4 Sexe_i \\
& \quad b_{i0} + b_{i1} t_{ij} + b_{i2} t_{ij}^2 \\
log(\sigma_{ij}) &= \xi_0 + \xi_1 t_{ij} + \xi_2 Age_i \\
& \quad u_{i0} + u_{i1} t_{ij} \\
logit(\tau_{ij}) &= \alpha_1 Age_i + \alpha_2 Sexe_i \\
& \quad a_{i0} + a_{i1} t_{ij}
\end{aligned}
$$

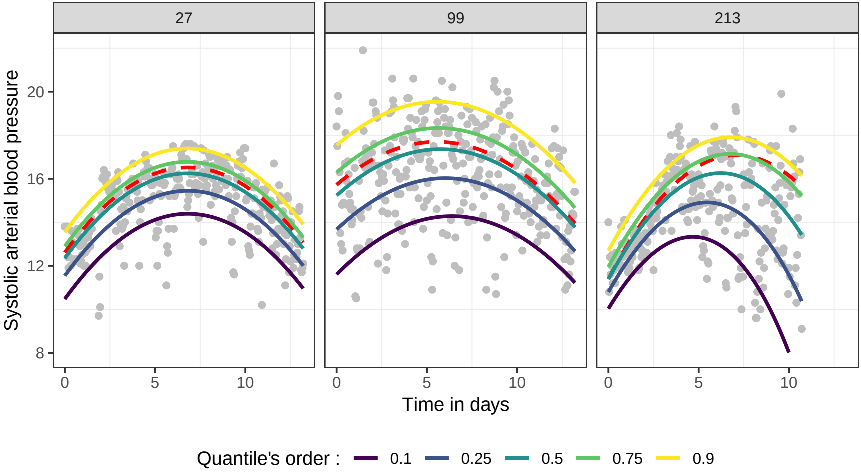
Application - Estimation results

Fixed effects (n.iter = 40000, n.burnin = 10000, n.thin = 10)

	$\widehat{\theta}$	sd	$CI_{95\%}(\theta)$	$\widehat{R}$
Location part				
$\beta_{Intercept}$	13.240	0.163	[12.922;13.559]	1.000
β_{time}	0.310	0.041	[0.231;0.392]	1.000
β_{time^2}	-0.030	0.004	[-0.038; -0.021]	1.000
β_{Age}	0.610	0.119	[0.380; 0.842]	1.000
β_{Sexe_m}	0.632	0.235	[0.17; 1.091]	1.000
Scale part				
$\xi_{Intercept}$	-0.555	0.019	[-0.592; -0.517]	1.022
ξ_{time}	-0.011	0.004	[-0.019; -0.003]	1.008
ξ_{Age}	0.084	0.016	[0.054; 0.114]	1.002
Skewness part				
α_{Age}	0.126	0.038	[0.052; 0.199]	1.003
α_{Sexe_m}	0.146	0.053	[0.041; 0.251]	1.003

Individual conditional distributions

Quantile, density and cumulative distributions over time



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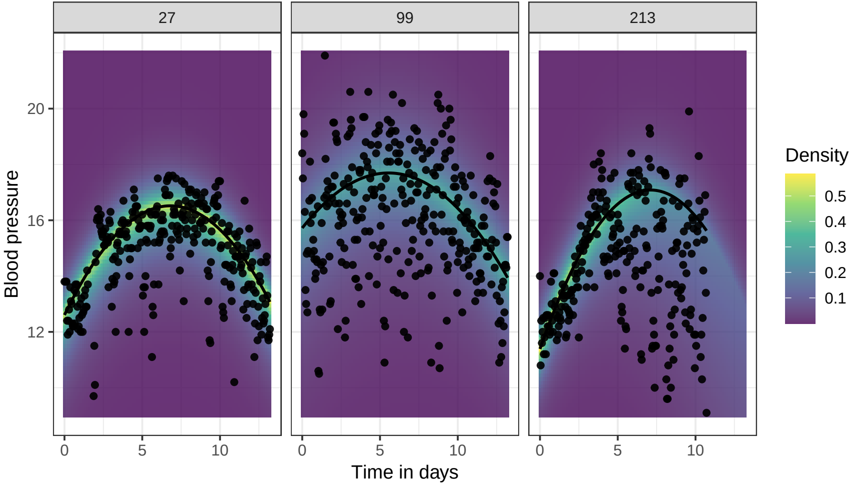

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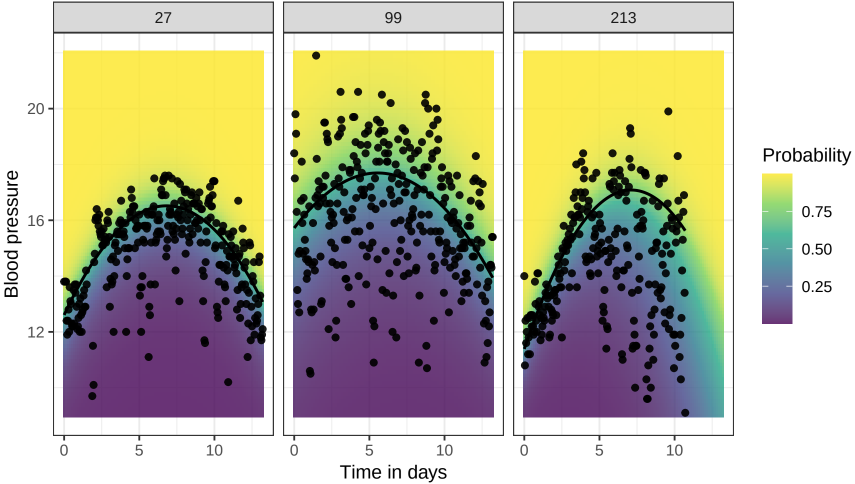


Model selection strategy

Choice of the probability distribution

- Which distribution to choose?
  - Use practical arguments (properties, parameter interpretation, flexibility, computational aspect)
  - Use criteria as AIC, DIC...

- New criteria for goodness-of-fit assessment
  - Focus on a set of quantiles
  - The best model is the one that minimizes

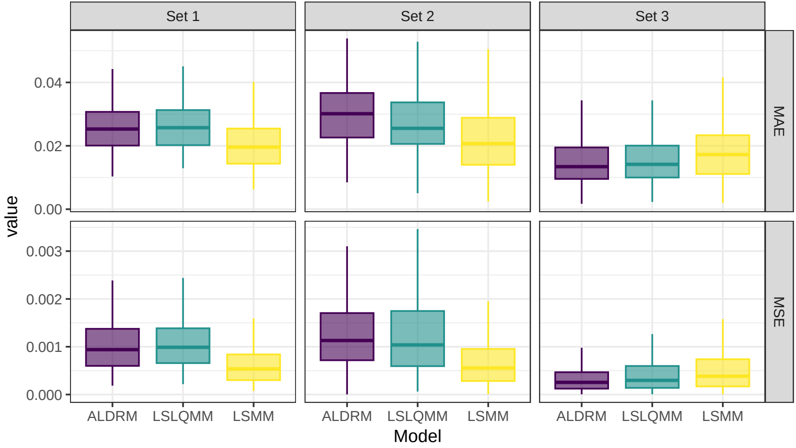
$$C_\Gamma = \frac{1}{n}\sum_{i=1}^{n} C_{i,\Gamma} \quad \text{with} \quad C_{i,\Gamma} = \frac{1}{\#\Gamma}\sum_{\gamma\in\Gamma} \ell\left(\widehat{\gamma}_i - \gamma\right)$$

  - ⋆ Γ a pre-fixed set of orders $\gamma \in]0,1[$ of the quantiles
  - ⋆ $\ell(.)$ a loss function
  - ⋆ $\widehat{\gamma}_i = \frac{n_i^\gamma}{n_i}$ with $n_i^\gamma = \sum_{j=1}^{n_i} \mathbb{1}\left\{y_{ij} < \widehat{\mathcal{Q}}_{Y_{ij}|\mathbf{r}_i}(\gamma)\right\}$

Application results

Distribution of $C_{i,\Gamma}$

- Sets: $\Gamma_1 = \{0.1, 0.2, \ldots, 0.9\}$, $\Gamma_2 = \{0.25, 0.5, 0.75\}$, $\Gamma_3 = \{0.1, 0.5, 0.9\}$
- Loss function $\ell(x) = x^2$ or $\ell(x) = |x|$ (MSE or MAE, resp.)



Discussion

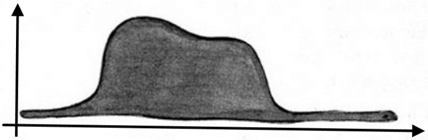
- ALDRM is a flexible distributional regression model
  - Deal with heteroskedasticity, asymmetry and *outliers*
  - Explore the entire distribution of interest
  - Provide various individual features (mode, dispersion, asymmetry, quantiles, cumulative probabilities...)

- All presented models are implemented in the R-package `BeQut`
  - Version in progress on `GitHub` and basic version on `CRAN`
  - Estimation procedure and model choice criterion validated by simulations
    - Conclusion: Everything is ok, trust me :) or see `https://arxiv.org/abs/2512.12362`

- Perspectives
  - Explore more the choice of the distribution based on data
  - Extension to join models for heterogeneous longitudinal and survival data
  - Improve computational aspects

Why use R?

- What is it?



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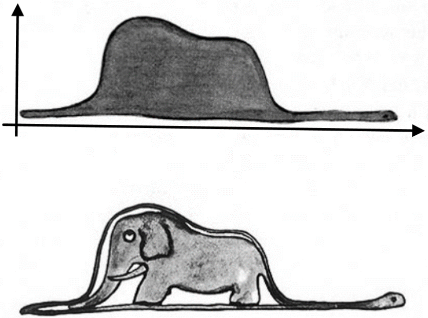

  - "*On ne voit bien qu'avec le coeur, l'essentiel est invisible pour les yeux*" (A de Saint-Exupéry, 1943)

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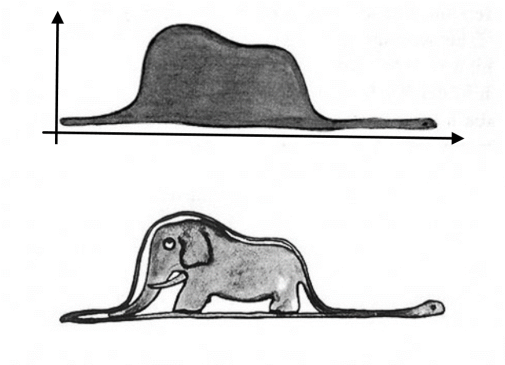

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- "*Love is in the* R " (John Paul Young, 1977)

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