APPROXIMATE CONFIDENCE REGIONS
IN THE ESTIMATION
OF ECOLOGICAL MODELS PARAMETERS

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How it all started

Our original goal was to associate *confidence regions* to estimated parameters.

We were looking for a numerical method to compute the *approximate* confidence regions.

Actually, we found *two* ….

- Linear approximation based on sensitivity functions (FIM)
- Second order approximation based on the Hessian matrix

Plus…

- A numerical method for computing the “exact” regions

The different nature of the two approximation suggested an accuracy check.

- If the two regions coincide, the estimates can be considered *accurate*
- If they differ, the estimation should be considered *critical*
Seminar material

Kinetic model to be estimated

Parameter Estimation

Error functional

Optimization algorithm

Sensitivity analysis

Practical Identifiability

Uncertainty Assessment

Covariance matrix

FIM

Hessian

Confidence Regions

Ellipsoid Approximation

Exact regions (level curves)

Applications: Monod, Richards, Dispersed Flow, Respirometry

Curvature
Summary

Confidence regions in a nutshell
- Theory of confidence regions
- A parameter estimation reliability test

PEAS Implemented methods
- Gridding
- Trajectory sensitivity
- Exact and approximate confidence regions
- Radii criterion
- Monte Carlo analysis

PEAS software organization
- Model implementation

PEAS software demonstration
- A dynamical simulation model
- An algebraic model
Papers on parameters estimation

- The original paper on optimised simplex search for parameter estimation

- Confidence regions

- Application to constructed wetland models

- Application to respirometric models

- This one

- Downloadable from: [http://www.dsi.unifi.it/~marsili/recent.htm](http://www.dsi.unifi.it/~marsili/recent.htm)
Confidence regions

Problem statement: find the minimum of the error functional

\[ E(p) = \sum_{j=1}^{N} \left( y_{j}^{exp} - y_{j}(p) \right)^{T} V_{j} \left( y_{j}^{exp} - y_{j}(p) \right) \]

given the model

\[
\begin{align*}
\frac{dx}{dt} &= f(x,u,p) \\
\frac{dt}{dt} &= g(x,u,p)
\end{align*}
\]

It is important to attach a measure of confidence to the estimates \( \hat{p} \)

For nonlinear in the parameters systems, only numerical methods are available
Confidence regions

- Determining the “best” parameter values is only a part of the estimation problem,
  - it is equally important to attach a measure of confidence to the estimates
- Most estimation techniques seek a valid set of parameters in terms of residuals, rather than a true model
- Many validation procedures involve model residuals and their correlation
- For linear systems the exact confidence regions can be computed
- For nonlinear in the parameters systems, only numerical methods are available
Statement of the estimation problem

Given a nonlinear system

\[
\begin{aligned}
\frac{dx}{dt} &= h(x, p, t) \\
y &= f(x, p)
\end{aligned}
\]

\[
\begin{align*}
x &\in \mathbb{R}^n \\
p &\in \mathbb{R}^{n_p} \\
y &\in \mathbb{R}^q \\
h : \mathbb{R}^n &\rightarrow \mathbb{R}^n \\
f : \mathbb{R}^n &\rightarrow \mathbb{R}^q
\end{align*}
\]

and a quadratic error functional

\[
E(p) = \sum_{i=1}^{N} \left[ y_i^s - y_i \right]^T V_i^{-1} \left[ y_i^s - y_i \right]
\]

Find the “best”, in the LS sense, parameter vector \( \hat{p} \)

\[
\hat{p} = \arg \min_p E(p)
\]
Estimation confidence regions

Confidence regions provide a way to judge the accuracy of parameter estimates.

Since the objective functional $E(p)$ represents the “closeness” of the experimental data to the fitted model, it is justifiable to base the confidence region on its contours.

This is OK if you can find the \textit{contour level} corresponding to a significant statistical level

\[
\begin{cases}
p : E(p) \leq \left(1 + \frac{n_p}{N - n_p} F_{n_p,N-n_p}^{1-\alpha} \right) E(\hat{p})
\end{cases}
\]
Exact and approximate confidence intervals

\[ \Delta E(p) \]

Exact confidence interval based on a \textit{statistical measure}

\[ \left(1 + \frac{n_p}{N - n_p} F_{n_p, N - n_p}^{1 - 0.95}\right) E(\hat{p}) \]

Approximate confidence interval based on the covariance matrix

\[ \hat{p} \pm \sigma_{\mu_{\text{max}}}^2 \sqrt{C_{ii}} \]

\[ \hat{p} = 0.45 \]
Approximate confidence regions

Confidence regions can be expressed as a function of the parameter covariance matrix $C$

$$\left\{ p : (p - \hat{p})^T C^{-1} (p - \hat{p})^T \leq n_p F_{n_p, N-n_p}^{1-\alpha} \right\}$$

for a linear model $C$ can be determined exactly

$$y = px + v \quad \Rightarrow \quad C = \sigma^2 \left( X^T V^{-1} X \right)^{-1}$$

For nonlinear models there is no exact way to obtain $C$ and the linear approximation may yield a poor estimate of the real confidence region.
Approximations of covariance matrix

- **Output linearisation (Jacobian) \( C \rightarrow C_J \)**
  \[
  C_J(\hat{p}) = \frac{E(\hat{p})}{N-n_p} \left( J^T V^{-1} J \right)^{-1} \quad J_{r,j}(\hat{p}) = \frac{\partial f}{\partial p_j} \bigg|_{(x_r,\hat{p})} = S^y_{p_j}
  \]
  A link with sensitivity

- **Fisher Information Matrix (FIM)**
  \[
  FIM = \sum_{i=1}^{N} \left( \frac{\partial y_i}{\partial p} \right)^T V_i^{-1} \left( \frac{\partial y_i}{\partial p} \right)
  \]
  If the residual distribution \( f \) is Gaussian and a LS estimator is used
  \[
  C_J(\hat{p}) = FIM^{-1}
  \]
  The LS estimator yields a minimum variance result (Cramér-Rao lower limit).

- **Error functional approximation (Hessian) \( C \rightarrow C_H \)**
  \[
  C_H(\hat{p}) = \frac{2E(\hat{p})}{N-n_p} H(\hat{p})^{-1} \quad \text{with} \quad H(\hat{p}) = \frac{\partial^2 E(p)}{\partial p \partial p^T} \bigg|_{\hat{p}}
  \]
  A link with the error functional shape
  Hessian numerical approximation
Are $C_J$ (FIM) and $C_H$ the same thing?

**NO, because**

**FIM**
- Is based on a linear approximation
- Relies on sensitivity functions, hence is sensitive to the system output function
- Is dependent on output parametrisation

**Hessian**
- Is based on a second order approximation
- It depends on the error functional $E(p)$
- Is independent of output parametrisation

Component-wise….

$$\hat{H}_{r,s} = 2 \frac{N - n_p}{E(\hat{p})} (FIM)_{r,s} - 2 \sum_{i=1}^{N} \left[ \left( y_i^s - y(x_i, \hat{p}) \right)^T V_i^{-1} \frac{d^2 y(x_i, \hat{p})}{dp_r dp_s} \right]$$

The *curvature* makes the difference
A digression on curvature

Curvature is the distortion induced by parametric nonlinearities.

It can be defined as the second derivative of the surface generated by the output function

$$\Omega : \left\{ y(t) = \varphi(x, p, t), \ p \in P \subseteq \mathbb{R}^n \right\}$$

$$\Omega$$ is also called the "expectation surface" because it contains all the possible values of the output.

For a nonlinear system the shape of the surface $$\Omega$$ may be heavily influenced by the curvature.

If the two representations do not agree, this means that the curvature term has significantly amplified the estimation error.

$$\left( y_i^s - y(x_i, \hat{p}) \right)^T V_i^{-1} \frac{d^2 y(x_i, \hat{p})}{dp_r dp_s}$$

Estimation error curvature
Components of curvature

- In the neighbourhood of $\hat{p}$, curvature is composed of a **tangent** and a **normal** component with respect to the surface $\Omega$.

- The **tangent** component is the **parameter curvature** and represents the degree of curvature induced by the **choice of parameters**.
  - It can be reduced or eliminated by a proper re-parametrisation.

- The **normal** component is the **intrinsic curvature**: it measures the degree of distortion of the surface due to the **nature of the output function in the solution space** $y(t) = \varphi(x, p, t)$.
  - It should become negligible around the minimum if the surface $\Omega$ is well-behaved (i.e. almost flat) around $\hat{p}$.
Assessment of nonlinearity through curvature

Through *curvature* the extent of model non-linearity can be assessed by comparing the maximum and minimum *curvature* radii

\[
    r_{\text{max}} = \left( 1 - \lambda_{\text{max}} \right) \frac{1}{2} \quad r_{\text{min}} = \left( 1 - \lambda_{\text{min}} \right) \frac{1}{2}
\]

where \( \lambda_{\text{max}} \) and \( \lambda_{\text{min}} \) are the extremal eigenvalues of the matrix \( B \), which relates the FIM and Hessian approximations

\[
    I_{n_p} - \hat{B} = \frac{1}{2} \hat{K}^T H \hat{K}
\]

where \( H \) is the Hessian \( \hat{K} = \hat{R}^{-1} \) and \( \hat{R}^T \hat{R} \xrightarrow{\text{Cholesky}} \frac{\text{FIM}}{s^2} \)

The closer \( r_{\text{max}} \) and \( r_{\text{min}} \) to 1, the smaller is the curvature
Method summary

- Confidence regions evaluation
  - Exact
  - Covariance Matrix
    - FIM
      - Approximate evaluation (Confidence ellipsoids)
    - Hessian
      - Approximate evaluation (Confidence ellipsoids)
  - Coincidence?
    - Criteria for consistency of estimates

- Numerical methods for computing the covariance matrix
- Confidence regions
- Curvature terms
Approximate confidence regions as discriminators

FIM approximation
\[
\left\{ p : (p - \hat{p})^T J_n^T V^{-1} J_n (p - \hat{p}) \leq s^2 n_p F_{n_p, N - n_p}^{1 - \alpha} \right\}
\]

Exact confidence regions
\[
\left\{ p : E(p) \leq c E(\hat{p}) \right\}
\]

Coincident regions?

Hessian approximation
\[
\left\{ p : (p - \hat{p})^T H_n (p - \hat{p}) \leq s^2 n_p F_{n_p, N - n_p}^{1 - \alpha} \right\}
\]

Doubtful estimates

YES

Reliable estimates

NO

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PEAS: Parameter Estimation Accuracy Software
Curvature effect

\[
\left[ \frac{\partial^2 f(p)}{\partial p_r \partial p_s} \right]_{\hat{p}} = \left[ \hat{f}_{rs} \right] \in \mathbb{R}^{N \times n_r \times n_p}
\]

- **Parametric**
  - \( f \) tangent component \( @ \hat{p} \)
  - Can be reduced through adequate re-parametrisation

- **Intrinsic**
  - \( f \) normal component \( @ \hat{p} \)
  - Independent from parameter choice
  - Evaluate max and min curvature radii
  - Radii close to unity indicate reliable linearisation

Accounts for the quadratic terms neglected in the output function linearisation

Distortion effect of the output solution space

\[
y(t) = \varphi(x, p, t)
\]
A less subjective test

Judging ellipses misalignment involves a good deal of subjectivity.

The new test is based on the distortion induced by the curvature, i.e. how much the ellipse differs from a sphere.

The curvature is responsible for the distortion in the transformed space.

$$\rho = \frac{r_{\text{max}}}{r_{\text{min}}} \rightarrow 1 \quad \text{in the perfect case}$$
Assessment of nonlinearity through curvature

Through *curvature* the extent of model non-linearity can be assessed by comparing the maximum and minimum *curvature radii*

\[
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\]

where \(\lambda_{\text{max}}\) and \(\lambda_{\text{min}}\) are the extremal eigenvalues of the matrix \(B\), which relates the FIM and Hessian approximations

\[
I_{n_p} - \hat{B} = \frac{1}{2} \hat{K}^T H \hat{K}
\]

where \(H\) is the Hessian \(\hat{K} = \hat{R}^{-1}\) and \(\hat{R}^T \hat{R} \xrightarrow{\text{Cholesky}} \frac{FIM}{s^2}\)

The radii criterion is obtained

\[
\bar{\rho} = 1 + \sqrt{\frac{n_p}{N - n_p} F_{n_p, N-n_p}^\alpha}
\]
Method summary

Confidence regions evaluation

Covariance Matrix

- FIM
- Hessian

Distortion in the transformed space

Comparison of the ratio $\rho$ with the threshold

$$B = I_{n_p} - \frac{1}{2} K^T HK$$

$$\rho = \frac{r_{\text{max}}}{r_{\text{min}}}$$

$$\bar{\rho} = 1 + \sqrt{\frac{n_p}{N-n_p}} F_{n_p, N-n_p}^\alpha$$

Reject estimates

Accept estimates

$\rho < \bar{\rho}$
Applications

» Ecological Kinetics
  - Monod
  - Richards
    - Identification difficulty induced by the shape of the error functional
    - Importance of proper initialisation

» Dispersed flow modelling
  - Horizontal subsurface constructed wetlands (HSCW)
    - Model selection assessment

» Respirometry
  - Reliability of estimation of a two-step nitrification model
  - Influence of the initial Ammonium-N injection on identifiability
    - Selection of critical parameters (second step)
Monod kinetics

- Well known estimation difficulties
  - Strong parameters correlation
- Test with synthetic noisy data
- Both substrate and biomass observed

![Graph showing substrate (S) and biomass (X) over time (h)]

- mg COD L⁻¹
- S = Substrate
- X = biomass
Estimation results for the Monod kinetics

\[
\begin{align*}
\frac{dS}{dt} &= -\frac{1}{Y} \frac{\mu_{\text{max}} S}{K_s + S} X \\
\frac{dX}{dt} &= \frac{\mu_{\text{max}} S}{K_s + S} X - K_d X \\
x &= [S \ X]^T \\
y &= x
\end{align*}
\]

Model

\[
S(0) = 10 \text{ mg/L} \quad X(0) = 0.1 \text{ mg/L}
\]

\[
\bar{p} : \mu_{\text{max}} = 0.5 \ (h^{-1}) ; \ K_s = 20 \ (mg \ COD \ L^{-1}) ; \ Y = 0.5 ; \ K_d = 0.03 \ (h^{-1})
\]

Estimation from noisy data \((\sigma = 0.05)\)

<table>
<thead>
<tr>
<th>(K_s \ (mg \ COD \ L^{-1}))</th>
<th>(\mu_{\text{max}} \ (h^{-1}))</th>
<th>(Y)</th>
<th>(K_d \ (h^{-1}))</th>
<th>Starting point</th>
<th>(E(\hat{p}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>True values</td>
<td>20.000</td>
<td>0.500</td>
<td>0.500</td>
<td>0.0030</td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>19.0997</td>
<td>0.483</td>
<td>0.525</td>
<td>0.0303</td>
<td>(22.0 \ 0.5 \ 0.37 \ 0.04)^T</td>
</tr>
<tr>
<td>Case 2</td>
<td>31.605</td>
<td>0.711</td>
<td>0.485</td>
<td>0.0289</td>
<td>(33.3 \ 0.8 \ 0.57 \ 0.08)^T</td>
</tr>
</tbody>
</table>

Case 1: Search successfully terminates at the minimum

Case 2: Search terminates at a wrong point, because of unsuitable initialisation
Confidence intervals

<table>
<thead>
<tr>
<th></th>
<th>$K_s\left(\text{mg CODL}^{-1}\right)$</th>
<th>$\mu_{\text{max}}\left(h^{-1}\right)$</th>
<th>$Y$</th>
<th>$K_d\left(h^{-1}\right)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>19.09968 ± 1.72181</td>
<td>0.48298 ± 0.03212</td>
<td>0.50524 ± 0.01139</td>
<td>0.03025 ± 0.00057</td>
</tr>
<tr>
<td>True values</td>
<td>20.000</td>
<td>0.5000</td>
<td>0.5000</td>
<td>0.0030</td>
</tr>
</tbody>
</table>

- $K_s$, with a 95% confidence interval of over 18% of the estimated value, has the largest uncertainty, though much less than that found by Holmberg (1982)
- $\mu_{\text{max}}$ has a 13% uncertainty
- $Y$ has a 4.4% uncertainty
- $K_d$ only 3.8%.
Shape of $E(p)$ for the Monod kinetics

Narrow valley at the bottom
Case (1): E(p) minimum reached

The two ellipsoids coincide and include the exact parameters

⇒ The minimum of E(p) was reached
⇒ Reliability of linearisation
⇒ No curvature effects
Case (2): E(p) minimum not reached but still in the valley

End point ≠ Optimal value

Only the Hessian approximation includes the exact values, because it conforms to the shape of E(p)

The Hessian approximation is more reliable

The H and J ellipses have axes with differing slopes, hence indicate differing parameter correlations
Case (3): the end point is not in the valley

Both approximations are unreliable

- $E(p)$ gradient not negligible
- Curvature effect is relevant
## Curvature radii

Minimum and maximum curvature radius for the two Monod calibration cases

<table>
<thead>
<tr>
<th>$K_s$</th>
<th>$\mu_{\text{max}}$</th>
<th>$Y$</th>
<th>$K_d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1: 0.9961 - 1.0009</td>
<td>Case 1: 0.9996 - 1.0004</td>
<td>Case 1: 0.9988 - 1.0004</td>
<td></td>
</tr>
<tr>
<td>Case 2: 0.9668 – 2.9963</td>
<td>Case 2: 0.9723- 1.1780</td>
<td>Case 2: 0.9698- 1.4414</td>
<td></td>
</tr>
<tr>
<td>$\mu_{\text{max}}$</td>
<td>--</td>
<td>Case 1: 0.9966 - 0.9998</td>
<td>Case 1: 0.9964 - 0.9991</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case 2: 0.9925 – 3.0541</td>
<td>Case 2: 0.9578 – 3.1749</td>
</tr>
<tr>
<td>$Y$</td>
<td>--</td>
<td>--</td>
<td>Case 1: 0.9988 - 0.9998</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Case 2: 0.9908 – 1.5607</td>
</tr>
</tbody>
</table>
Residual autocorrelation (RAC)

- Even Case 1 yields partially correlated residuals
- Though Case 2 performs slightly worse, it is hard to discriminate
- In both cases, some samples fall outside the zero-confidence limit
- The discriminatory power of RAC is much less than confidence ellipsoids.

Case (1)

Case (2)
The Richards growth function

- Widely used in leaf and plant growth
- Saturation kinetics like the logistic, but with a further tuning parameter: the exponent $n$
- Model parameters calibrated on real experimental data (Selenastrum algae)

\[
\frac{dG}{dt} = G^r \left( 1 - \frac{G^n}{K^n} \right)
\]
Parameter estimation

The simplex search was initiated from three different points. Not each choice terminated the search in the right place.

Richards growth estimates from experimental data.

<table>
<thead>
<tr>
<th></th>
<th>$r$</th>
<th>$K$</th>
<th>$n$</th>
<th>Starting point</th>
<th>$E(\hat{p})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>0.02559</td>
<td>0.07530</td>
<td>0.05129</td>
<td>$[0.0239 \ 0.08 \ 0.05]^T$</td>
<td>1.40293 e-04</td>
</tr>
<tr>
<td>Case 2</td>
<td>0.01723</td>
<td>0.07793</td>
<td>-0.37804</td>
<td>$[0.090 \ 0.095 \ -0.65]^T$</td>
<td>2.04105 e-04</td>
</tr>
<tr>
<td>Case 3</td>
<td>0.02642</td>
<td>0.07459</td>
<td>0.08807</td>
<td>$[0.0800 \ 0.09 \ 0.15]^T$</td>
<td>2.04104 e-04</td>
</tr>
</tbody>
</table>

Case 1 estimated parameters

<table>
<thead>
<tr>
<th></th>
<th>$r$</th>
<th>$K$</th>
<th>$n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>0.02559 ± 0.00445</td>
<td>0.07530 ± 0.00131</td>
<td>0.05129 ± 0.1947</td>
</tr>
</tbody>
</table>
Estimation problems with the Richards function

The “true” parameters being not known, the ellipsoids method is the only way of assessing the reliability of the estimates.

*Case 1* corresponds to a correct estimation: the search terminates in the minimum as confirmed by the exact coincidence of the Hessian and FIM ellipsoids. The intrinsic curvature correction factor has no effect.

*Case 2* corresponds to a search termination at a point far from the minimum, where the gradient is still considerable.

*Case 3* represents the opposite situation: the search stopped in a flat region near, but not exactly at the minimum.

The exponent $n$ is the most difficult parameter, with the possibility to obtain negative values.

95% confidence interval vary widely:

- over 700% for $n$; less than 35% for $r$; only 3.5% for $K$. 
Location of search end-points

Only Case 1 reaches the minimum.

Case 2 in high gradient zone

Case 3 in flat region far from the minimum
Case 1 Ellipsoids: coincidence

![Graph showing ellipsoids for Case 1 with two sets of data: FIM and Hessian. The graphs display the relationship between K, n, and r.]
Case 2 Ellipsoids: Hessian larger than FIM
Case 3 Ellipsoids: FIM larger than Hessian
Application to dispersed flow

- Modelling the flow in Horizontal Subsurface Constructed Wetlands (HSCW)
- Flow behaviour is similar to a diffusive reactor (DR)
- If a DR is approximated with a combination of CSTR and Plug-Flow, the questions arise:
  - What is the best approximating structure?
  - How can we estimate its parameters?
- The theory is used here to answer both questions:
  - Propose a structure
  - Estimate the parameters

- If the structure **fails** the confidence regions it is rejected
- If the structure **passes** the confidence criterion it is retained

Manuscript submitted to *Ecological Modelling*
No reliable, simple flow model exists to date, which takes into account the variable porosity of the medium (gravel + roots)
Approximate structures

Model A

\[ F_{in} \rightarrow C_1 \rightarrow C_2 \rightarrow C_3 \rightarrow \text{Plug-Flow} \rightarrow F_{out} \]

Model B

\[ F_{in} \rightarrow C_1 \rightarrow C_2 \rightarrow C_3 \rightarrow C_4 \]

\[ F \cdot (1-b) \]

\[ C_4 \rightarrow V_2 \rightarrow C_5 \rightarrow \text{Plug-Flow} \rightarrow F_{out} \]

\[ F \cdot b \]

\[ V_3 \rightarrow C^* \]

\[ \delta \]
Model A was fitted to the literature data from a HSCW in Carville (USA) Data from EPA.
Assessment of model fitting: model A

Though the visual agreement between data and model is good, the ellipsoids show a modelling deficiency.
Model B was fitted to the Lithium tracer data from a small HSCW in Tuscany.
In addition the visual agreement between data and model, the ellipsoids show a structural consistency, though the model is difficult to estimate........
Structural problems with model B
PEAS Structure

- **GUI Introductory section**
- **User interface**
  - Input menu
  - Parameter menu
  - Data menu

**Model representations**
- Simulink model
- S-function model
- M.file model

**Computational engines**
- Gridding
- Parameter estimation
- Exact regions
- Confidence regions
- Monte Carlo analysis

**Legend**
- Interfaces
- Methods
- Models
Software engineering

- Model definition
  - accepts model definitions
    - *.mdl
    - *.m

- Model specifications
  - model parameters (to be calibrated),
  - model constants (not to be calibrated)
  - initial conditions.

- Calibration specifications
  - choice of the optimization algorithm
  - estimation tolerances and termination criteria

- Accuracy assessment
  - exact regions
  - approximate regions
  - Monte Carlo analysis
Monte Carlo Analysis (MCA)

There are cases in which the ellipsoid method is not applicable, e.g. in the case of “patched” models containing hard switching functions to introduce discontinuities in time-varying parameters.

With MCA the parameters confidence limits are obtained based on a large number of estimations obtained by running the model with perturbed observations \( \widetilde{y} = y(\hat{p}) \cdot (1 + \varepsilon) \quad \varepsilon \in N(0, \sigma^2) \).

A gaussian distribution \( N(\hat{m}_i, \hat{s}_i^2) \) is then fitted to the histogram of the estimates

\[
\hat{p}_i \cong \hat{m}_i ; \quad \hat{\sigma}_p_i \cong \pm t_{N_{\text{simul}}-1}^{\alpha/2} \hat{s}_i
\]

with the variance approximated by

\[
\hat{s}_i^2 = \frac{1}{N_{\text{simul}}-1} \sum_{j=1}^{N_{\text{simul}}} (p_j - \hat{m}_i)^2
\]
Example of MCA results

\[ \hat{p} \]

\[ 2\delta_p \]
PEAS main interface
Model definition

Simulink model (block diagram)  Simulink model (S-function)

Simulink level

S-function level

C level

DLL

#define S_FUNCTION_NAME MODEL
#define S_FUNCTION_LEVEL 2
#include "simstruc.h"
#include <stdio.h>
#include <stdlib.h>
#include <string.h>

...BODY of C source code

#ifdef MATLAB_MEX_FILE    /* Is this file
being compiled as a MEX-file? */
#include "simulink.c"    /* MEX-file
interface mechanism */
#else
#include "cg_sfun.h"   /* Code
generation registration function */
#endif
A dynamical model example

A simple Monod model with respirometric observations

\[
\begin{align*}
    \frac{dS}{dt} &= -\frac{1}{Y} \frac{mu S}{k_s + S} X + q(S_i - S) \\
    \frac{dX}{dt} &= \frac{mu S}{k_s + S} X - k_d X
\end{align*}
\]

In PEAS notation becomes

**Model equations**

\[
\begin{align*}
    \frac{dx_1}{dt} &= -\frac{1}{P_{calib}(3)} P_{calib}(1) \cdot x_1 \cdot \frac{x_2}{P_{calib}(2) + x_1} + P_{cost}(1) \cdot (Input - x_1) \\
    \frac{dx_2}{dt} &= P_{calib}(1) \cdot x_1 \cdot \frac{x_2}{P_{calib}(2) + x_1} - P_{calib}(4) \cdot x_2
\end{align*}
\]

**Output equations**

\[
\begin{align*}
    y_1 &= x_1 \\
    y_2 &= x_2 \\
    y_3 &= \frac{1 - P_{calib}(3) P_{calib}(1) \cdot x_1 \cdot x_2}{P_{calib}(3) P_{calib}(2) + x_1} + P_{calib}(4) \cdot x_2
\end{align*}
\]

**Error functional**

\[
E(p) = \sum_{j=1}^{N} (y_1^{exp}(j) - y_1(j))^2 + \sum_{j=1}^{N} (y_2^{exp}(j) - y_2(j))^2 + \sum_{j=1}^{N} (y_3^{exp}(j) - y_3(j))^2
\]
Calibration results
Confidence regions

Confidence test result:
- Parameter estimation reliability test: $R_{max}/R_{min} = 1.1368$
- Threshold value: $1.1793$
- Radii test passed

Estimated parameters:
- $\mu$: 0.41316
- $k_s$: 10.3359
- $Y$: 0.30881
- $k_d$: 0.031335

Graphs showing confidence regions for $k_s$, $Y$, $k_d$, and $\mu$.
Bad result due to improper initialization
## Comparison of algorithmic performance

The Simplex method is the most accurate and, in this case, the application of the Quasi-Newton method brings no improvement. The other algorithms are faster but produce less accurate results.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>True value</th>
<th>Initial value</th>
<th>Optimization algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Simplex</td>
</tr>
<tr>
<td>mu</td>
<td>0.4</td>
<td>0.3</td>
<td>0.4055</td>
</tr>
<tr>
<td>ks</td>
<td>10</td>
<td>12</td>
<td>10.1022</td>
</tr>
<tr>
<td>Y</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3029</td>
</tr>
<tr>
<td>kd</td>
<td>0.03</td>
<td>0.04</td>
<td>0.0298</td>
</tr>
<tr>
<td>run time (s)</td>
<td></td>
<td></td>
<td>63.703</td>
</tr>
<tr>
<td>E(p)</td>
<td></td>
<td></td>
<td>16.1021</td>
</tr>
</tbody>
</table>
Confidence interval comparison

Confidence bounds obtained with the approximate confidence regions based on the Hessian matrix approximation and with the Monte Carlo analysis for an estimated measurement error $s^2 = 0.05$.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>True value</th>
<th>Estimated value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Simplex (Hessian)</td>
</tr>
<tr>
<td>mu</td>
<td>0.4</td>
<td>0.40552 ± 0.0120</td>
</tr>
<tr>
<td>ks</td>
<td>10.0</td>
<td>10.1022 ± 0.7097</td>
</tr>
<tr>
<td>Y</td>
<td>0.3</td>
<td>0.30287 ± 0.0037</td>
</tr>
<tr>
<td>kd</td>
<td>0.03</td>
<td>0.02979 ± 0.0007</td>
</tr>
</tbody>
</table>
Monte Carlo analysis
An algebraic model

The oxygen dynamics

\[ \frac{dS_o}{dt} = K_L a (S_{sat} - S_o) - r \]

and its analytical solution obtained by calculus

\[ S(t) = S_{sat} \cdot (1 - e^{-K_L a \cdot t}) + S_o(0) \cdot e^{-K_L a \cdot t} - \frac{r}{K_L a} \cdot (1 - e^{-K_L a \cdot t}) \]

PEAS notations \( P_{calib}(1) = K_L a; \ P_{calib}(2) = r; \ P_{cost}(1) = S_{sat}; \ X_o(1) = S_o \)

yield

\[ S = P_{cost}(1) \cdot (1 - e^{-P_{calib}(1) t}) + X_o \cdot e^{-P_{calib}(1) t} - \frac{P_{calib}(2)}{P_{calib}(1)} \cdot (1 - e^{-P_{calib}(1) t}) \]

Coded as an m. file

```matlab
function [S,tsim]=Rear(t)
global P_calib P_cost X_0 Input Q
S=(P_cost(1)).*(1-exp(-P_calib(1).*(t)))+...
(X_0(1).*exp(-P_calib(1).*(t)))-...
(P_calib(2)./P_calib(1)).*(1-exp(-P_calib(1).*(t)));
tsim=t;
```
Algebraic model calibration results

Figure No. 2: Calibration

Figure No. 1: Dynamic Sensitivity

SIGMA test T

K\text{la} = 0.29127 \pm 0.016887
\text{r} = 0.50563 \pm 0.061301

Confidence Test
R_{\text{max}}/R_{\text{min}} = 1.0147
Threshold value = 1.4985

S. Marsili-Libelli
Conclusions

- **Confidence regions** provide a way to assess estimation consistency

- Two differing approximations can be used:
  - **FIM** involving model linearisation and sensitivity analysis
  - **Hessian**, based on a second order approximation of the error functional
  - Their difference involves curvature

- PEAS implements both the estimation AND the accuracy analysis
  - Both exact and approximate confidence regions can be computed
  - A numerical "pass" test based on curvature radii is included
  - If the ellipsoids method is not applicable, Monte Carlo analysis is available
"That's all Folks!"