（4）応用

逆問題とは？

- 順問題:

原因 ➡ 結果

- 逆問題:

原因 ⬅ 結果

(i) 電子顕微鏡の画像再構成

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実問題に対する応用 1/3

提案法の有効性を実問題で評価するために
電子顕微鏡の画像再構成問題に適用した

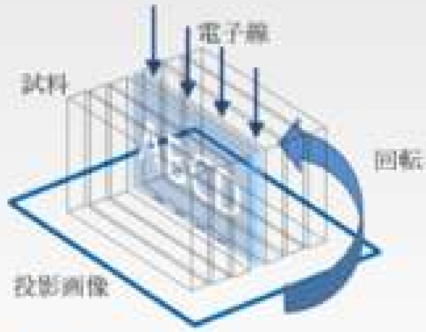


Figure: 電子顕微鏡の画像再構成問題.

Inverse problems: Image reconstruction

In order to evaluate the proposed methods in practice, we apply the them to image reconstruction problems

Consider approximating a solution x^* of linear systems of equations

$$Ax^* = b^*,$$

where $A \in \mathbf{R}^{m \times n}$ is a discretized Radon transform, $m \leq n$, $x^* \geq 0$ is an image data, and b^* is a projection data.

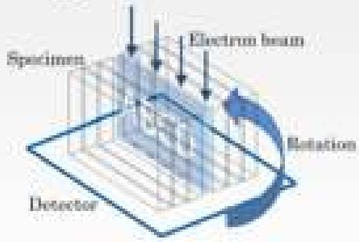


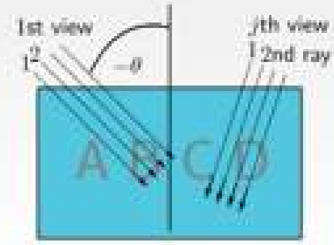
Figure: Projection image.

Difficulties 1/2

For simplicity, consider one slice of a specimen, i.e., 2D reconstruction.

Artifacts
Since the range of the angle θ of rotation of the specimen is limited due to physical constraints, reconstructed images may suffer artifacts. For instance,

$$-70^\circ < \theta < 70^\circ.$$



Difficulties 2/2

Observation error
Since an observation error δ perturbs b^*, we actually treat

$$Ax = b \quad \text{or} \quad \min_{x \in \mathbb{R}^n} \|b - Ax\|_2,$$

to obtain $x \simeq x^*$, where $b = b^* + \delta$.
Hence, a tight fitting $\min_{x \in \mathbb{R}^n} \|b - Ax\|_2$ gives an error-contaminated solution.


Figure: Exact image


Figure: Reconstructed image given by ART without observation error

Previous methods 1/5

Algebraic Reconstruction Technique [Herman *et al.* '73]

- ART $\Longleftrightarrow$ the SOR method for the normal equations
  $$AA^{\mathsf{T}}\boldsymbol{u} = \boldsymbol{b}, \quad \boldsymbol{x} = A^{\mathsf{T}}\boldsymbol{u}.$$
- Given $\boldsymbol{x}^{(0,1)}$, for $k = 0, 1, \ldots,$
  $$\boldsymbol{x}^{(k,i+1)} = \boldsymbol{x}^{(k,i)} + \omega \frac{b_i - (\boldsymbol{\alpha}_i, \boldsymbol{x}^{(k,i)})}{\|\boldsymbol{\alpha}_i\|_2{}^2} \boldsymbol{\alpha}_i, \quad i = 1, \ldots, m,$$
  $$\boldsymbol{x}^{(k+1,1)} = \boldsymbol{x}^{(k,m+1)},$$
  where $\omega \in (0, 2)$ is the relaxation parameter and $\boldsymbol{\alpha}_i$ is the ith row of A.
- If $\boldsymbol{x}^{(0,1)} = \mathbf{0}$, then ART gives the minimum-norm (pseudo-inverse) solution $\forall \boldsymbol{b} \in \mathcal{R}(A)$.

Previous methods 2/5

Simultaneous Iterative Reconstruction Technique (SIRT) [Gilbert '72]

- SIRT $\Longleftrightarrow$ Richardson method for $A^{\mathsf{T}}A\boldsymbol{x} = A^{\mathsf{T}}\boldsymbol{b}$.
- Given $\boldsymbol{x}^{(0,1)}$, for $k = 0, 1, \ldots,$
  $$\boldsymbol{x}^{(k)} = \boldsymbol{x}^{(k-1)} + \omega A^{\mathsf{T}}(\boldsymbol{b} - A\boldsymbol{x}^{(k-1)}),$$
  where $\omega \in (0, 2/\|A^{\mathsf{T}}A\|_2)$ is the relaxation parameter.
- SIRT gives the pseudo-inverse solution $\forall \boldsymbol{b} \in \mathbf{R}^m$.

実問題に対する応用 2/3

提案法の有効性を数値実験で検討した

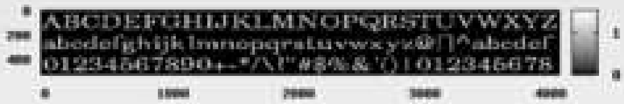


Figure: 再構成したい画像.

Figure: 従来法．相対誤差 0.621．計算時間 180 秒.

Figure: 提案法．相対誤差 0.498．計算時間 472 秒．
（相対誤差 0.617 のときは 72 秒．）

実問題に対する応用 3/3

実際の観測データを用いた解法の性能比較

Figure: 従来法 A による再構成画像.

Figure: 従来法 B による再構成画像.

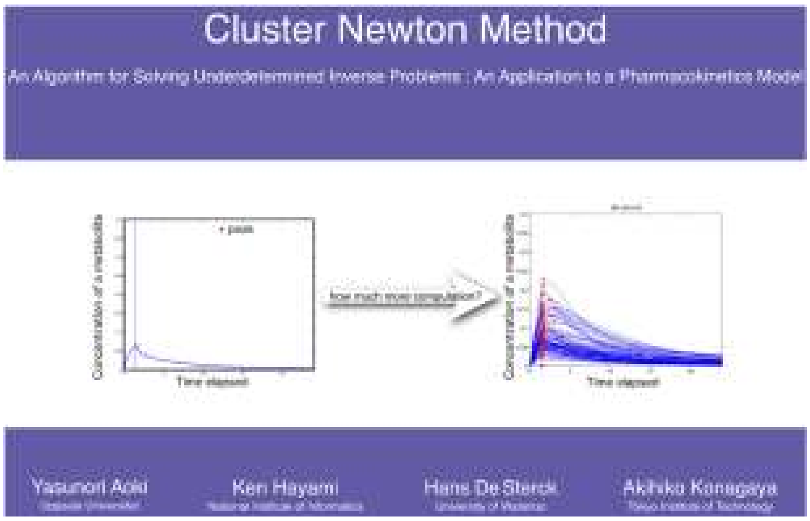
Figure: 提案法による再構成画像.

参考文献

・保國 惠一, 細田 陽介, 速水 謙,
電子顕微鏡の画像再構成逆問題,
平成24年 電気学会 電子・情報・システム部門大会 講演論文集, pp. 931-933,
2012年9月5日-7日, 弘前大学.

・Keiichi Morikuni,
Inner-iteration Preconditioning for Least Squares Problems,
Doctoral thesis, Department of Informatics, School of Multidisciplinary Sciences,
The Graduate University for Advanced Studies, June 10, 2013.

(ii) 薬物動態モデルの逆問題



Personalized Pharmacokinetics Model of CPT-11

Parameters → Reasonably Observable data

Personalized model parameters

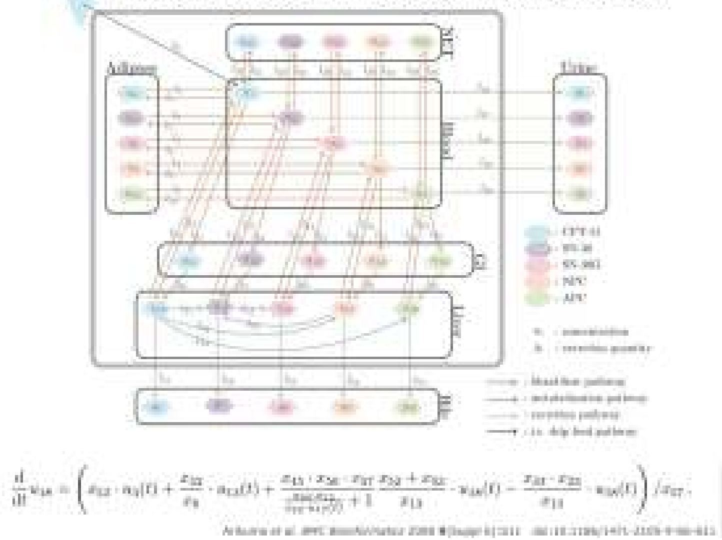
A regular patient (few data)

60 Parameters

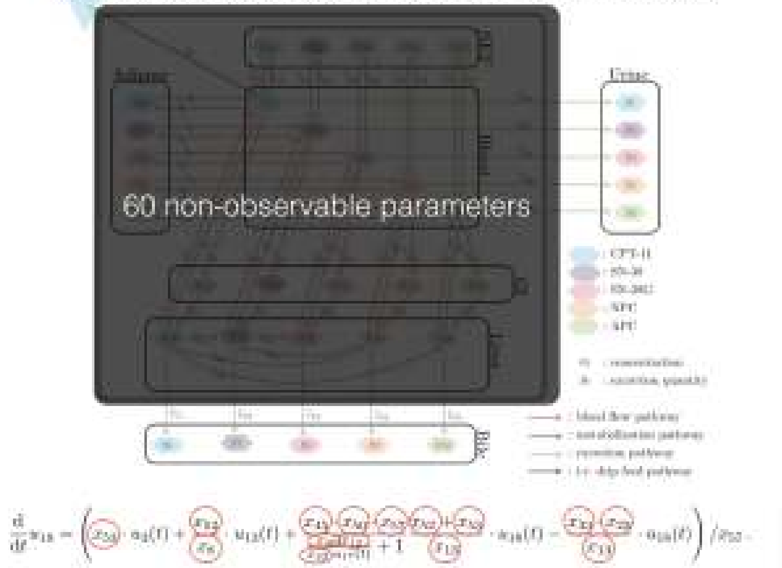
10 Measurements

Underdetermined Inverse problem

Arikuma et al's Irinotecan PBPK model

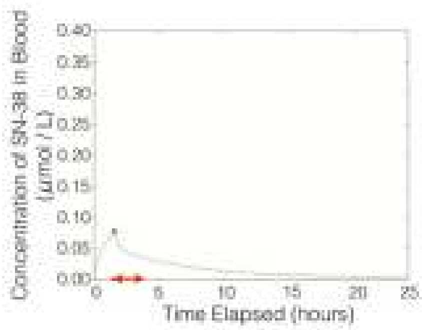


Arikuma et al's Irinotecan PBPK model



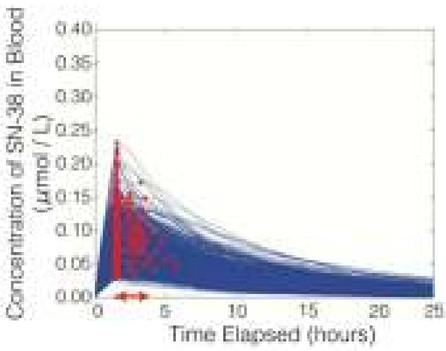
Arikuma et al. BMC Bioinformatics 2008 9(Suppl 6):S11 doi:10.1186/1471-2105-9-S6-S11

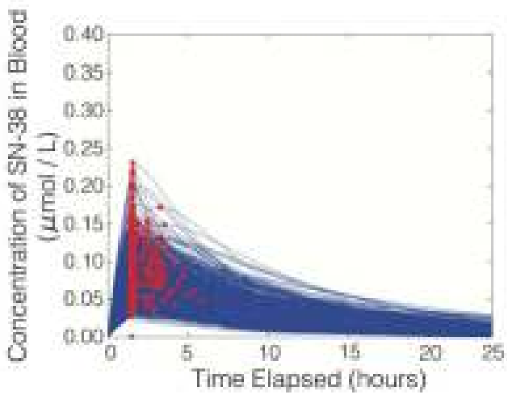
This underdetermined inverse problem can easily be solved by the Levenberg-Marquardt method which finds a solution close to the initial model parameters.



However, the clinical observation suggests that the maximum concentration should happen 2.5 ±1 hour.

By solving this underdetermined inverse problem multiple times with different initial model parameters, we obtain various solutions which fits clinical observation.





7~8 hours on a server machine with two quad-core 3GHz Intel Xeon

Why is this so time consuming?

- Function evaluation requires numerical solution of the system of non-linear ODEs.
- Jacobian is approximated by finite differences at each iteration for each solution.
- ODEs need to be solved fairly accurately in order for the LM method to converge to the root.

Example 1 : Level curve tracing of a rough surface

Find a set of 100 points near $\mathcal{X}^0$, s.t.

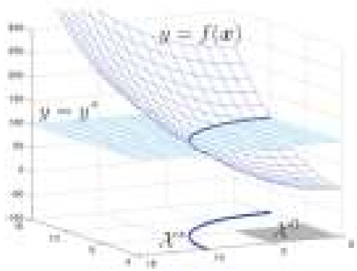
$$f(\boldsymbol{x}) = y^*$$

where

$$f(\boldsymbol{x}) = (x_1^2 + x_2^2) + \sin(10000x_1)\sin(10000x_2)/100$$

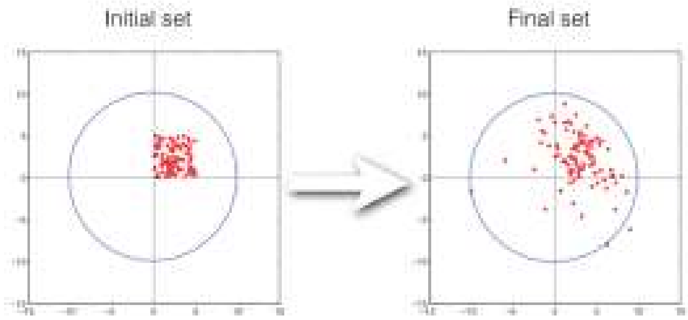
$$y^* = 100$$

$$\mathcal{X}^0 = \{\boldsymbol{x} \in \mathbb{R}^2 : \max_{i=1,2} \left| \frac{x_i - 2.5}{2.5} \right| < 1\}$$



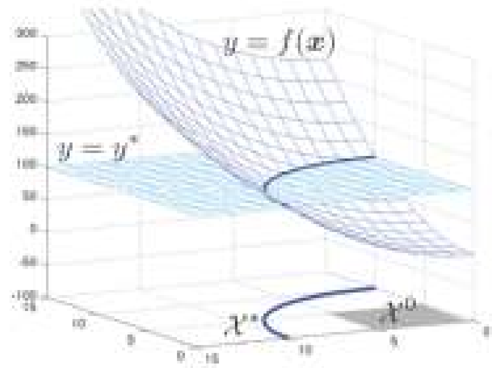
Levenberg Marquardt method

For all of the initial points, the algorithm terminated with an error
"Algorithm appears to be converging to a point that is not a root."



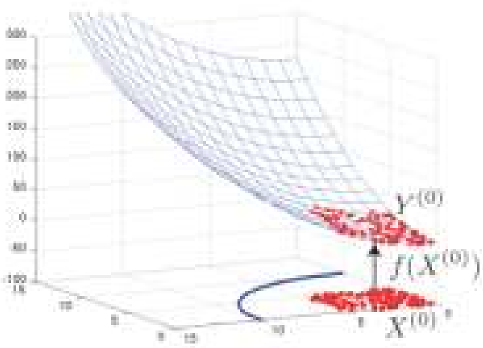
Cluster Newton method

- Stage 1 (Regularized Newton's method applied to a cluster of points)
  - Linear approximation with least squares fitting
    (least square solution of an overdetermined system of linear equations which acts as regularization)
  - Moore-Penrose inverse using the linear approximation
    (minimum norm solution of an underdetermined system of linear equations)
- Stage 2 (Broyden's method, i.e. multi-dimensional secant method)
  - Use the linear approximation in Stage 1 as initial Jacobian
    (start with reasonable Jacobian approximation)
  - Use the points found by the Stage 1 as initial points
    (start with the initial points already close to the solution)



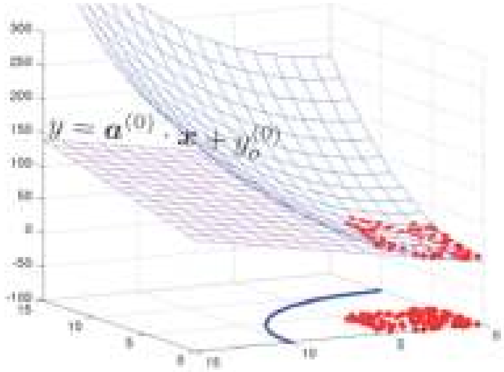
Stage 1

1st iteration step1



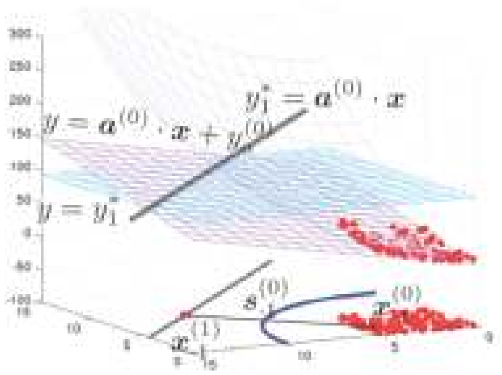
Stage 1

1st iteration step2



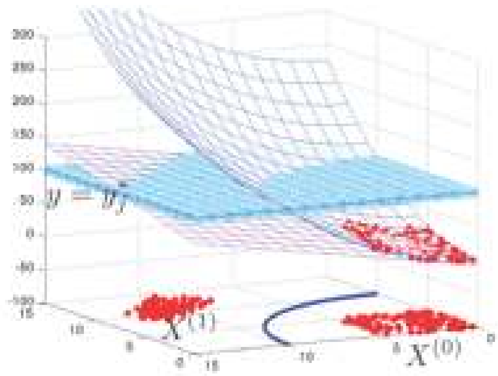
Stage 1

1st iteration step3



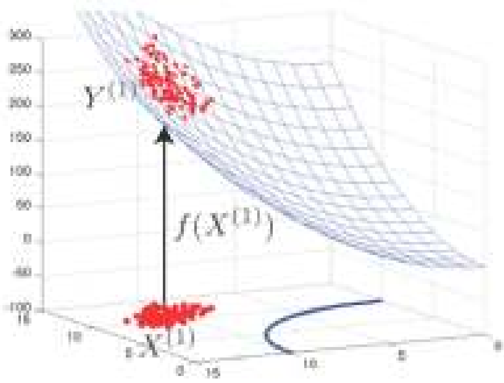
Stage 1

1st iteration step4



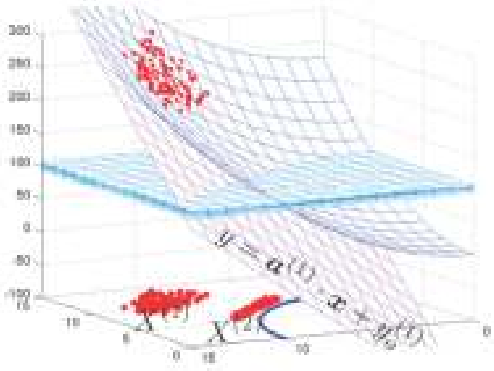
Stage 1

2nd iteration step1



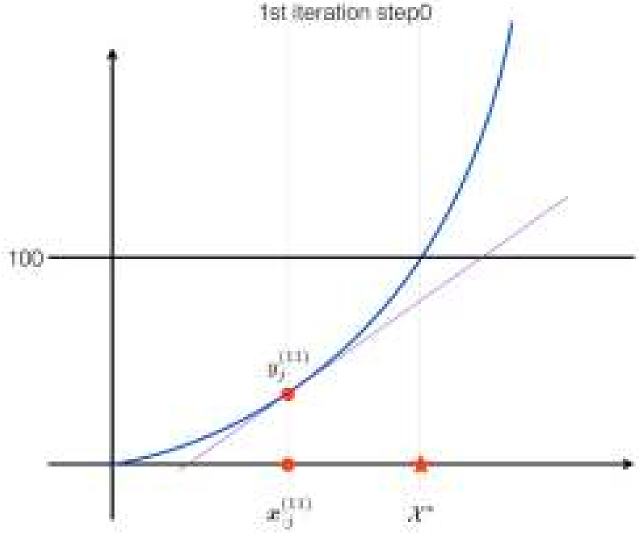
Stage 1

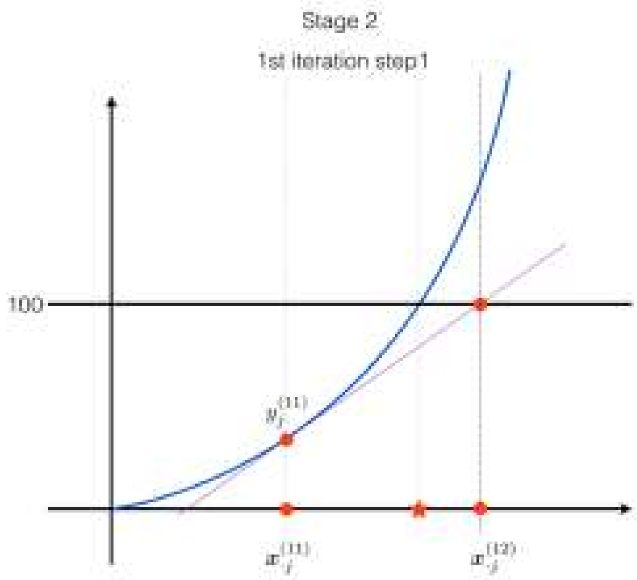
2nd iteration step2-3

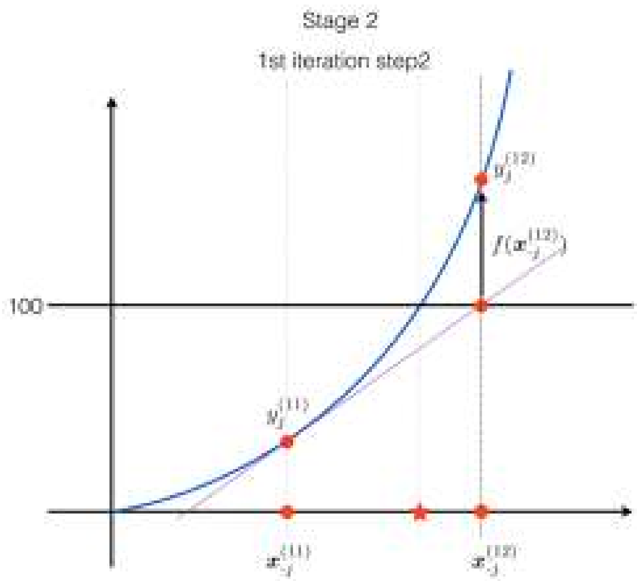


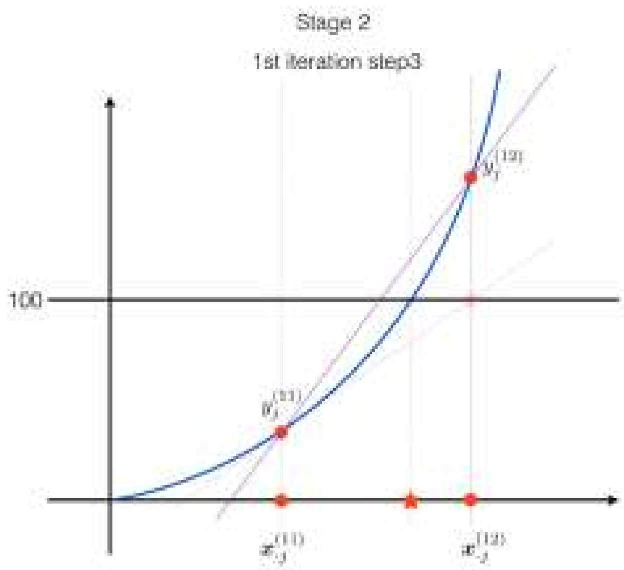
Stage 2

1st iteration step0

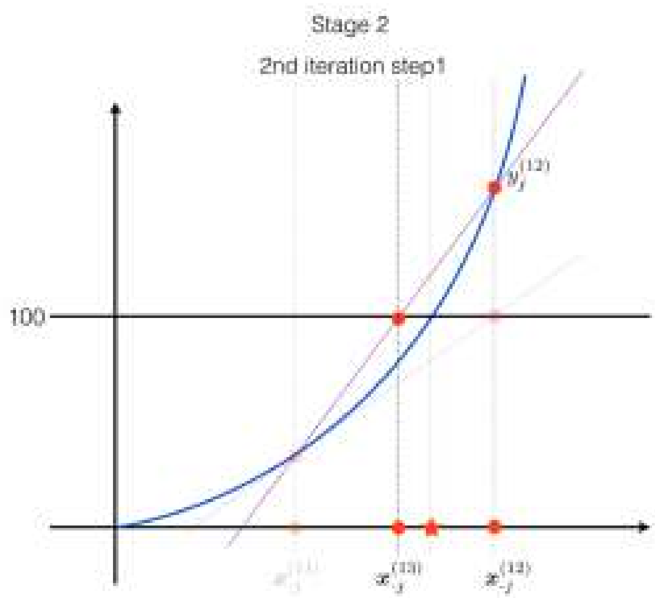



Stage 2
1st iteration step1
100

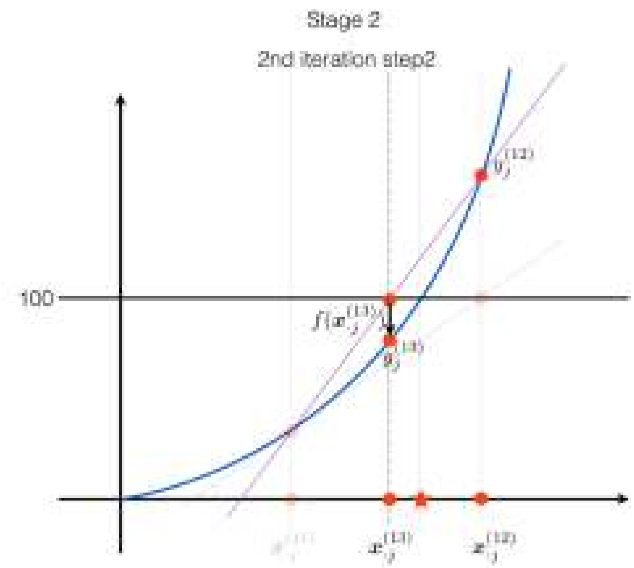

Stage 2
1st iteration step2
100

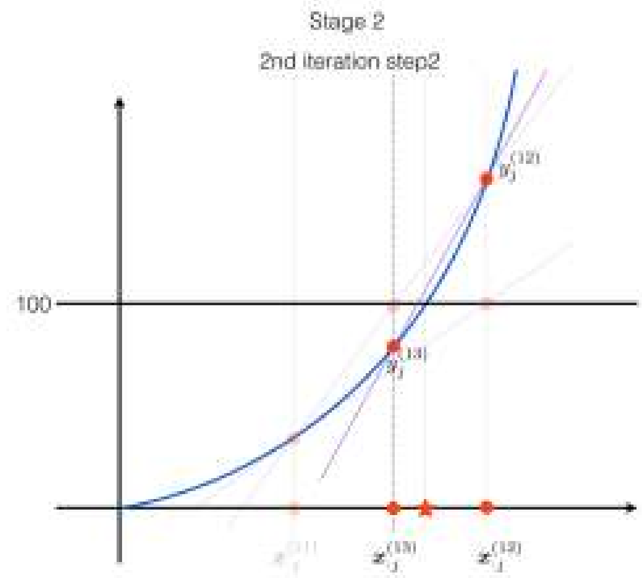


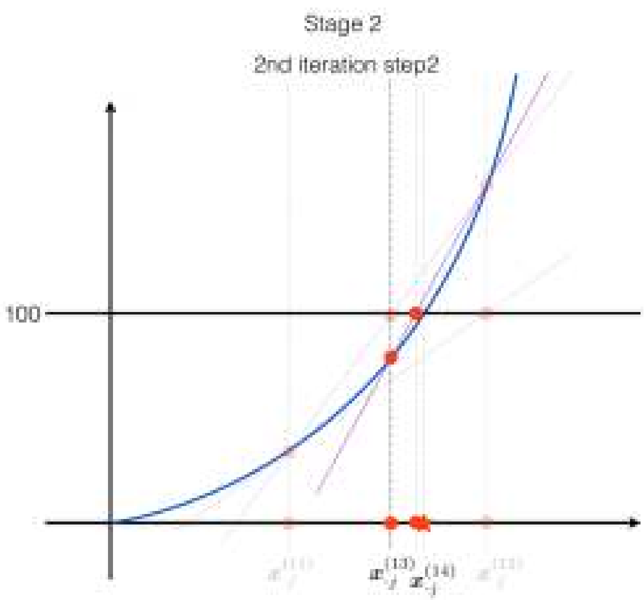
2013.7.22. 最小2乗法_速水 75



2013.7.22. 最小2乗法_速水 76


Stage 2
2nd iteration step2
100

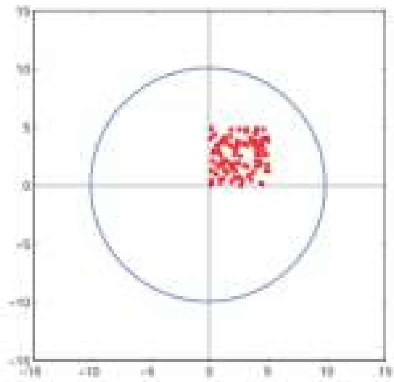

Stage 2
2nd iteration step2
100



Cluster Newton Method

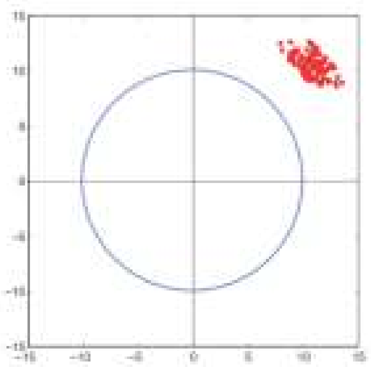
- 1 function evaluation / iteration / solution
- No Jacobian approximation based on the local info

Initial set



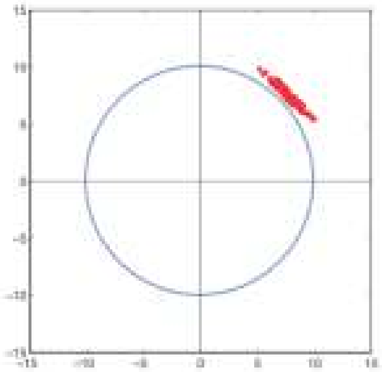
Stage 1

1st iteration



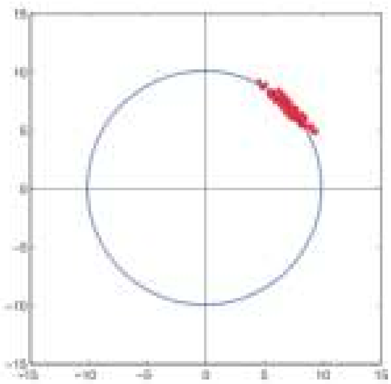
Stage 1

2nd iteration



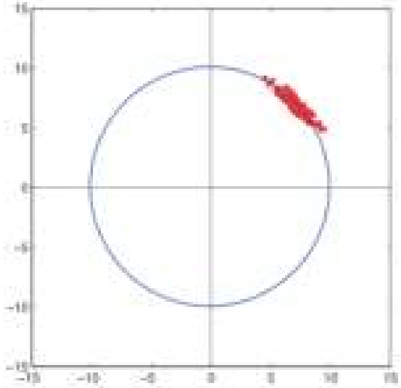
Stage 1

3rd iteration



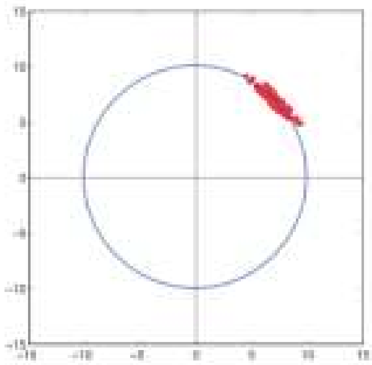
Stage 1

4th iteration



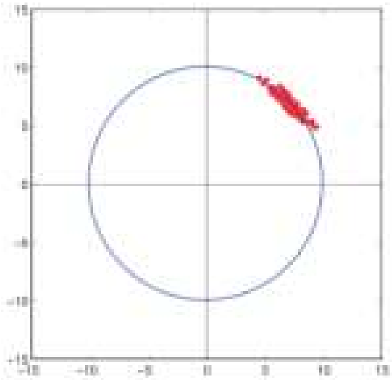
Stage 1

5th iteration



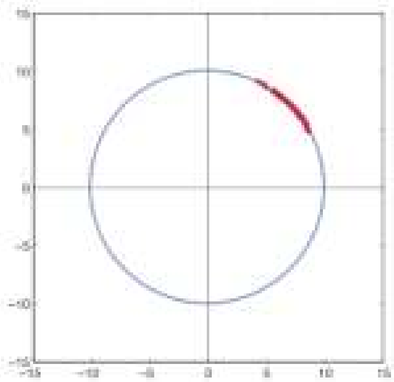
Stage 1

6th iteration



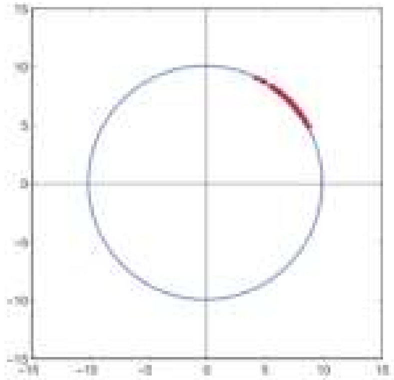
Stage 2

1st iteration



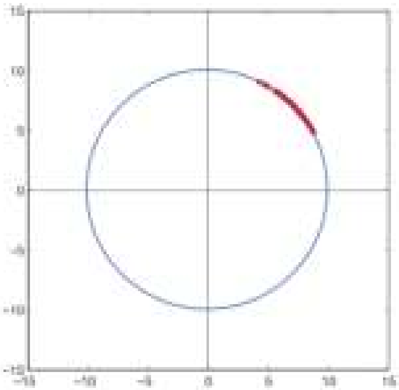
Stage 2

2nd iteration



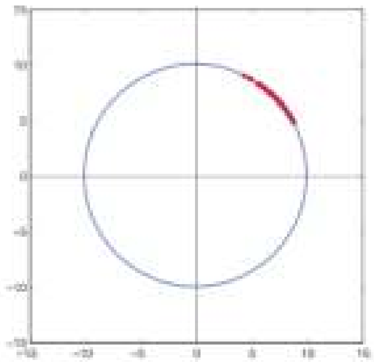
Stage 2

3rd iteration



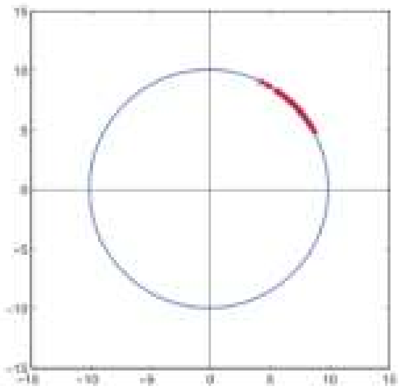
Stage 2

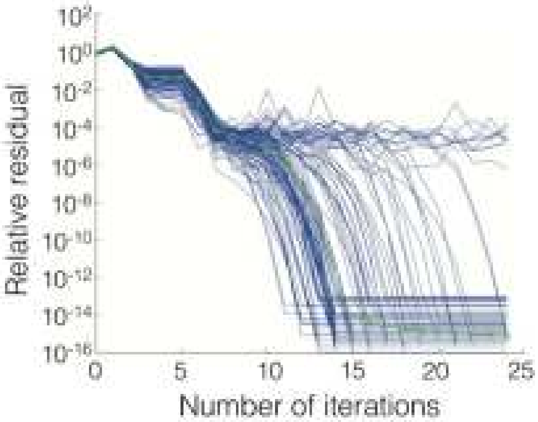
4th iteration



Stage 2

5th iteration





Relative residual : $r_j^{(k)} = \dfrac{|y_j^{(k)} - y^*|}{y^*}$

Example 2 : ODE coefficients identification

Forward Problem

Pharmacokinetics model of CPT-11 (Arikuma et al. 2008):

$$\frac{\mathrm{d}}{\mathrm{d}t}\boldsymbol{u} = \boldsymbol{h}(\boldsymbol{u}, t; \boldsymbol{x})$$

where

$u_{1,2,\ldots,25}(t;\boldsymbol{x})$: concentration of drug/metabolites

$u_{26,\ldots,35}(t;\boldsymbol{x})$: cumulative excretion quantity of drug/metab.

t : time

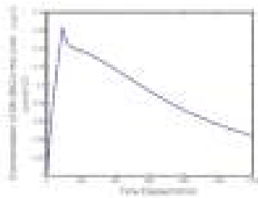
$\boldsymbol{x}$: set of model parameters ($\boldsymbol{x} \in \mathbb{R}^{60}$)

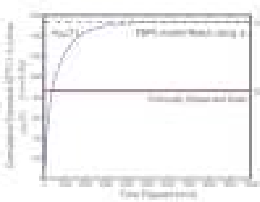
Map from model parameters to observable data:

$$\boldsymbol{f}(\boldsymbol{x}) = \boldsymbol{y}$$

where $\boldsymbol{y}$ is a part of the steady state solution of the ODE

$$y_i(\boldsymbol{x}) = \lim_{t\to\infty} u_{i+25}(t;\boldsymbol{x}) \qquad \text{for } i = 1, 2, \ldots, 10$$





Inverse Problem

Find 1000 sets of parameters $\boldsymbol{x}$, s.t.

$$\boldsymbol{f}(\boldsymbol{x}) = \boldsymbol{y}^*$$

where

$\boldsymbol{f} : \mathbb{R}^{60} \to \mathbb{R}^{10}$

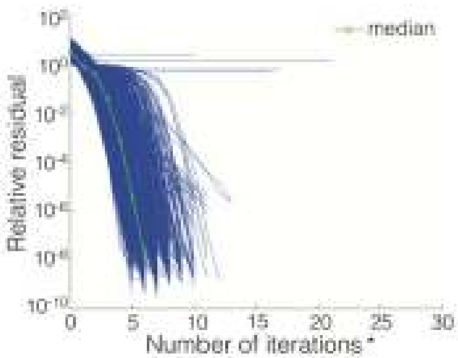
$\boldsymbol{y}^*$: clinically observed data

(Slatter et al. 2000)

clinically observed data

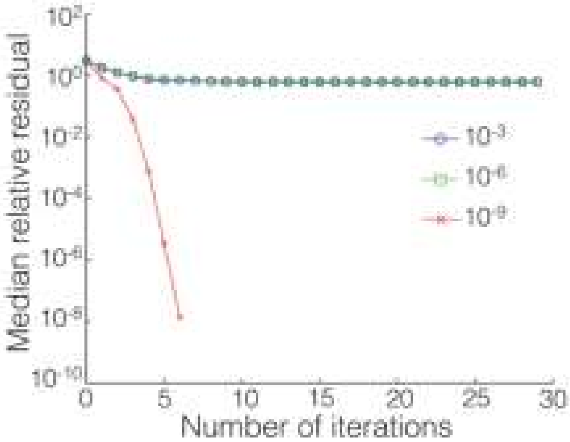
		patient 1	patient 2
CPT-11 in Urine	y_1^*	859.0	957.9
SN-38 in Urine	y_2^*	35.5	18.4
SN-38G in Urine	y_3^*	473.8	129.1
NPC in Urine	y_4^*	3.55	5.89
APC in Urine	y_5^*	305.0	86.4
CPT-11 in Bile + Faeces	y_6^*	975.4	1381.7
SN-38 in Bile + Faeces	y_7^*	127.1	352.4
SN-38G in Bile + Faeces	y_8^*	105.4	11.5
NPC in Bile + Faeces	y_9^*	24.5	58.2
APC in Bile + Faeces	y_{10}^*	218.4	354.5
total dosage	$\sum_{i=1}^{10} y_i^*$	3846	4376

Levenberg Marquardt method

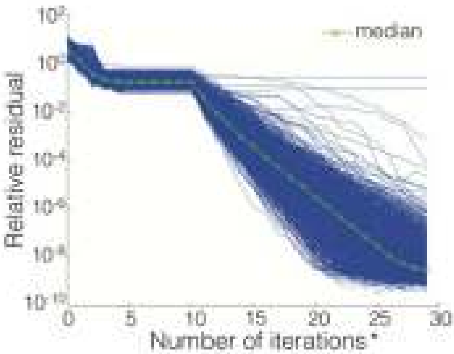


* : at least 61 function evaluations / iteration / solution

Levenberg Marquardt method

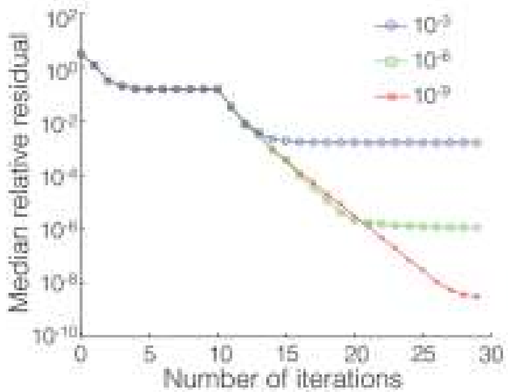


Cluster Newton method



* : only 1 function evaluations / iteration / solution

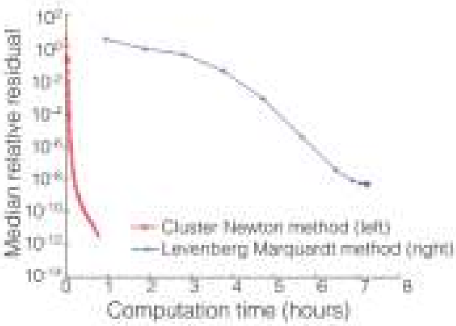
Cluster Newton method



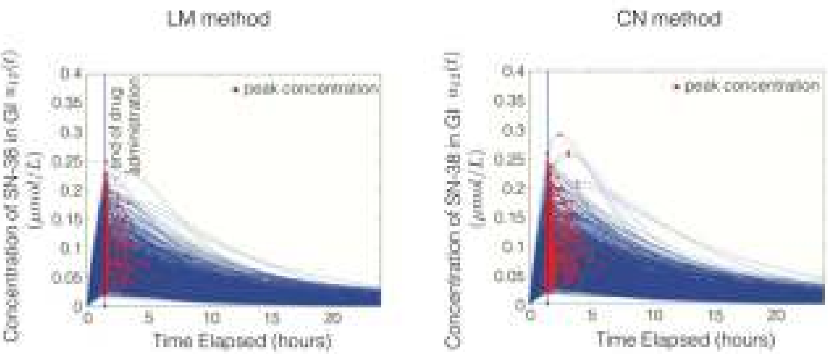
Cluster Newton method

- Less number of function evaluations
- Less sensitive to the error in function evaluations

Levenberg Marquardt method v.s. Cluster Newton method



Predicting un-measurable quantity through a mathematical model (concentration of SN-38 in gastrointestinal tract)



Conclusion

We have introduced ...

- Idea of sampling multiple solutions in the solution manifold of an underdetermined inverse problem
- CN method efficiently finds multiple solutions.

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