

Markov Chain Monte Carlo methods

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- ▶ Gentle introduction: Monte Carlo (MC) example
- ▶ Markov Chain Monte Carlo (MCMC)
 - ▶ Need (Bayes) and idea
 - ▶ Metropolis-Hastings
 - ▶ Diagnostics and other MCMC
 - ▶ Issues
- ▶ MCMC applied: Immunoassays

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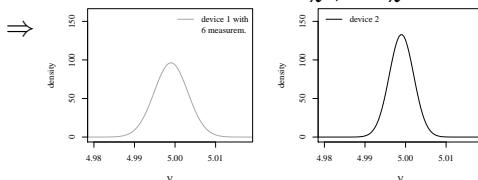
MCMC applied

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Table 8 — A series of $n = 6$ sets of simultaneous indication values, obtained independently, of the input quantities for the measurement of resistance and reactance (9.4.1.3)

	Set	V/V	I/mA	ϕ/rad
device 1	1	5.007	19.663	
	2	4.994	19.639	
	3	5.005	19.640	
	4	4.990	19.685	
	5	4.999	19.678	
	6	4.999	19.661	
				— device 2 (high precision)

- measurand: V , I and $Z = V/I$
- assume: bivariate N-distribution with means $\begin{pmatrix} \hat{V} \\ \hat{I} \end{pmatrix}$, known covariances $\mathbf{u}_x^1 \neq \mathbf{u}_x^2$



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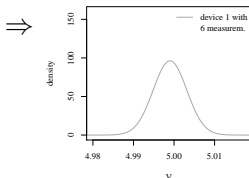
⇒ GUM not applicable

GUM example (S2 [BIPM et al., 2011, Ex. 9.4], Revision [Ex. 5.3])

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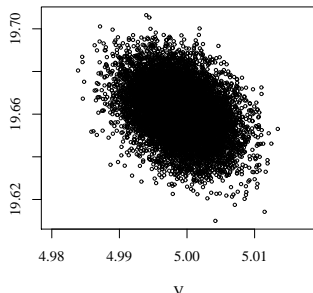
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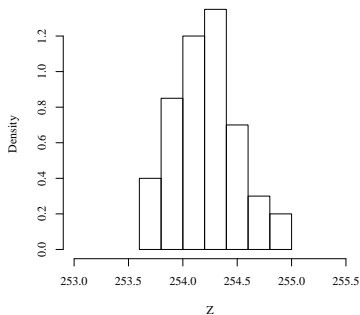
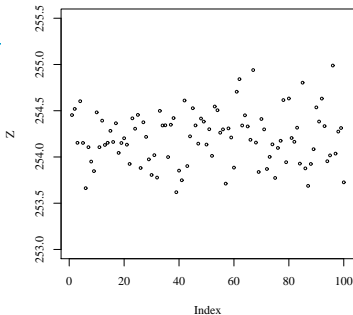
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- measurand: V , I and $Z = V/I$
- assume: bivariate N-distribution with mean $\begin{pmatrix} \hat{V} \\ \hat{I} \end{pmatrix}$, known covariance $\mathbf{U}_x^1 = \mathbf{U}_x^2$

⇒ **Monte Carlo** (R code with mvtnorm package, [R Core Team, 2015])

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MC=rmvnorm(n=10^4,mean=colMeans(data),sigma=Ux)
Z=MC[,1]/MC[,2]*1000
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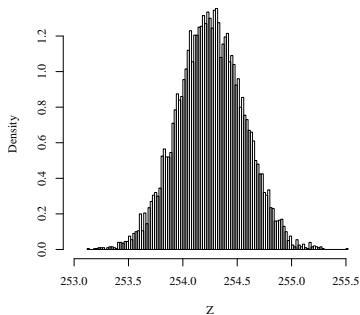
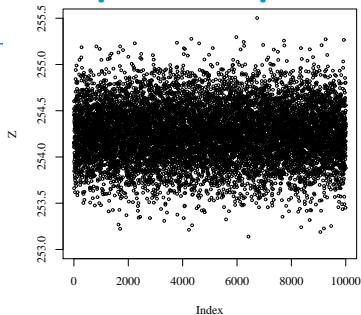


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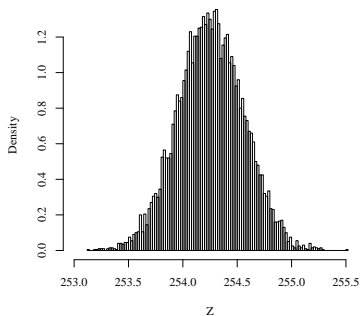
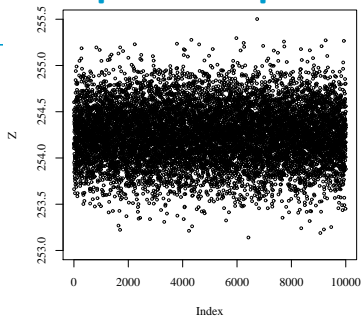


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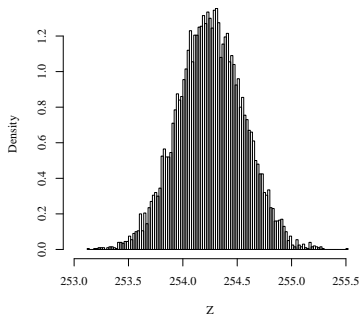
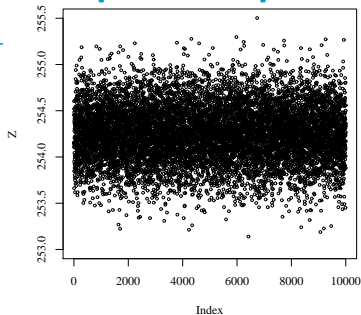
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⇒ **Monte Carlo** (Matlab[®] code with statistics toolbox, [MATLAB, 2015])

```
MC=mvnrnd(mean(data),Ux,1e4);
```

```
Z=1000*MC(:,1)./MC(:,2);
```

A Simple Example for MC



► measurand: V , I and $Z = V/I$

► assume: bivariate N-distribution with mean $\begin{pmatrix} \hat{V} \\ \hat{I} \end{pmatrix}$,
known covariance $\mathbf{U}_x^1 = \mathbf{U}_x^2$

⇒ **Monte Carlo**

► draw independent samples from input pdf

► transform by measurement fct.

⇒ estimates, uncertainties, coverage intervals, ... (if existent)

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⇒ Bayesian framework:

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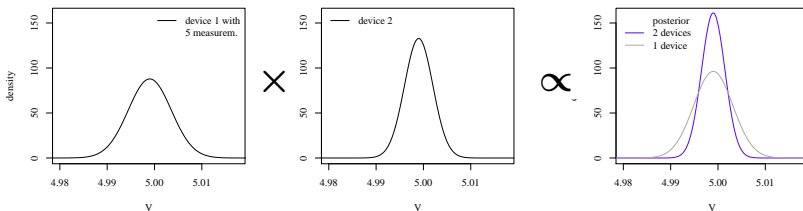
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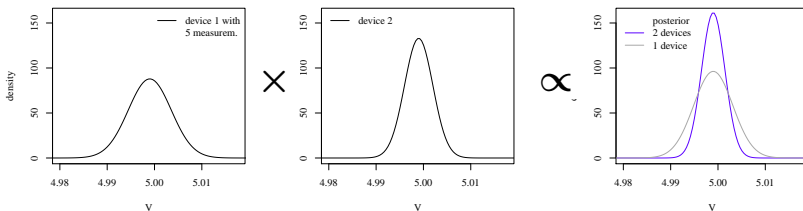
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$$\text{posterior} \propto \text{likelihood} \times \text{prior}$$

posterior distribution:

⇒ integration (for normalization, estimate, uncertainty, CI, ...)

- | | |
|--|--|
| ▶ analytically | usually impossible |
| ▶ numerically
(deterministic methods) | often difficult
(high dimension) |
| ▶ direct sampling (MC) | often impossible
(non-stand./high-dim. pdf) |

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 \Rightarrow integration (for normalization, estimate, uncertainty, CI, ...)

\Rightarrow A Markov Chain Monte Carlo (MCMC) method for the simulation of a distribution f is any method producing an ergodic Markov Chain whose stationary distribution is f .

[Robert and Casella, 2004]

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[Robert and Casella, 2004]

Markov Chain: dependent samples (not independent)

ergodic & stationary: after some time all samples are from f

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Metropolis-Hastings algorithm [Hastings, 1970]:

- ▶ simple, versatile method to construct an 'ergodic Markov Chain with stationary distribution f '

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- ▶ simple, versatile method to construct an 'ergodic Markov Chain with stationary distribution f '

- ▶ choose a proposal distribution q
choose a starting value X_0

For $t = 1, 2, \dots$

Sample point Y from $q(\cdot|X_t)$

Take $X_{t+1} = Y$ with probability $\alpha(X_t, Y)$

$X_{t+1} = X_t$ otherwise

$$\alpha(X_t, Y) = \min \left(1, \frac{f(Y)q(X_t|Y)}{f(X_t)q(Y|X_t)} \right)$$

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- ▶ converges to f : no matter which X_0 or q (wide enough)
[Metropolis et al., 1953]

Metropolis-Hastings algorithm [Hastings, 1970]:

- ▶ simple, versatile method to construct an 'ergodic Markov Chain with stationary distribution f '

- ▶ choose a proposal distribution $q=U(x-\delta, x+\delta)$
choose a starting value $X_0, x=(4.95, 19.66)$

For $t = 1, 2, \dots$

Sample point Y from $q(\cdot|X_t)$

Take $X_{t+1} = Y$ with probability $\alpha(X_t, Y)$

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For $t = 1, 2, \dots$

$y=\text{runif}(2, \text{min}=x-\text{delta}, \text{max}=x+\text{delta})$

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For $t = 1, 2, \dots$

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y=runif(2,min=x-delta,max=x+delta)
if (runif(1)>f(y)/f(x)) y=x
Y[t,]=y, x=y
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Metropolis-Hastings algorithm [Hast

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- ▶ choose a proposal distribution q
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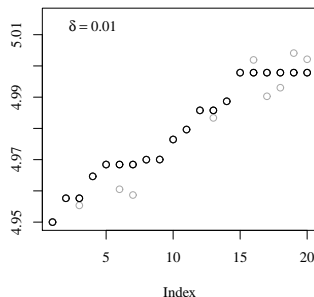
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y = runif(2, min = x - delta, max = x + delta)
if (runif(1) > f(y) / f(x)) y = x
Y[t,] = y, x = y
    
```

```

f <- function(x) {
  dmvtmnorm(x, mean = colMeans(data1), sigma = U1) *
  dmvtmnorm(x, mean = data[6, 1:n], sigma = U2)
}
    
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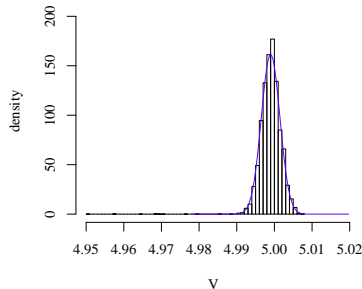
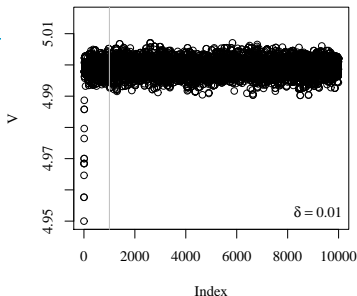
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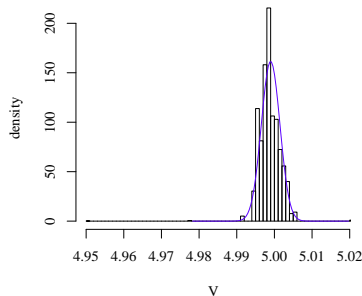
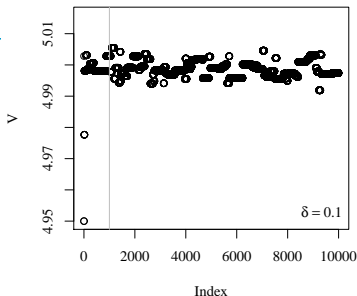
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- converges to f : no matter which X_0 or q (wide enough)
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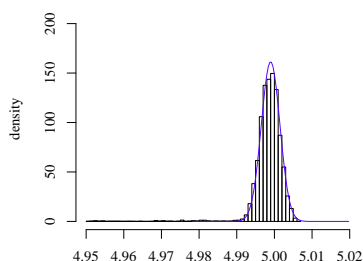
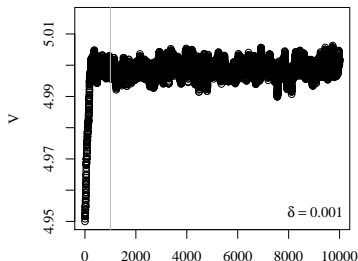
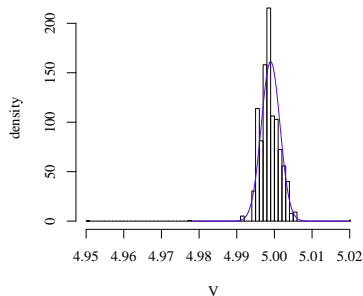
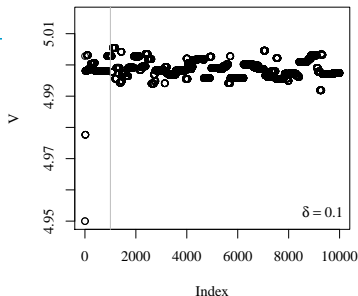
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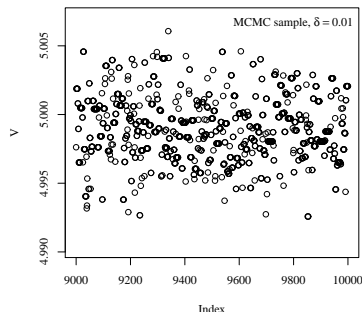
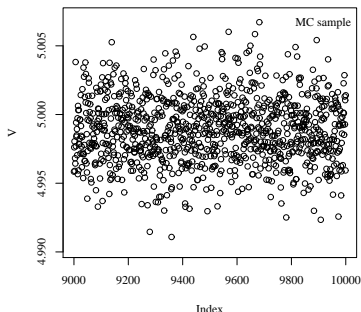
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Metropolis-Hastings algorithm [Hastings, 1970]:

- simple, versatile method to construct an 'ergodic **Markov Chain** with stationary distribution f '

dependence between samples \Rightarrow information \downarrow or time \uparrow



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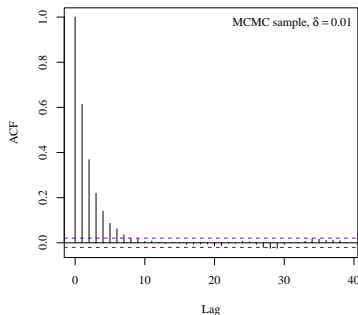
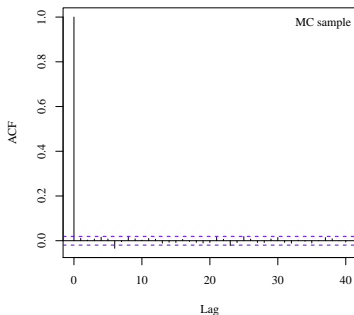
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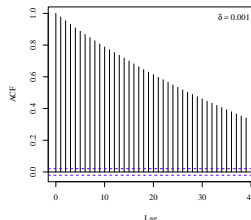
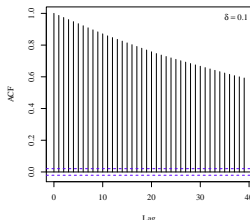
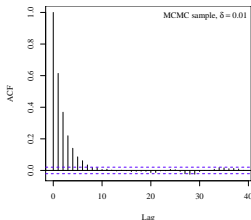
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- ▶ simple, versatile method to construct an 'ergodic **Markov Chain** with stationary distribution f '
 - ▶ proposal distr. q is of practical importance: dependence between samples \Rightarrow information \downarrow or time \uparrow
- \Rightarrow calibrate M-H algorithm (with little knowledge about f)

Toolkit:

- ▶ diagnostics
- ▶ common classes of proposals q
- ▶ transformations of parameters
- ▶ other MCMC methods (e.g. Hamiltonian MC: STAN)

[Stan Development Team, 2014]

- initial samples discarded (here 10%, burn-in)
- acceptance rate

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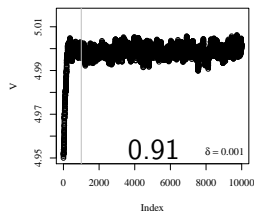
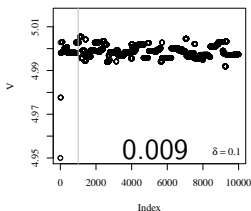
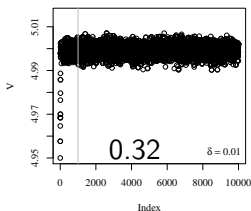
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- ▶ initial samples discarded (here 10%, burn-in)
- ▶ acceptance rate: most efficient when close to 0.25 (rule of thumb for random walk M-H) [Roberts et al., 1997]

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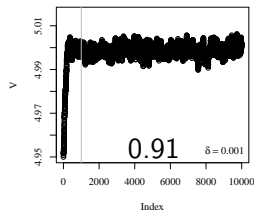
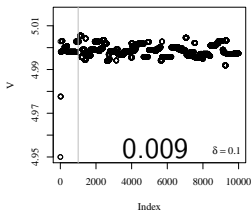
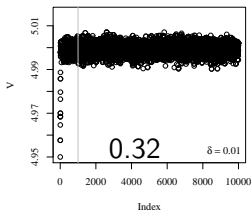
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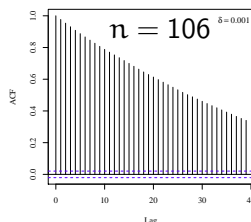
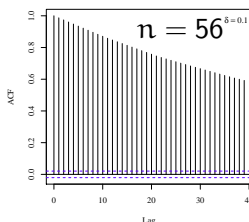
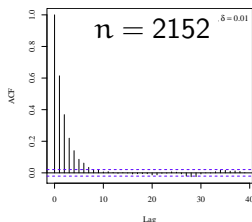
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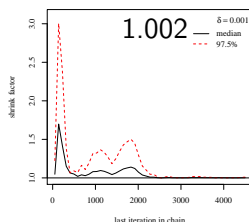
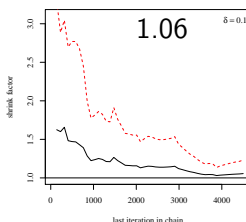
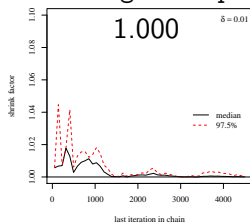


- ▶ initial samples discarded (here 10%, burn-in)
- ▶ acceptance rate: most efficient when close to 0.25 (rule of thumb for random walk M-H) [Roberts et al., 1997]
- ▶ effective sample size: correlation reduces information
`effectiveSize(Y[,1])`, or
⇒ subsampling to reduce space (thinning)



- ▶ initial samples discarded (here 10%, burn-in)
- ▶ acceptance rate: most efficient when close to 0.25 (rule of thumb for random walk M-H) [Roberts et al., 1997]
- ▶ effective sample size: correlation reduces information \Rightarrow subsampling to reduce space (thinning)
- ▶ Gelman-Rubins convergence diagn.: on multiple chains, comparison of variance within & between chains

gelman.plot(MCMC) [Gelman and Rubin, 1992]



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- random walk M-H: local exploration

$$\text{e.g. } Y_t = X_t + \epsilon_t \text{ with } \epsilon_t \sim N(0, \Sigma)$$

implemented in standard software:

R (`mcmc` for N-proposal), Matlab (`statistics: mhsample`)

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- ▶ Metropolis (symmetric), independence sampler, single component M-H, Gibbs sampler (free software: BUGS [Lunn et al., 2009, Thomas et al., 2006]), . . .

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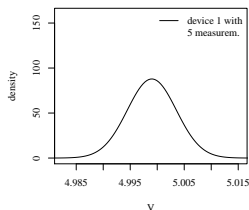
R (`mcmc` for N-proposal), Matlab (statistics: `mhsample`)

- ▶ Metropolis (symmetric), independence sampler, single component M-H, Gibbs sampler (free software: BUGS [Lunn et al., 2009, Thomas et al., 2006]), . . .
- ▶ adaptive schemes: tune proposal during warm-up

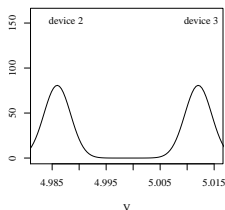
BUT

► 'you've only seen where you've been'

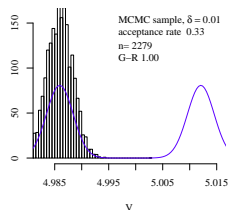
[Robert and Casella, 2004, p.464]



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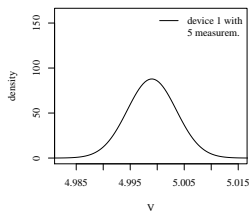
MCMC applied

Summary

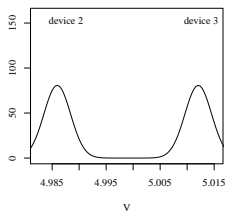
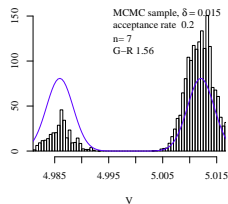
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[Robert and Casella, 2004, p.464]



X

 \propto 

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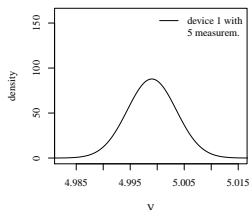
MCMC applied

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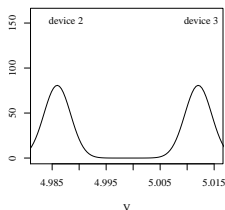
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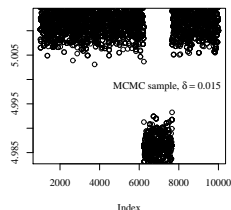
[Robert and Casella, 2004, p.464]



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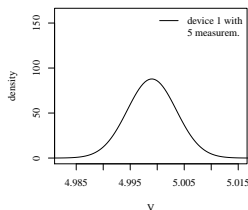
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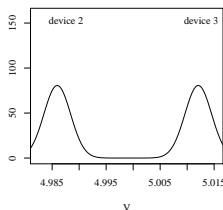
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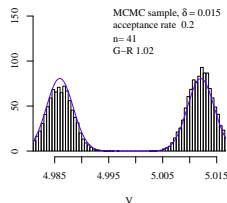
[Robert and Casella, 2004, p.464]



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► convergence assured theoretically – practically it may

- take a long time
- not ‘ve been reached (correctness of result)
- posterior may not exist [Hobert and Casella, 1996]

⇒ ‘Beware: MCMC sampling can be dangerous!’

[Spiegelhalter et al., 2003]

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IA Bayes

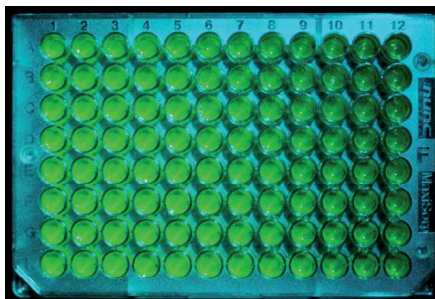
Immunoassays MCMC

Summary

Immunoassays are bio-analytical tests

- ▶ measure even very small amounts of substance
- ▶ to detect: infection, hormones or drugs

⇒ means of diagnosis in health care



ELISA microtiter plate [Voigt et al., 2008, Fig. 1]

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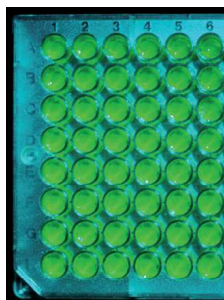
Immunoassays MCMC

Summary

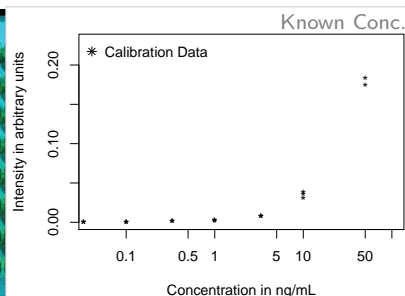
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ELISA microtiter plate [Voigt et al., 2008, Fig. 1]



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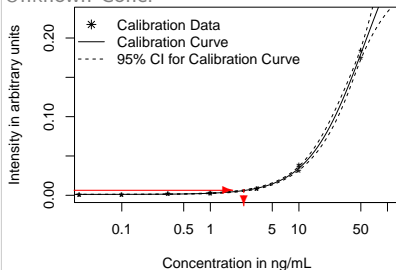
Summary

Immunoassays are bio-analytical tests

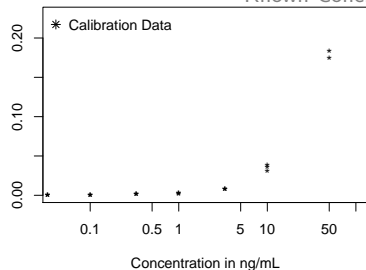
- ▶ measure even very small amounts of substance
- ▶ to detect: infection, hormones or drugs

⇒ means of diagnosis in health care

Unknown Conc.



Known Conc.



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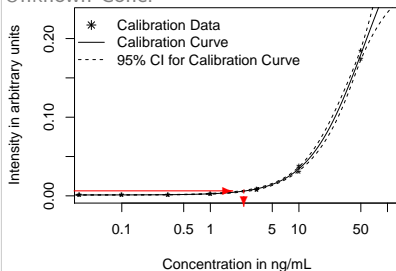
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IA Bayes

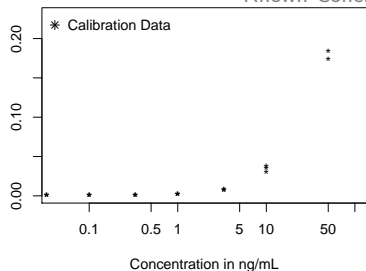
Immunoassays MCMC

Summary

Unknown Conc.



Known Conc.



non-linear regression

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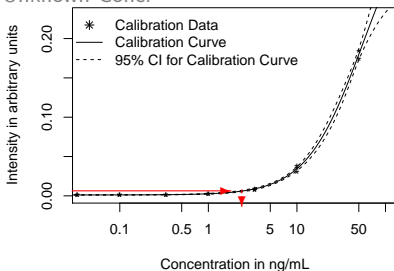
IA Intro

IA Bayes

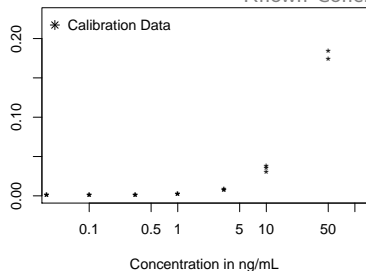
Immunoassays MCMC

Summary

Unknown Conc.



Known Conc.



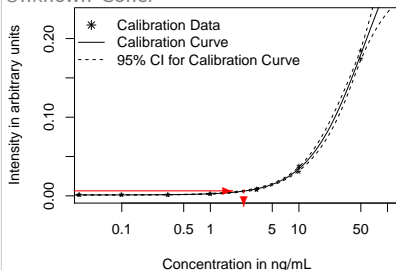
non-linear regression

2x Bayes' theorem:

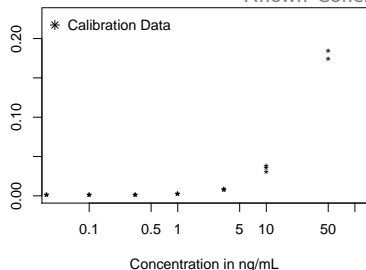
- calibration
- unknown concentration

regression
parameters

Unknown Conc.



Known Conc.



non-linear regression

2x Bayes' theorem:

- calibration (include prior info)
 - unknown concentration
- regression parameters

⇒ propagates all information / uncertainty

Calibration:

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MCMC basi

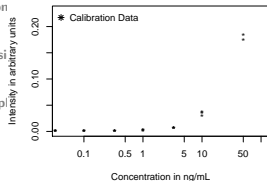
MCMC app

IA Intro

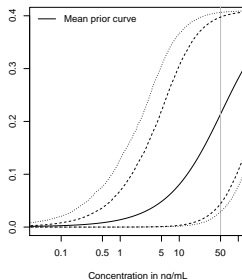
IA Bayes

Immunoassays MCMC

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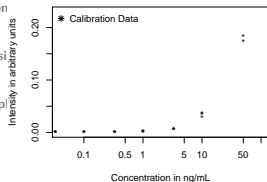


\times

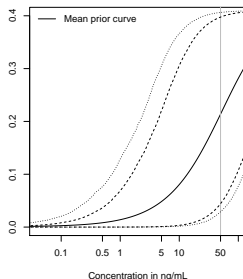


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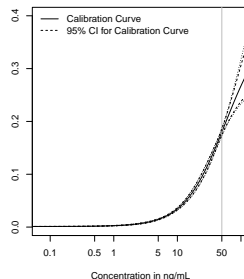
Calibration:



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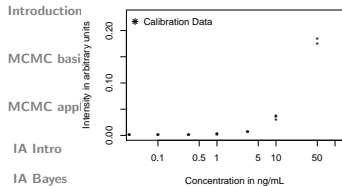


- No analytic solution
- ⇒ MCMC: Gibbs sampling
 - as implemented in BUGS [Lunn et al., 2009]
 - source code in New04-Guide [Elster et al., 2015]

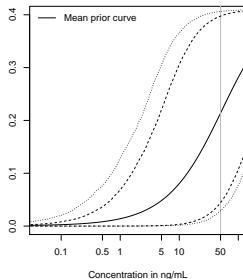
Details: 10 chains, 800,000 iterations each
(retain every 10th sample of 2nd half)

- convergence: no reason to suspect contrary from acf, G-R but time-consuming

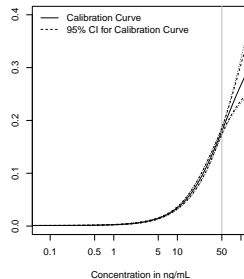
Calibration:



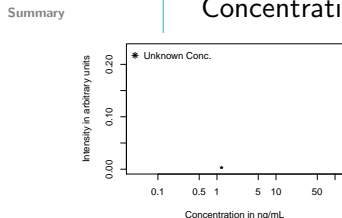
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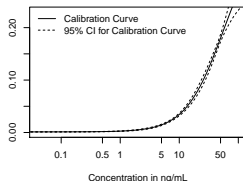
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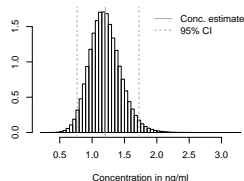
Concentration estimation:



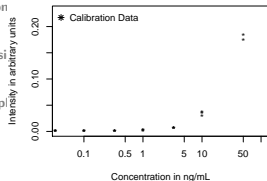
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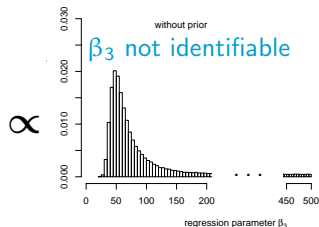
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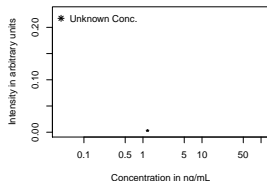
Calibration:



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Concentration estimation:



IA not analysable

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Summary

⇒ Prior information can make parameters identifiable

⇒ Bayes enables IA analysis

⇒ MCMC enables Bayesian approach

Klaunberg, K., Walzel, M., Ebert, B., and Elster, C. (2015). Informative prior distributions for ELISA analyses. Biostatistics, 16(3):465 – 479

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Markov Chain Monte Carlo sampling

- ▶ useful
- ▶ default method (M-H) easy to implement
- ⇒ showed simple code
- ▶ hard to calibrate for efficiency
- ⇒ gave diagnostics & different proposals
- ▶ software available (partially automatic calibration)
- ⇒ still: knowledge required to assure correctness of results

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Simple example & Immunassay analysis

- ▶ Bayes is worth doing (but often intractable without MCMC)
 - ▶ include all information (prior)
 - ▶ coherent propagation of uncertainty

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Robert, C. P. (2015). The Metropolis-Hastings algorithm. ArXiv e-print arXiv:1504.01896 [stat.CO]

Elster, C., Klauenberg, K., Walzel, M., Wübbeler, G., Harris, P., Cox, M., et al. (2015). A Guide to Bayesian Inference for Regression Problems. Deliverable of EMRP project NEW04 'Novel mathematical and statistical approaches to uncertainty evaluation'

Robert, C. P. and Casella, G. (2004). Monte Carlo statistical methods. Springer Texts in Statistics. New York: Springer, 2nd edition

Gilks, W., Richardson, S., and Spiegelhalter, D. (1996). Markov Chain Monte Carlo in practice. Interdisciplinary Statistics. London: Chapman & Hall/CRC, 1st edition

Most Bayes books:

Gelman, A., Carlin, J. B., Stern, H., and Rubin, D. B. (2003). Bayesian data analysis. Texts in Statistical Science. London: Chapman & Hall/CRC, 2nd edition

Robert, C. P. (2007). The Bayesian choice: From Decision-Theoretic Foundations to Computational Implementation. Springer Texts in Statistics. New York: Springer

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Part of this work has been funded by EMRP-project NEW 04 'Novel mathematical and statistical approaches to uncertainty evaluation'. The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union.

EMRP

European Metrology Research Programme
■ Programme of EURAMET



The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union

Markov Chain Monte Carlo sampling

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<p>Introduction</p> <p>MCMC basics</p> <p>MCMC applied</p> <p>Summary</p> <p>Literature</p>	<p>BIPM, IEC, IFCC, ILAC, ISO, IUPAC, IUPAP, and OIML (2011). <u>Evaluation of measurement data – Supplement 2 to the ‘Guide to the expression of uncertainty in measurement’ – Extension to any number of output quantities</u>. Joint Committee for Guides in Metrology, JCGM 101.</p> <p>Elster, C., Klauenberg, K., Walzel, M., Wübbeler, G., Harris, P., Cox, M., Matthews, C., Smith, I., Wright, L., Allard, A., Fischer, N., Cowen, S., Ellison, S., Wilson, P., Pennecchi, F., Kok, G., van der Veen, A., and Pendrill, L. (2015). A Guide to Bayesian Inference for Regression Problems. Deliverable of EMRP project NEW04 “Novel mathematical and statistical approaches to uncertainty evaluation”.</p> <p>Gelman, A., Carlin, J. B., Stern, H., and Rubin, D. B. (2003). <u>Bayesian data analysis</u>. Texts in Statistical Science. London: Chapman & Hall/CRC, 2nd edition.</p> <p>Gelman, A. and Rubin, D. B. (1992). Inference from iterative simulation using multiple sequences. <u>Statistical Science</u>, 7(4):457–472.</p> <p>Gilks, W., Richardson, S., and Spiegelhalter, D. (1996). <u>Markov Chain Monte Carlo in practice</u>. Interdisciplinary Statistics. London: Chapman & Hall/CRC, 1st edition.</p> <p>Hastings, W. K. (1970). Monte carlo sampling methods using Markov chains and their applications. <u>Biometrika</u>, 57(1):97–109.</p> <p>Hobert, J. P. and Casella, G. (1996). The effect of improper priors on Gibbs sampling in hierarchical linear mixed models. <u>Journal of the American Statistical Association</u>, 91:1461–1473.</p> <p>Klauenberg, K., Walzel, M., Ebert, B., and Elster, C. (2015). Informative prior distributions for ELISA analyses. <u>Biostatistics</u>, 16(3):465 – 479.</p> <p>Lunn, D., Spiegelhalter, D., Thomas, A., and Best, N. (2009). The BUGS project: Evolution, critique and future directions. <u>Statistics in Medicine</u>, 28:3049–3067.</p> <p>MATLAB (2015). <u>Release 2015a</u>. The MathWorks, Inc., Natick, Massachusetts.</p>
<p>MCMC methods</p>	<p>BIPM Workshop on Measurement Uncertainty, Paris, 15/06/2015 – p. 18/18</p>

<p>Introduction</p> <p>MCMC basics</p> <p>MCMC applied</p> <p>Summary</p> <p>Literature</p>	<p>Metropolis, N., Rosenbluth, A. W., Rosenbluth, M. N., Teller, A. H., and Teller, E. (1953). Equation of state calculations by fast computing machines. <u>The Journal of Chemical Physics</u>, 21(6):1087–1092.</p> <p>R Core Team (2015). <u>R: A Language and Environment for Statistical Computing</u>. R Foundation for Statistical Computing, Vienna, Austria.</p> <p>Robert, C. P. (2007). <u>The Bayesian choice: From Decision-Theoretic Foundations to Computational Implementation</u>. Springer Texts in Statistics. New York: Springer.</p> <p>Robert, C. P. (2015). The Metropolis-Hastings algorithm. ArXiv e-print arXiv:1504.01896 [stat.CO].</p> <p>Robert, C. P. and Casella, G. (2004). <u>Monte Carlo statistical methods</u>. Springer Texts in Statistics. New York: Springer, 2nd edition.</p> <p>Roberts, G. O., Gelman, A., and Gilks, W. R. (1997). Weak convergence and optimal scaling of random walk metropolis algorithms. <u>The Annals of Applied Probability</u>, 7:110–120.</p> <p>Spiegelhalter, D., Thomas, A., Best, N., and Lunn, D. (2003). <u>WinBUGS User Manual</u>, version 1.4 edition.</p> <p>Stan Development Team (2014). Stan: A c++ library for probability and sampling, version 2.5.0.</p> <p>Thomas, A., O'Hara, B., Ligges, U., and Sturtz, S. (2006). Making BUGS open. <u>R news</u>, 6(1):12–17.</p> <p>Voigt, J., Ebert, B., Hoffman, A., and Macdonald, R. (2008). Validierung eines 'Fluorescent Enzyme Linked Immuno Sandwich Assay' (ELISA). <u>PTB-Mitteilungen</u>, 118(4):255–260.</p>
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