# Large-scale Linear and Nonlinear Optimization in Quad Precision 

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US-Mexico Workshop on Optimization and its Applications
Mérida, Yucatán, Mexico, Jan 4-8, 2016
From INFORMS SFO Nov 9-12, 2014
1st Fletcher-Powell Lecture, Strathclyde, Glasgow, June 23-26, 2015

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## Abstract

For challenging numerical problems, William Kahan has said that "default evaluation in Quad is the humane option" for avoiding severe unexpected error in floating-point computations. The IEEE 754-2008 standard includes Quad precision (about 34 significant digits) and is provided by some compilers as a software library. For example, gfortran provides a real(16) datatype. This is the humane option for producing Quad-precision software.

We describe experiments on multiscale linear and nonlinear optimization problems using Double and Quad implementations of MINOS. On a range of examples we find that Quad MINOS achieves exceptionally small primal and dual infeasibilities (of order $1 \mathrm{e}-30$ ) when "only" $1 \mathrm{e}-15$ is requested. The motivation has been large multiscale LP and NLP problems arising in systems biology (flux balance analysis models of metabolic networks). Standard solvers are not sufficiently accurate, and exact simplex solvers are extremely slow. Quad precision offers a reliable compromise.

Partially supported by the
National Institute of General Medical Sciences
of the National Institutes of Health (NIH)
Award U01GM102098
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## Motivation

## Multiscale LPs in systems biology

Normal approach for LP solvers (simplex or interior)

- Scale (to reduce large matrix values)
- Solve with Feasibility/Optimality tols $=1 \mathrm{e}-6$ say
- Unscale


## Difficulty

- Unscaling magnifies residuals
- Solution may be far from feasible or optimal


## Stoichiometric matrices $S$

$$
2 \mathrm{H}_{2}+\mathrm{O}_{2} \rightarrow 2 \mathrm{H}_{2} \mathrm{O}
$$

|  | $\cdot$ | $\cdot$ | $\cdot$ | $W$ | $\cdot$ | $\cdot$ | $\cdot$ |
| :---: | ---: | :---: | :---: | ---: | :---: | :---: | :---: |
| $\mathrm{H}_{2}$ | $\cdot$ | $\cdot$ | $\cdot$ | -2 | $\cdot$ | $\cdot$ | $\cdot$ |
| $\mathrm{O}_{2}$ | $\cdot$ | $\cdot$ | $\cdot$ | -1 | $\cdot$ | $\cdot$ | $\cdot$ |
| $\mathrm{H}_{2} \mathrm{O}$ | $\cdot$ | $\cdot$ | $\cdot$ | 2 | $\cdot$ | $\cdot$ | $\cdot$ |

chemicals $\times$ reactions

$62000 \times 77000$

## Constraint Based Reconstruction and Analysis (COBRA)

A biochemical network (inherently multiscale) is represented by a stoichiometric matrix $S$ with $m$ rows corresponding to metabolites (chemicals) and $n$ columns representing reactions. $S$ is part of the ODE that governs the time-evolution of concentrations:

$$
\begin{equation*}
\frac{d}{d t} x(t)=S v(t) \tag{1}
\end{equation*}
$$

where $x(t) \in \mathbf{R}^{m}$ is a vector of time-dependent concentrations and $v(t) \in \mathbf{R}^{n}$ is a vector of reaction fluxes. The objective of maximizing growth rate at steady state leads to an LP:

$$
\begin{align*}
\max _{v} & c^{T} v  \tag{2a}\\
\text { s.t. } & S v=0,  \tag{2b}\\
& I \leq v \leq u, \tag{2c}
\end{align*}
$$

where growth is defined as the biosynthetic requirements of experimentally determined biomass composition, and biomass generation is a set of reaction fluxes linked in the appropriate ratios.

## ME models (FBA with coupling constraints)

Flux Balance Analysis (FBA) has been used by Ines Thiele (2012) for the first integrated stoichiometric multiscale model of Metabolism and macromolecular Expression (ME) for Escherichia coli K12 MG1655. Added coupling constraints

$$
\begin{equation*}
c_{\min } \leq \frac{v_{i}}{v_{j}} \leq c_{\max } \tag{3}
\end{equation*}
$$

become linear constraints

$$
\begin{equation*}
c_{\min } v_{j} \leq v_{i}, \quad v_{i} \leq c_{\max } v_{j} \tag{4}
\end{equation*}
$$

for various pairs of fluxes $v_{i}, v_{j}$. They are linear approximations of nonlinear constraints and make $S$ in (2b) even less well-scaled because of large variations in reaction rates. Quad precision is evidently more appealing.

## Coupling constraints

Two fluxes could be related by

$$
\begin{equation*}
0.0001 \leq \frac{v_{1}}{v_{2}} \leq 10000 \tag{5}
\end{equation*}
$$

Lifting approach (Yuekai Sun, ICME, 2012)
Transform into sequences of constraints involving auxiliary variables with reasonable coefficients. The second inequality in (5) becomes $v_{1} \leq 10000 v_{2}$, which is equivalent to

$$
\begin{equation*}
v_{1} \leq 100 s_{1}, \quad s_{1} \leq 100 v_{2} \tag{6}
\end{equation*}
$$

If the first inequality in (5) were presented as $v_{1} \geq 0.0001 v_{2}$, we would leave it alone, but the equivalent inequality $10000 v_{1} \geq v_{2}$ would be transformed to

$$
v_{2} \leq 100 s_{2}, \quad s_{2} \leq 100 v_{1}
$$

## The desirability of Quad precision

"Carrying somewhat more precision in the arithmetic than twice the precision carried in the data and available for the result will vastly reduce embarrassment due to roundoff-induced anomalies."
"Default evaluation in Quad is the humane option."

## Methods for achieving Quad precision

Hand-code calls to auxiliary functions
Even $\mathrm{q}=\mathrm{qdotdd}(\mathrm{v}, \mathrm{w})$ needs several double functions twosum, split, twoproduct sum2, dot2
to compute double $\mathrm{x}, \mathrm{y}$
and hence quad result $\mathrm{q}=$ quad $(\mathrm{x})+$ quad $(\mathrm{y})$
Double-double datatype ( $\approx 32$ digits)
QD: http://crd-legacy.lbl.gov/~dhbailey/mpdist/
C++ with interfaces to $\mathrm{C}++$ and F 90
DDFUN90: entirely F90
Minor changes to source code
Quad datatype ( $\approx 34$ digits)
Some f90 compilers such as gfortran
Again minor changes to source code
We use this humane approach to Quad implementation

## System and Methods

## quadMINOS

The GNU GCC compilers make Quad available via 128-bit data types. We have therefore been able to make a Quad version of the Fortran 77 linear and nonlinear optimization solver MINOS using the gfortran compiler ${ }^{1}$ with real (8) changed to real(16) everywhere.

Double is implemented in hardware, while Quad is a software library.
Our aim is to explore combined use of the Double and Quad MINOS simplex solvers for the solution of large multiscale linear programs. We seek greater efficiency than is normally possible with exact simplex solvers.

[^0]
## quadSNOPT

In the f90 implementations of SQOPT and SNOPT, we select one of the modules

```
snPrecision32.f90
```

snPrecision64.f90
snPrecision128.f90
For example, snPrecision128.f90:

```
module snModulePrecision
    implicit none
    public
    integer(4), parameter :: ip = 8, rp = 16 ! quad precision
end module snModulePrecision
```


## quadSNOPT

In the f90 implementations of SQOPT and SNOPT, we select one of the modules

```
snPrecision32.f90
snPrecision64.f90
snPrecision128.f90
```

For example, snPrecision128.f90:

```
module snModulePrecision
    implicit none
    public
    integer(4), parameter :: ip = 8, rp = 16 ! quad precision
end module snModulePrecision
```

Later:

```
module sn50lp
    use snModulePrecision, only : ip, rp
    subroutine s5solveLP ( x, y )
    real(rp), intent(inout) :: x(nb), y(nb)
```


## MINOS and quadMINOS

The primal simplex solver in MINOS includes

- geometric-mean scaling of the constraint matrix
- the EXPAND anti-degeneracy procedure
- partial pricing (but no steepest-edge pricing, which would generally reduce total iterations and time)
- Basis LU factorizations and updates via LUSOL

$$
\begin{array}{rll}
\text { quadMINOS } \equiv \text { MINOS with } \begin{array}{ll}
\text { real }(8) & \rightarrow r e a l(16) \\
& e p s=2.22 e-16
\end{array} \rightarrow \text { eps }=1.93 e-34
\end{array}
$$

# DQQ procedure 

Step D: Double MINOS Step Q1: Quad MINOS<br>Step Q2: Quad MINOS with no scaling

## DQQ procedure

(1) Cold start Double MINOS with scaling and somewhat strict settings, save basis
(2) Warm start Quad MINOS with scaling and tighter Featol/Opttol, save basis
(3) Warm start Quad MINOS without scaling but tighter LU tols


## MINOS runtime options for DQQ procedure

|  | Default | Step D | Step Q1 | Step Q2 |
| :--- | ---: | ---: | ---: | ---: |
| Scale option | 2 | 2 | 2 | 0 |
| Feasibility tol | $1 \mathrm{e}-6$ | $1 \mathrm{e}-7$ | $1 \mathrm{e}-15$ | $1 \mathrm{e}-15$ |
| Optimality tol | $1 \mathrm{e}-6$ | $1 \mathrm{e}-7$ | $1 \mathrm{e}-15$ | $1 \mathrm{e}-15$ |
| LU Factor tol | 100.0 | 10.0 | 10.0 | 5.0 |
| LU Update tol | 10.0 | 10.0 | 10.0 | 5.0 |

Table: Three pilot models from Netlib, eight Mészáros problematic LPs, and three ME biochemical network models. Dimensions of $m \times n$ constraint matrices $A$ and size of the largest optimal primal and dual variables $x^{*}, y^{*}$.

| model | m | $n$ | nnz( $A$ ) | $\max \left\|A_{i j}\right\|$ | $\left\\|x^{*}\right\\|_{\infty}$ | $\left\|y^{*}\right\| \mid$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| pilot4 | 411 | 1000 | 5145 | $3 \mathrm{e}+04$ | 1e+05 | $3 \mathrm{e}+02$ |
| pilot | 1442 | 3652 | 43220 | $2 \mathrm{e}+02$ | $4 \mathrm{e}+03$ | $2 \mathrm{e}+02$ |
| pilot87 | 2031 | 4883 | 73804 | $1 \mathrm{e}+03$ | $2 \mathrm{e}+04$ | $1 \mathrm{e}+01$ |
| de063155 | 853 | 1488 | 5405 | $8 \mathrm{e}+11$ | 3e+13 | $6 \mathrm{e}+04$ |
| de063157 | 937 | 1488 | 5551 | $2 \mathrm{e}+18$ | $2 \mathrm{e}+17$ | $6 \mathrm{e}+04$ |
| de080285 | 937 | 1488 | 5471 | $1 \mathrm{e}+03$ | $1 \mathrm{e}+02$ | $3 \mathrm{e}+01$ |
| gen1 | 770 | 2560 | 64621 | $1 \mathrm{e}+00$ | $3 \mathrm{e}+00$ | $1 \mathrm{e}+00$ |
| gen2 | 1122 | 3264 | 84095 | $1 \mathrm{e}+00$ | $3 \mathrm{e}+00$ | $1 \mathrm{e}+00$ |
| gen4 | 1538 | 4297 | 110174 | $1 \mathrm{e}+00$ | $3 \mathrm{e}+00$ | $1 \mathrm{e}+00$ |
| 130 | 2702 | 15380 | 64790 | $1 \mathrm{e}+00$ | $1 \mathrm{e}+09$ | $4 \mathrm{e}+00$ |
| iprob | 3002 | 3001 | 12000 | $1 \mathrm{e}+04$ | $3 \mathrm{e}+02$ | $1 \mathrm{e}+00$ |
| TMA_ME | 18210 | 17535 | 336302 | 2e+04 | $6 \mathrm{e}+00$ | $1 \mathrm{e}+00$ |
| GlcAerWT | 68300 | 76664 | 926357 | $8 \mathrm{e}+05$ | $6 \mathrm{e}+07$ | $2 \mathrm{e}+07$ |
| GlcAlift | 69529 | 77893 | 928815 | $3 \mathrm{e}+05$ | $6 \mathrm{e}+07$ | $2 \mathrm{e}+07$ |

Table: Itns and runtimes in secs for Step 1 (Double MINOS) and Steps 2-3 (Quad MINOS). Pinf and Dinf $=\log _{10}$ final maximum primal and dual infeasibilities. Problem iprob is infeasible. Bold figures show Pinf and Dinf at the end of Step 3. Pinf/ $\left\|x^{*}\right\|_{\infty}$ and Dinf/ $\left\|y^{*}\right\|_{\infty}$ are all $O\left(10^{-30}\right)$ or smaller, even though only $O\left(10^{-15}\right)$ was requested. This is an unexpectedly favorable empirical finding.

| model | Itns | Times | Final objective | Pinf | Dinf |
| :--- | ---: | ---: | :---: | ---: | ---: |
| pilot4 | 1571 | 0.1 | $-2.5811392602 \mathrm{e}+03$ | -05 | -13 |
|  | 6 | 0.0 | $-2.5811392589 \mathrm{e}+03$ | -39 | -31 |
|  | 0 | 0.0 | $-2.5811392589 \mathrm{e}+03$ | - | -30 |
| pilot | 16060 | 5.7 | $-5.5739887685 \mathrm{e}+02$ | -06 | -03 |
|  | 29 | 0.7 | $-5.5748972928 \mathrm{e}+02$ | - | -27 |
|  | 0 | 0.2 | $-5.5748972928 \mathrm{e}+02$ | - | -32 |
| pilot87 | 19340 | 15.1 | $3.0171038489 \mathrm{e}+02$ | -09 | -06 |
|  | 32 | 2.2 | $3.0171034733 \mathrm{e}+02$ | - | -33 |
|  | 0 | 1.2 | $3.0171034733 \mathrm{e}+02$ | - | -33 |


| model | Itns | Times | Final objective | Pinf | Dinf |
| :--- | ---: | ---: | ---: | ---: | ---: |
| de063155 | 921 | 0.0 | $1.8968704286 \mathrm{e}+10$ | -13 | +03 |
|  | 78 | 0.1 | $9.8830944565 \mathrm{e}+09$ | - | -17 |
|  | 0 | 0.0 | $9.8830944565 \mathrm{e}+09$ | - | -24 |
| de063157 | 488 | 0.0 | $1.4561118445 \mathrm{e}+11$ | +20 | +18 |
|  | 476 | 0.5 | $2.1528501109 \mathrm{e}+07$ | -27 | -12 |
|  | 0 | 0.0 | $2.1528501109 \mathrm{e}+07$ | - | -12 |
| de080285 | 418 | 0.0 | $1.4495817688 \mathrm{e}+01$ | -09 | -02 |
|  | 132 | 0.1 | $1.3924732864 \mathrm{e}+01$ | -35 | -32 |
|  | 0 | 0.0 | $1.3924732864 \mathrm{e}+01$ | - | -32 |
| gen1 | 369502 | 205.3 | $-1.6903658594 \mathrm{e}-08$ | -06 | -12 |
|  | 246428 | 9331.3 | $1.2935699163 \mathrm{e}-06$ | -12 | -31 |
|  | 2394 | 81.6 | $1.2953925804 \mathrm{e}-06$ | -45 | -30 |
| gen2 | 44073 | 60.0 | $3.2927907828 \mathrm{e}+00$ | -04 | -11 |
|  | 1599 | 359.9 | $3.2927907840 \mathrm{e}+00$ | - | -29 |
| gen4 | 0 | 10.4 | $3.2927907840 \mathrm{e}+00$ | - | -32 |
|  | 45369 | 212.4 | $1.5793970394 \mathrm{e}-07$ | -06 | -10 |
|  | 53849 | 14812.5 | $2.8932268196 \mathrm{e}-06$ | -12 | -30 |
|  | 37 | 10.4 | $2.8933064888 \mathrm{e}-06$ | -54 | -30 |


| model | Itns | Times | Final objective | Pinf | Dinf |
| :--- | ---: | ---: | ---: | ---: | ---: |
| I30 | 1229326 | 876.7 | $9.5266141574 \mathrm{e}-01$ | -10 | -09 |
|  | 275287 | 7507.1 | $-7.5190273434 \mathrm{e}-26$ | -25 | -32 |
|  | 0 | 0.2 | $-4.2586876849 \mathrm{e}-24$ | -24 | -33 |
| iprob | 1087 | 0.2 | $2.6891551285 \mathrm{e}+03$ | +02 | -11 |
|  | 0 | 0.0 | $2.6891551285 \mathrm{e}+03$ | +02 | -31 |
|  | 0 | 0.0 | $2.6891551285 \mathrm{e}+03$ | +02 | -28 |
| TMA_ME | 12225 | 37.1 | $8.0051076669 \mathrm{e}-07$ | -06 | -05 |
|  | 685 | 61.5 | $8.7036315385 \mathrm{e}-07$ | -24 | -30 |
|  | 0 | 6.7 | $8.7036315385 \mathrm{e}-07$ | - | -31 |
| GlcAerWT | 62856 | 9707.3 | $-2.4489880182 \mathrm{e}+04$ | +04 | -05 |
|  | 5580 | 3995.6 | $-7.0382449681 \mathrm{e}+05$ | -07 | -26 |
|  | 4 | 60.1 | $-7.0382449681 \mathrm{e}+05$ | -19 | -21 |
| GlcAlift | 134693 | 14552.8 | $-5.1613878666 \mathrm{e}+05$ | -03 | -01 |
|  | 3258 | 1067.1 | $-7.0434008750 \mathrm{e}+05$ | -09 | -26 |
|  | 2 | 48.1 | $-7.0434008750 \mathrm{e}+05$ | -20 | -22 |

## DRR procedure

Step D: Double MINOS<br>Step R1: Refinement<br>Step R2: Refinement with no scaling

## Plausible alternative to DQQ

## DRR procedure

(1) Cold start Double MINOS with scaling and somewhat strict settings
(2) Warm start with scaling and Iterative Refinement and tighter Featol/Opttol
(3) Warm start with no scaling but Iterative Refinement and tighter LU tols

- We need Quad residuals for $B x_{B}=b-N x_{n}$ after LU and for $B y=a, B^{T} y=c_{B}$ each iteration


## DRR procedure

(1) Cold start Double MINOS with scaling and somewhat strict settings
(2) Warm start with scaling and Iterative Refinement and tighter Featol/Opttol
(3) Warm start with no scaling but Iterative Refinement and tighter LU tols

- We need Quad residuals for $B x_{B}=b-N x_{n}$ after LU and for $B y=a, B^{T} y=c_{B}$ each iteration
- Quad $r=a-B y \quad$ needs $\quad r \leftarrow r-y_{k} B_{k} \quad$ (qaxpy)

Compiler converts $B$ to Quad every iteration

## DRR procedure

(1) Cold start Double MINOS with scaling and somewhat strict settings
(2) Warm start with scaling and Iterative Refinement and tighter Featol/Opttol
(3) Warm start with no scaling but Iterative Refinement and tighter LU tols

- We need Quad residuals for $B x_{B}=b-N x_{n}$ after LU and for $B y=a, B^{T} y=c_{B}$ each iteration
- Quad $r=a-B y \quad$ needs $\quad r \leftarrow r-y_{k} B_{k} \quad$ (qaxpy)

Compiler converts $B$ to Quad every iteration

- Quad $r=c_{B}-B^{T} y$ needs Quad dotproducts (qdot)

Again, compiler converts $B$ to Quad every iteration

## DRR procedure

(1) Cold start Double MINOS with scaling and somewhat strict settings
(2) Warm start with scaling and Iterative Refinement and tighter Featol/Opttol
(3) Warm start with no scaling but Iterative Refinement and tighter LU tols

- We need Quad residuals for $B x_{B}=b-N x_{n}$ after LU and for $B y=a, B^{T} y=c_{B}$ each iteration
- Quad $r=a-B y \quad$ needs $\quad r \leftarrow r-y_{k} B_{k} \quad$ (qaxpy)

Compiler converts $B$ to Quad every iteration

- Quad $r=c_{B}-B^{T} y$ needs Quad dotproducts (qdot)

Again, compiler converts $B$ to Quad every iteration

- James Ho (1975) SRR procedure?


## LPnetlib test problems

Unexpectedly high accuracy in Quad

## 62 classic LP problems (ordered by file size)

```
afiro
stocfor1
adlittle
scagr7
sc205
share2b
recipe
vtpbase
share1b
bore3d
scorpion
capri
brandy
scagr25
sctap1
israel
scfxm1
pilot4
scsd6
```

pilotja

```
ship04s
seba
grow15
fffff800
scfxm3
ship04l
ganges
sctap2
grow22
ship08s
stocfor2
pilotwe
ship12s
25fv47
sierra
czprob
```


## DRR procedure on LPnetlib problems

```
Pinf = max Primal infeasibility
Dinf = max Dual infeasibility/(1+|y*||
```

Pinf $\leq$ Feasibility tol<br>Default 1e-6<br>Dinf $\leq$ Optimality tol<br>Default $1 \mathrm{e}-6$

Plot $\log _{10}($ Pinf $)$ and $\log _{10}($ Dinf $)$ for steps D, R1, R2

Primal/dual infeasibilities:

Scale option 2
Feasibility tol 1e-7
Optimality tol 1e-7

LU Partial Pivoting
LU Factor tol 10.0
LU Update tol 10.0
Quad refinement 0

$$
\epsilon=2.2 \mathrm{e}-16
$$

Step D: Double MINOS, cold start, scale


Primal/dual infeasibilities:

Scale option 2
Feasibility tol 1e-9
Optimality tol 1e-9

LU Partial Pivoting
LU Factor tol 1.9
LU Update tol 1.9
Quad refinement 1

$$
\epsilon=2.2 \mathrm{e}-16
$$

Step R1: Double MINOS, warm start, scale, refine


| Scale option 0 |  |
| :--- | ---: |
| Feasibility tol | $1 \mathrm{e}-9$ |
| Optimality tol | $1 \mathrm{e}-9$ |
|  |  |
| LU Partial Pivoting |  |
| LU Factor tol | 1.9 |
| LU Update tol | 1.9 |
| Quad refinement | 1 |

$$
\epsilon=2.2 \mathrm{e}-16
$$




## DQQ procedure on LPnetlib problems

Pinf $=$ max Primal infeasibility
Dinf $=\max$ Dual infeasibility $/\left(1+\left\|y^{*}\right\|_{\infty}\right)$

MINOS stops when $\begin{aligned} & \text { Pinf } \leq \text { Feasibility tol } \\ & \text { Dinf } \leq \text { Optimality tol }\end{aligned}$

Plot $\log _{10}($ Pinf $)$ and $\log _{10}($ Dinf $)$ for steps D, Q1, Q2

Primal/dual infeasibilities:

Scale option 2
Feasibility tol 1e-7
Optimality tol 1e-7

LU Partial Pivoting
LU Factor tol 10.0
LU Update tol 10.0
Expand freq 100000

$$
\epsilon=2.2 \mathrm{e}-16
$$

Step D: Double MINOS, cold start, scale (repeat)


D: Cold, scale: $\log ($ Dinf $)$


Primal/dual infeasibilities:

Scale option 2
Feasibility tol 1e-15
Optimality tol 1e-15

LU Partial Pivoting
LU Factor tol 10.0
LU Update tol 10.0

$$
\epsilon=1.9 \mathrm{e}-35
$$

Step Q1: Quad MINOS, warm start, scale



Primal/dual infeasibilities:

Scale option 0
Feasibility tol 1e-15
Optimality tol 1e-15

LU Partial Pivoting
LU Factor tol 5.0
LU Update tol 5.0

$$
\epsilon=1.9 \mathrm{e}-35
$$

Step Q2: Quad MINOS, warm start, no scale


## Multiscale NLPs

## Systems biology FBA problems with variable $\mu$ (Palsson Lab, UC San Diego, 2014)

## ME models with nonlinear constraints

As coupling constraints are often functions of the organism's growth rate $\mu$, Lerman et al. (UCSD) consider growth-rate optimization nonlinearly with the single $\mu$ as the objective instead of via a linear biomass objective function. Nonlinear constraints of the form
represented as

$$
\begin{equation*}
\frac{v_{i}}{v_{j}} \leq \mu \tag{7}
\end{equation*}
$$

$$
\begin{equation*}
v_{i} \leq \mu v_{j} \tag{8}
\end{equation*}
$$

are added to (2b), where $v_{i}, v_{j}, \mu$ are all variables. Constraints (8) are linear if $\mu$ is fixed at a specific value $\mu_{k}$. Lerman et al. employ a binary search to find the largest $\mu_{k} \in\left[\mu_{\text {min }}, \mu_{\text {max }}\right]$ that keeps the associated LP feasible. Thus, the procedure requires reliable solution of a sequence of related LPs.

## tinyME

Nonlinear FBA formulation, Laurence Yang, UCSD, Dec 2014

```
max }\mu\quad\operatorname{max}
    st }\muAx+Bx=
    Sx =b \equiv
    bounds on x
```

$$
\begin{aligned}
\max \mu & \\
\text { st } \quad \mu A x+w & =0 \\
B x-w & =0 \\
S x & =b
\end{aligned}
$$

bounds on $x$, no bounds on $w$

- Tiny example: $\approx 2500 \times 3000$
- $\mu=x_{1}$ and the first columns of $A, B$ are empty
- Constraints are linear if $\mu$ is fixed 25 LP subproblems would give 8 digits
suggests binary search on sequence of LPs (really need quad Simplex)
- Instead, apply quad MINOS LCL method = Linearly Constrained Lagrangian 6 NLP subproblems (with linearized constraints) give 20 digits


## Quadratic convergence of major iterations (Robinson 1972)



EXIT -- optimal solution found

| Problem name | tinyME |  |  |
| :---: | :---: | :---: | :---: |
| No. of iterations | 912 | Objective value 8. | 94810579E-01 |
| No. of major iterations | 6 | Linear objective 0. | 00000000E+00 |
| Penalty parameter | 1.000000 | Nonlinear objective 8. | 94810579E-01 |
| No. of calls to funobj | 98 | No. of calls to funcon | 98 |
| No. of superbasics | 0 | No. of basic nonlinears | 786 |
| No. of degenerate steps | 0 | Percentage | 0.00 |
| Max x (scaled) 12 | 5.6E-01 | Max pi (scaled) | 103 8.3E+05 |
| Max x 1020 | 6.1E+01 | Max pi | 103 9.7E+03 |
| Max Prim inf (scaled) | 0.0E+00 | Max Dual inf(scaled) | $92.9 \mathrm{E}-14$ |
| Max Primal infeas | 0.0E+00 | Max Dual infeas | 9 1.3E-18 |
| Nonlinear constraint violn | $1.9 \mathrm{E}-20$ |  |  |
| funcon called with nstate $=2$ |  |  |  |
| Final value of $\mathrm{mu}=0.84694810578563166175146802332321527$ |  |  |  |
| Time for solving problem |  | 13.50 seconds |  |

## ME 2.0

Large FBA and FVA problems, Laurence Yang, UCSD, Sep 2015

FBA model iJL1678: $\quad 71,000 \times 80,000$ LP
Quad MINOS cold start:
FVA problems:
$\sim 3$ hours
$\min$ and max individual variables $v_{j}$

|  |  | Double CPLEX |  | Quad MINOS |  |
| :--- | :--- | ---: | ---: | ---: | ---: |
| Reaction | Protein | $v_{\min }$ | $v_{\max }$ | $v_{\min }$ | $v_{\text {max }}$ |
| translation_b0169 | RpsB | 30.715011 | 30.712581 | 30.719225 | 30.719225 |
| translation_b0025 | RibF | 0.212807 | 0.211712 | 0.210161 | 0.210161 |
| translation_b0071 | LeuD | 0.303304 | 0.765585 | 0.303634 | 0.303634 |
| translation_b0072 | LeuC | 0.303304 | 0.681146 | 0.303634 | 0.303634 |

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- If the comma's omitted, the which is wicked.


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Thanks for the quick reply.
Thanks for your quick reply.
Peter, thanks for your quick reply.

## Philosophy

## -

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Jan 5<br>Tues, Jan 5

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- Urge chip-makers to implement hardware quad precision.


## Conclusions

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## References

- Y. Sun, R. M. T. Fleming, I. Thiele, and M. A. Saunders. Robust flux balance analysis of multiscale biochemical reaction networks, BMC Bioinformatics 14:240, 2013, 6 pp.
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## Special thanks

- George Dantzig, born 101 years ago (8 Nov 1914)
- William Kahan, IEEE floating-point standard, including Quad, Boulder.pdf (2011)
- GNU gfortran
- Ronan Fleming, Ines Thiele (Luxembourg)
- Bernhard Palsson, Josh Lerman, Teddy O'Brien, Laurence Yang (UCSD)
- Ed Klotz (IBM CPLEX), Yuekai Sun, Jon Dattorro (Stanford)
- Frank Curtis, Jose Luis Morales, Katya Scheinberg, Andreas Wächter
- Is quadMINOS available?

Yes, in the openCOBRA toolbox http://opencobra.github.io/cobratoolbox/

- Can quadMINOS be called from Matlab or Tomlab? Yes via system call (not Mex)
- Is quadMINOS available in GAMS? Soon Yes
- How about AMPL?

No, but should be feasible

- Is there a quadSNOPT?

Yes, in 990 SNOPT9 we can change 1 line

- Can CPLEX / Gurobi / Mosek / ...help? Yes, they can provide Presolve and Warm start, especially from GAMS
- Will Quad hardware eventually be standard?

We hope so but Kahan is pessimistic


[^0]:    ${ }^{1}$ GNU Fortran (GCC) 4.6.2 20111019 on Mac OS X (now version 5.2.0)

