

# The DQQ procedure for multiscale optimization

Ding Ma and Michael Saunders

MS&E and ICME, Stanford University

ICCOPT 2016  
Tokyo, Japan, August 6–11, 2016

## Abstract

Systems biology models of metabolic networks can lead to challenging optimization problems for which standard solvers are not sufficiently accurate, while the rational arithmetic of exact simplex solvers is extremely slow. Quad-precision floating-point (even in software) offers a practical compromise. We combine Double and Quad versions of MINOS, with and without scaling, to overcome the difficulty of unscaling multiscale problems. This has enabled solution of the Meszaros "problematic" LPs and increasingly large linear and nonlinear ME models in systems biology.

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



## 1 Motivation

## 2 Quad Precision

## 3 DQQ procedure

## 4 DRR procedure

## 5 62 LPnetlib test problems

## 6 Multiscale NLPs

## 7 Conclusions

# Motivation

# Multiscale LPs in systems biology

$$\max_v c^T v \text{ s.t. } S v = 0, \quad l \leq v \leq u$$

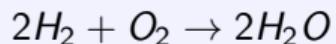
## Normal for LP (simplex or interior)

- Scale to reduce large  $A_{ij}$
- Solve with Feasibility/Optimality tols 1e-6
- Unscale

## Difficulty

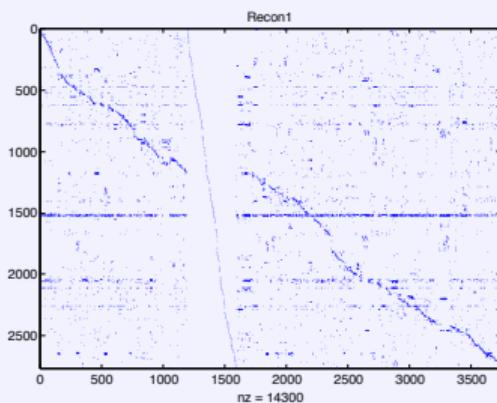
- Unscaling magnifies residuals
- Solution may be far from feasible or optimal

# Stoichiometric matrices $S$

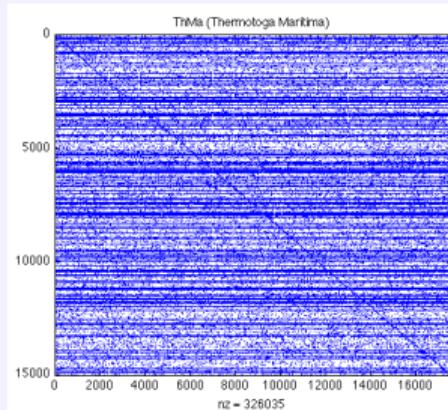


$$\begin{array}{c|cccccc} & \cdot & \cdot & \cdot & W & \cdot & \cdot & \cdot \\ \hline H_2 & \cdot & \cdot & \cdot & -2 & \cdot & \cdot & \cdot \\ O_2 & \cdot & \cdot & \cdot & -1 & \cdot & \cdot & \cdot \\ H_2O & \cdot & \cdot & \cdot & 2 & \cdot & \cdot & \cdot \end{array}$$

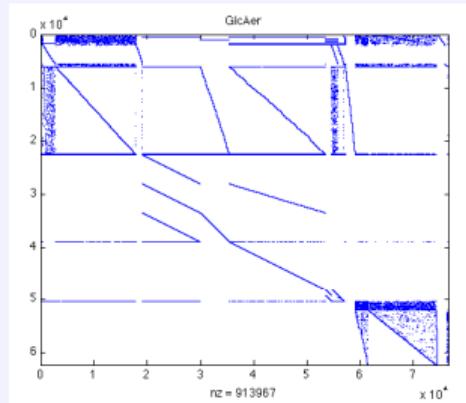
chemicals  $\times$  reactions



$2800 \times 3700$



$15000 \times 18000$



$62000 \times 77000$

# ME models (Metabolism and macromolecular Expression)

## Coupling constraints

$$c_{\min} \leq \frac{v_i}{v_j} \leq c_{\max} \quad \equiv \quad c_{\min} v_j \leq v_i, \quad v_i \leq c_{\max} v_j$$

## Lifting

$$v_1 \leq 10000v_2 \quad \equiv \quad v_1 \leq 100s_1, \quad s_1 \leq 100v_2$$

# 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.”*

— William Kahan

## Methods for achieving Quad precision

### Double auxiliary functions (hand-coded)

Even `qdotdd(v,w)` needs `twosum`, `split`, `twoproduct` `sum2`, `dot2` to compute `x,y` such that `q = vTw = quad(x) + quad(y)`

### Double-double datatype ( $\approx 32$ digits)

QD: <http://crd-legacy.lbl.gov/~dhbailey/mpdist/>

Minor changes to source code (except I/O), uses floating-point hardware

### Quad datatype ( $\approx 34$ digits)

`real(16)` in gfortran, ifort      `float128` in gcc

Minor changes

We use this humane approach to Quad implementation

# Double MINOS and Quad MINOS

real(8)

eps = 2.22e-16

Hardware

real(16)

eps = 1.93e-34

Software

## snopt9 = Double or Quad SQOPT, SNOPT

### snPrecision.f90

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

### module sn50lp

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

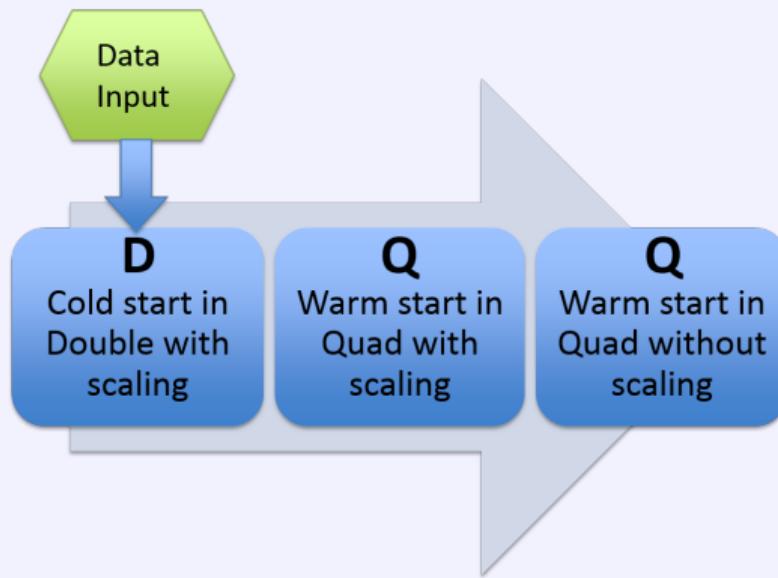
## DQQ procedure

**Step D: Double MINOS**

**Step Q1: Quad MINOS**

**Step Q2: Quad MINOS with no scaling**

# DQQ procedure



## MINOS runtime options for DQQ procedure

	Default	Step D	Step Q1	Step Q2
Scale option	2	2	2	0
Feasibility tol	1e-6	1e-7	1e-15	1e-15
Optimality tol	1e-6	1e-7	1e-15	1e-15
Expand frequency	10000	100000	100000	100000
LU Factor tol	100.0	1.9	10.0	5.0
LU Update tol	10.0	1.9	10.0	5.0

pilot models from Netlib  
Mészáros problematic LPs  
ME biochemical network models

	$m$	$n$	$\text{nnz}(A)$	$\max  A_{ij} $	$\ x^*\ _\infty$	$\ y^*\ _\infty$
pilot4	411	1000	5145	3e+04	1e+05	3e+02
pilot	1442	3652	43220	2e+02	4e+03	2e+02
pilot87	2031	4883	73804	1e+03	2e+04	1e+01
de063155	853	1488	5405	8e+11	3e+13	6e+04
de063157	937	1488	5551	2e+18	2e+17	6e+04
de080285	937	1488	5471	1e+03	1e+02	3e+01
gen1	770	2560	64621	1e+00	3e+00	1e+00
gen2	1122	3264	84095	1e+00	3e+00	1e+00
gen4	1538	4297	110174	1e+00	3e+00	1e+00
I30	2702	15380	64790	1e+00	1e+09	4e+00
iprob	3002	3001	12000	1e+04	3e+02	1e+00
TMA_ME	18210	17535	336302	2e+04	6e+00	1e+00
GlcAerWT	68300	76664	926357	8e+05	6e+07	2e+07
GlcAlift	69529	77893	928815	3e+05	6e+07	2e+07

Itns and runtimes in secs for DQQ Steps 1,2,3 (Double MINOS and Quad MINOS).

Pinf and Dinf =  $\log_{10}$  max primal/dual infeasibilities.

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

Step 3 Pinf/  $\|x^*\|_\infty$  and Dinf/  $\|y^*\|_\infty$  are  $O(10^{-30})$

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

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

Step 3 Pinf/  $\|x^*\|_\infty$  and Dinf/  $\|y^*\|_\infty$  are  $O(10^{-30})$   
except iprob is infeasible

## DRR procedure

**Step D: Double MINOS**

**Step R1: Refinement**

**Step R2: Refinement with no scaling**

**Plausible alternative to DQQ**

## DRR procedure

- We need **Quad residuals** for solving  $Bx_B = b - Nx_n$  after LU and for solving  $Bp = a$ ,  $B^T y = c_B$  each iteration
- Quad  $r = a - Bp$  needs  $r \leftarrow r - p_k B_k$  (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

# LPnetlib test problems

Compare DRR and DQQ

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

afiro	scfxm1	ship04s	pilotja
stocfor1	bandm	seba	ship081
adlittle	e226	grow15	nesm
scagr7	grow7	fffff800	ship121
sc205	etamacro	scfxm3	cycle
share2b	agg	ship04l	greenbea
recipe	scsd1	ganges	greenbeb
vtpbase	standata	sctap2	80bau3b
share1b	beaconfd	grow22	d2q06c
bore3d	gfrdpnc	ship08s	woodw
scorpion	stair	stocfor2	d6cube
capri	scrs8	pilotwe	pilot
brandy	shell	ship12s	wood1p
scagr25	scfxm2	25fv47	pilot87
sctap1	pilot4	sierra	
israel	scsd6	czprob	

## DRR procedure on LPnetlib problems

$P_{\text{inf}} = \max$  Primal infeasibility

$D_{\text{inf}} = \max$  Dual infeasibility/ $(1 + \|y^*\|_\infty)$

MINOS stops when	$P_{\text{inf}} \leq$ Feasibility tol	Default $1e-6$
	$D_{\text{inf}} \leq$ Optimality tol	Default $1e-6$

Plot  $\log_{10}(P_{\text{inf}})$  and  $\log_{10}(D_{\text{inf}})$  for steps D, R1, R2

## Primal/dual infeasibilities:

## Step D: Double MINOS, cold start, scale

Scale option 2

Feasibility tol  $1e-7$

Optimality tol  $1e-7$

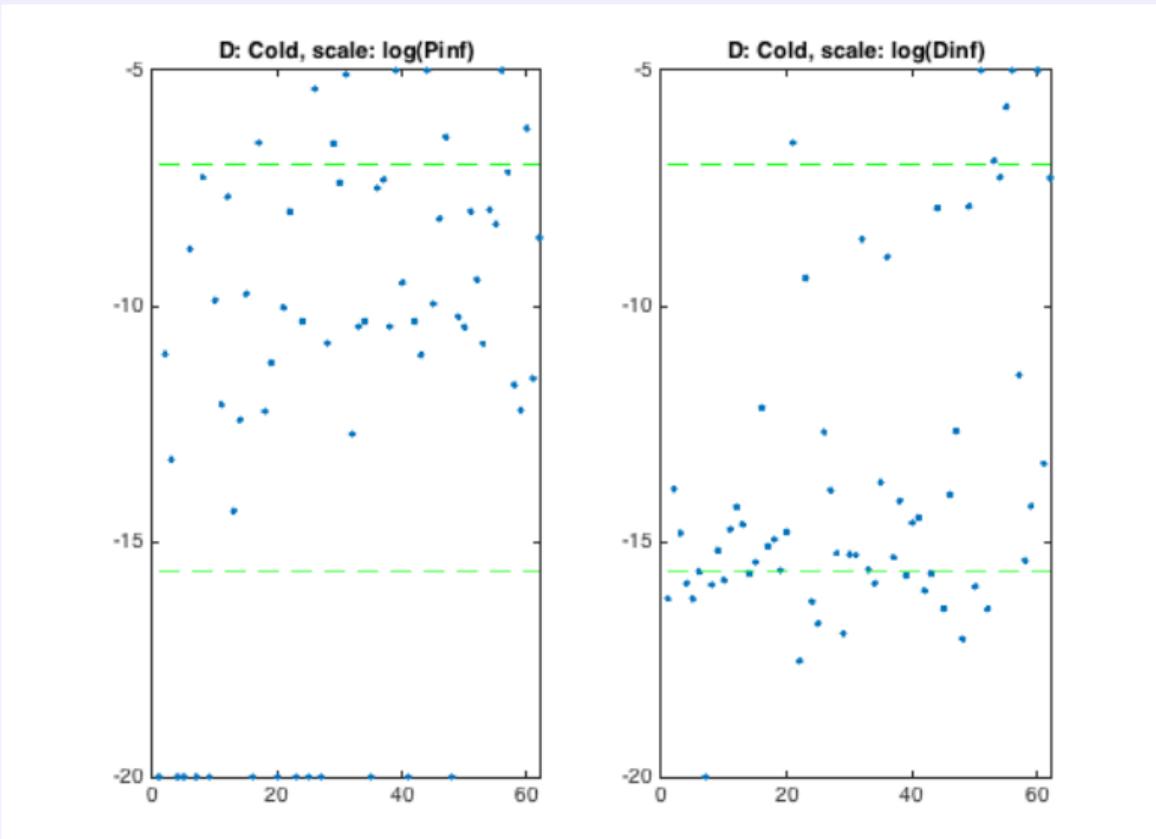
LU Partial Pivoting

LU Factor tol 10.0

LU Update tol 10.0

Quad refinement 0

$$\epsilon = 2.2e-16$$



## Primal/dual infeasibilities:

Scale option 2

Feasibility tol  $1e-9$

Optimality tol  $1e-9$

LU Partial Pivoting

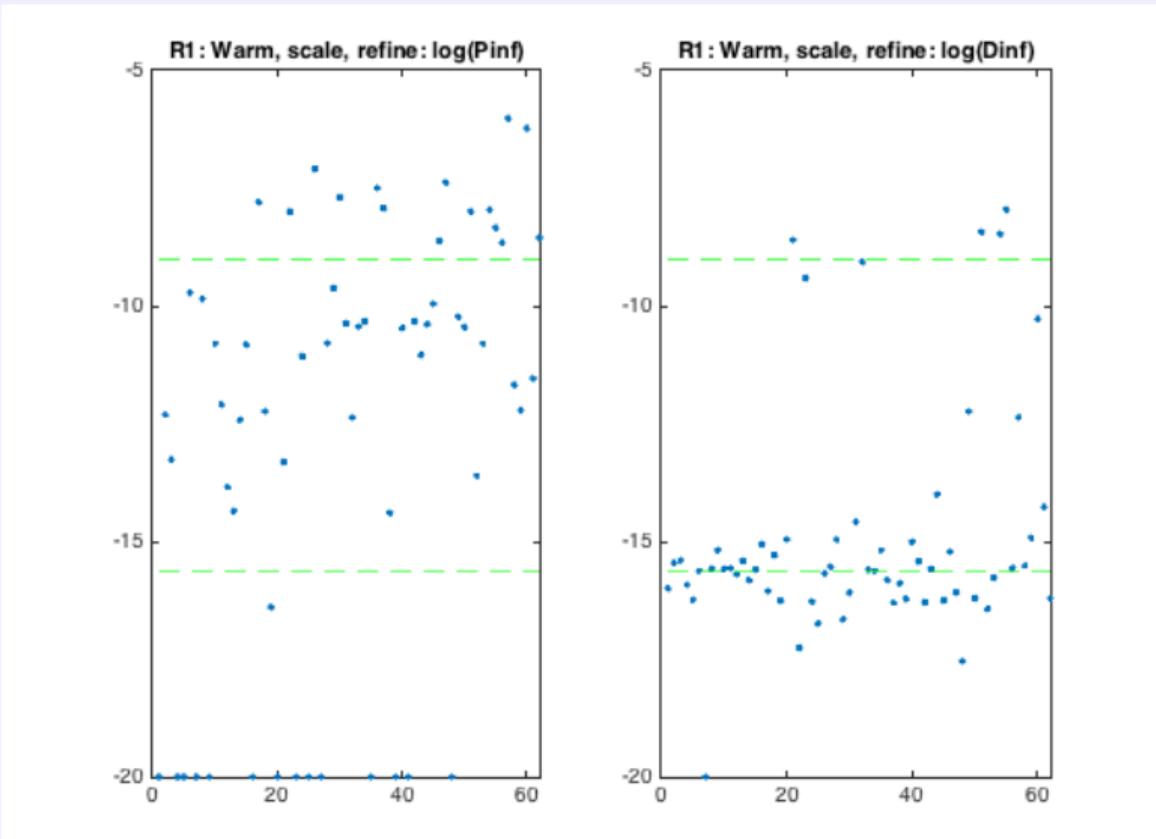
LU Factor tol 1.9

LU Update tol 1.9

Quad refinement 1

$$\epsilon = 2.2e-16$$

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



## Primal/dual infeasibilities:

## Step R2: Double MINOS, warm start, no scale, refine

Scale option 0

Feasibility tol  $1e-9$

Optimality tol  $1e-9$

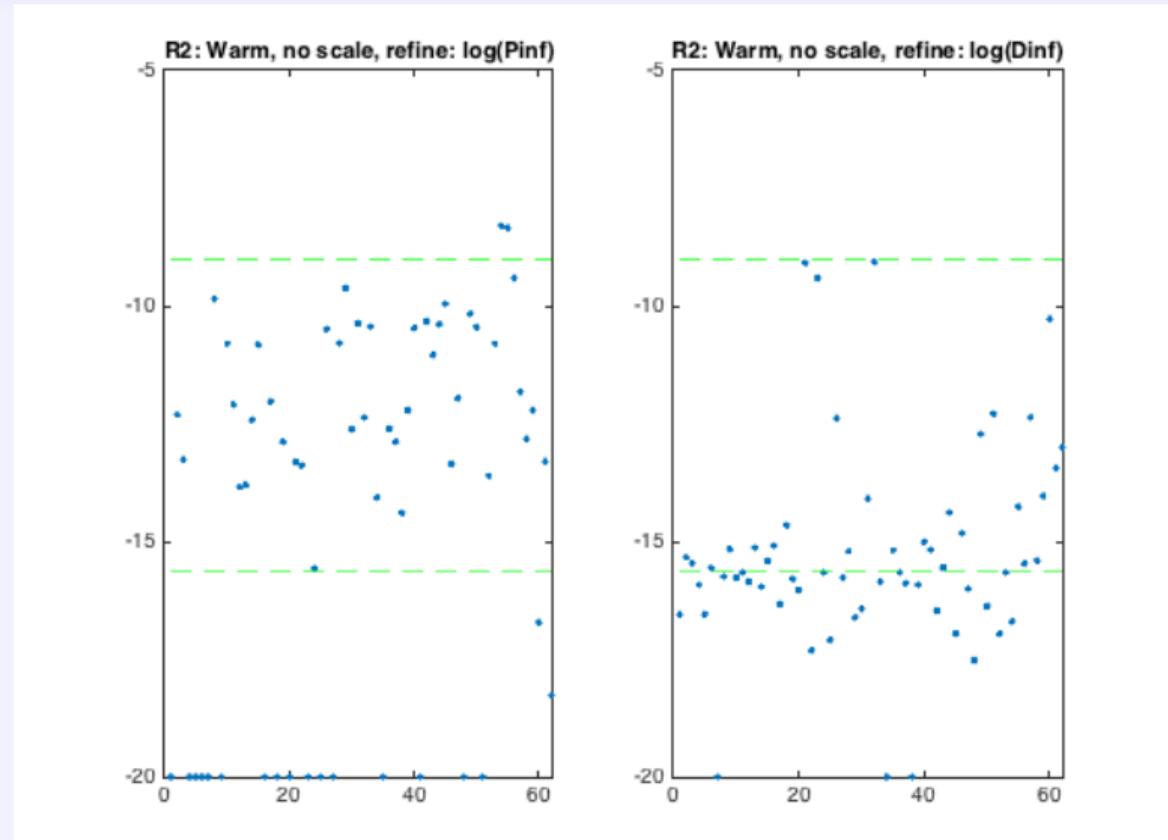
LU Partial Pivoting

LU Factor tol 1.9

LU Update tol 1.9

Quad refinement 1

$$\epsilon = 2.2e-16$$



## DQQ procedure on LPnetlib problems

$P_{\text{inf}} = \max$  Primal infeasibility

$D_{\text{inf}} = \max$  Dual infeasibility/ $(1 + \|y^*\|_\infty)$

MINOS stops when     $P_{\text{inf}} \leq$  Feasibility tol  
                                   $D_{\text{inf}} \leq$  Optimality tol

Plot  $\log_{10}(P_{\text{inf}})$  and  $\log_{10}(D_{\text{inf}})$  for steps D, Q1, Q2

## Primal/dual infeasibilities:

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

Scale option 2

Feasibility tol  $1e-7$

Optimality tol  $1e-7$

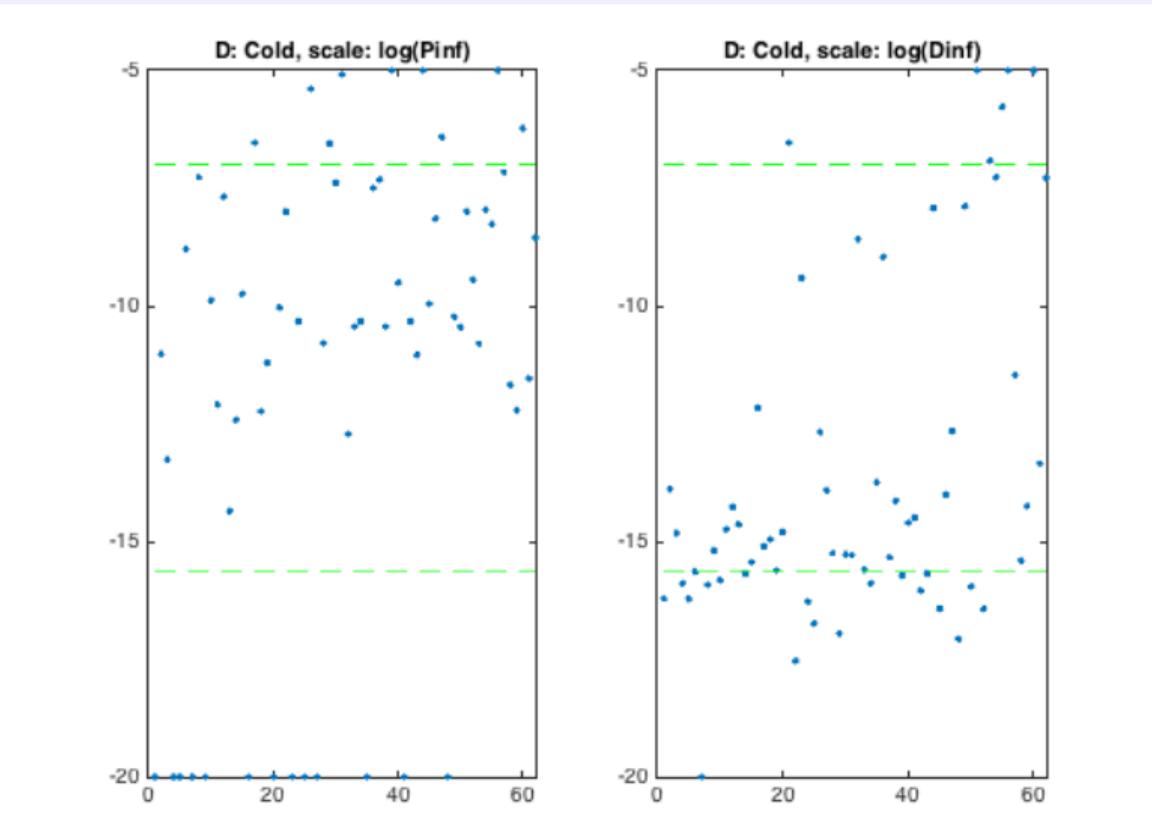
LU Partial Pivoting

LU Factor tol 10.0

LU Update tol 10.0

Expand freq 100000

$$\epsilon = 2.2e-16$$



## Primal/dual infeasibilities:

## Step Q1: Quad MINOS, warm start, scale

Scale option 2

Feasibility tol 1e-15

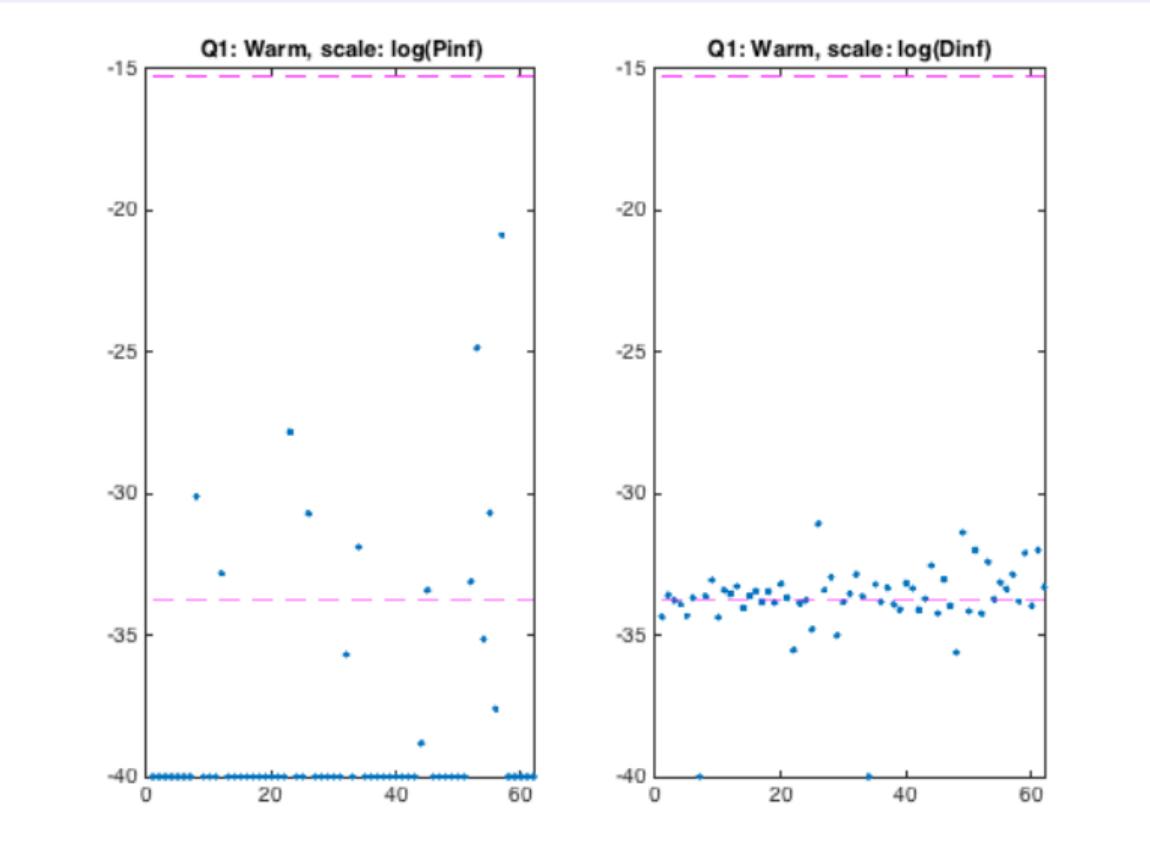
Optimality tol 1e-15

LU Partial Pivoting

LU Factor tol 10.0

LU Update tol 10.0

$$\epsilon = 1.9 \times 10^{-35}$$



## Primal/dual infeasibilities:

## Step Q2: Quad MINOS, warm start, no scale

Scale option 0

Feasibility tol 1e-15

Optimality tol 1e-15

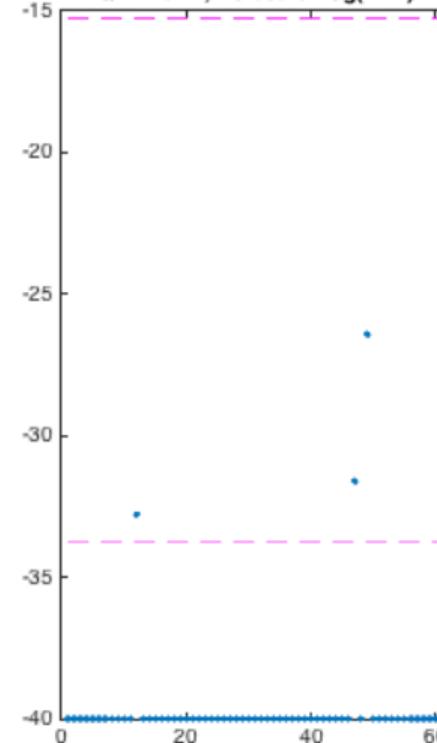
LU Partial Pivoting

LU Factor tol 5.0

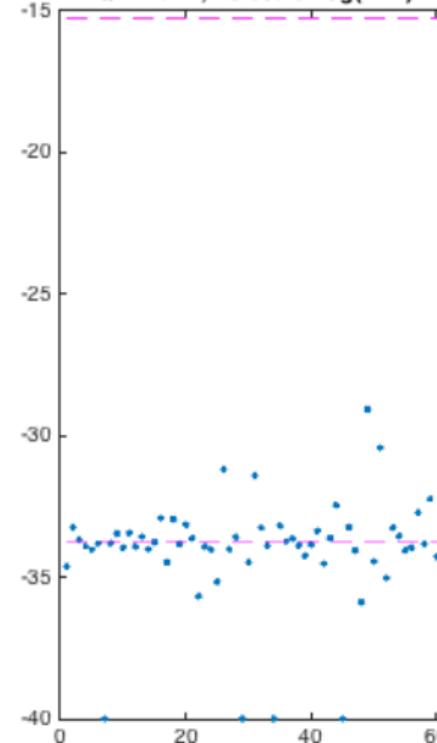
LU Update tol 5.0

$$\epsilon = 1.9 \times 10^{-35}$$

Q2: Warm, no scale: log(Pinf)



Q2: Warm, no scale: log(Dinf)



# Multiscale NLPs

Systems biology FBA problems with variable  $\mu$   
Palsson Lab, UC San Diego, 2014–2016

## ME models with nonlinear constraints

Coupling constraints can be functions of the organism's growth rate  $\mu$ .

Lerman et al. (UCSD) consider growth-rate optimization nonlinearly with a single  $\mu$  as the objective. Nonlinear constraints

$$\frac{v_i}{v_j} \leq \mu \quad \equiv \quad v_i \leq \mu v_j$$

are linear if  $\mu$  is fixed. Can use a binary search to find the largest  $\mu \in [\mu_{\min}, \mu_{\max}]$  that keeps the associated LP feasible.

Requires reliable solution of a sequence of related LPs.

# tinyME ( $2500 \times 2800$ nonlinear ME model)

Nonlinear FBA formulation, Laurence Yang, UCSD, Dec 2014

$$\begin{array}{ll} \max & \mu \\ \text{st} & \mu Ax + Bx = 0 \\ & Sx = b \\ & \text{bounds on } x \end{array} \equiv$$

$$\begin{array}{ll} \max & \mu \\ \text{st} & \mu Ax + w = 0 \\ & Bx - w = 0 \\ & Sx = b \\ & \text{bounds on } x, \text{ no bounds on } w \end{array}$$

- $\mu = x_1$  First columns of  $A$ ,  $B$  are empty
- Binary search  
25 LP subproblems would give 8 digits (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)

quadMINOS 5.6 (Nov 2014)

Major	minor	step	objective	Feasible	Optimal	nsb	ncon	penalty
1	304T	0.0E+00	8.00000E-01	6.1E-03	2.1E+03	0	4	1.0E+02
2	561T	1.0E+00	8.00000E-01	2.6E-14	3.2E-04	0	46	1.0E+02
3	40T	1.0E+00	8.28869E-01	5.4E-05	3.6E-05	0	87	1.0E+02
4	7	1.0E+00	8.46923E-01	1.2E-05	2.9E-06	0	96	1.0E+02
5	0	1.0E+00	8.46948E-01	4.2E-10	2.6E-10	0	97	1.0E+02
6	0	1.0E+00	8.46948E-01	7.9E-23	1.2E-20	0	98	1.0E+01

EXIT -- optimal solution found

13.5 secs

# solveME ( $11000 \times 19000$ nonlinear ME model)

2600 nonlinear constraints, 16000 nonlinear variables  
 Laurence Yang, UCSD, Sep 2015

```
Itn      32 -- linear constraints satisfied.  

Calling funcon. mu = 0.832815729997476367249118875820191994
```

Major	minor	step	objective	Feasible	Optimal	nsb	ncon	penalty	BSwap
1	32T	0.0E+00	8.32816E-01	4.3E-13	1.0E+03	0	4	1.0E+02	0
19	40T	1.0E+00	8.32816E-01	2.5E-16	1.0E-03	0	743	1.0E+02	0
20	40T	1.0E+00	8.32816E-01	1.0E-21	9.3E-04	0	784	1.0E+02	0
23	40T	1.0E+00	8.55337E-01	3.4E-07	5.7E-05	0	907	1.0E+02	0
24	40T	1.0E+00	8.55664E-01	2.1E-08	6.6E-07	0	948	1.0E+02	0
25	11	1.0E+00	8.55664E-01	7.0E-17	1.8E-11	0	961	1.0E+02	0
26	0	1.0E+00	8.55664E-01	9.3E-19	8.0E-29	0	962	1.0E+01	0

EXIT -- optimal solution found

# ME 2.0 (large FBA and FVA problems)

$71,000 \times 80,000$  LPs

Laurence Yang, UCSD, Sep 2015

Quad MINOS cold start:  $\sim 3$  hours

FVA problems: min and max individual variables  $v_j$

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

## quadQP

Laurence Yang, UCSD, Jul 2016

$$\min c^T x + \frac{1}{2} x^T H x \text{ st } Ax + s = b \text{ and bounds,}$$

$$\begin{array}{ll} H & 4146 \times 4146 \\ A & 12667 \times 21126 \end{array}$$

Itn	rg	ninf	sinf	objective
-----	----	------	------	-----------

1	-1.1E+11	159	7.715E+00	0.00000000E+00
---	----------	-----	-----------	----------------

500	-1.9E+10	159	7.715E+00	0.00000000E+00
-----	----------	-----	-----------	----------------

900	-1.3E+14	159	7.715E+00	0.00000000E+00
-----	----------	-----	-----------	----------------

3000	-1.5E+05	11	9.784E-04	0.00000000E+00
------	----------	----	-----------	----------------

3400	-5.1E-02	4	6.616E-05	0.00000000E+00
------	----------	---	-----------	----------------

Itn	3554	-- feasible solution.	Objective =	7.634331271E-03
-----	------	-----------------------	-------------	-----------------

Itn	rg	ninf	sinf	objective	nobj	nsb
-----	----	------	------	-----------	------	-----

4000	-4.8E-02	0	0.000E+00	3.08300094E-03		
------	----------	---	-----------	----------------	--	--

5000	-1.9E-04	0	0.000E+00	1.03117165E-03	1406	1
------	----------	---	-----------	----------------	------	---

5200	-1.9E-05	0	0.000E+00	1.02662098E-03	1436	2
------	----------	---	-----------	----------------	------	---

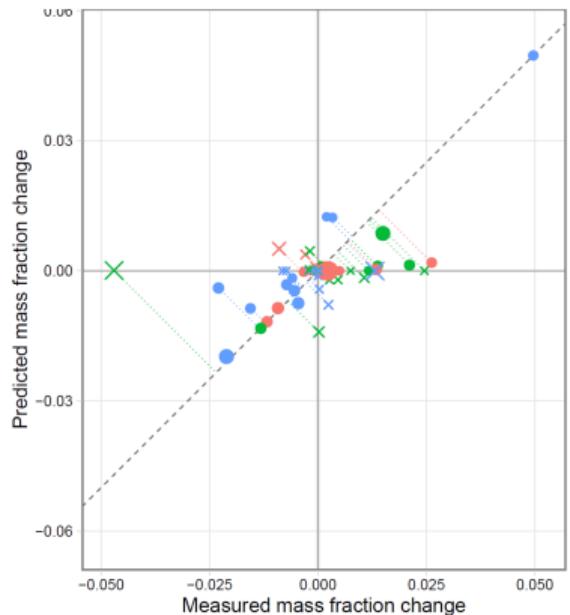
5300	-4.6E-09	0	0.000E+00	1.02660849E-03	1466	4
------	----------	---	-----------	----------------	------	---

## quadQP

Laurence Yang, UCSD, Jul 2016

246 secs

# Refining ME-computed proteomes



**Proteome:** the set of all proteins that is or can be expressed by an organism

**Mass fraction:** relative abundance of a given protein relative to all proteins (i.e., the proteome)

Includes solving quad-precision QP

Itn	rg	ninf	sinf	objective	nobj	nsb
4700	-2.9E-03	0	0.000E+00	1.35572488E-03		
4800	-1.2E-03	0	0.000E+00	1.03964380E-03		
4900	-4.1E-04	0	0.000E+00	1.03667479E-03		

Itn	rg	ninf	sinf	objective	nobj	nsb
5000	-1.9E-04	0	0.000E+00	1.03117165E-03	1406	1
5100	-6.6E-05	0	0.000E+00	1.02674422E-03	1423	1
5200	-1.9E-05	0	0.000E+00	1.02662098E-03	1436	2
5300	-4.6E-09	0	0.000E+00	1.02660849E-03	1466	4

Itn 5318 -- 25 nonbasics set on bound, basics recomputed  
Itn 5318 -- feasible solution. Objective = 1.026608483E-03

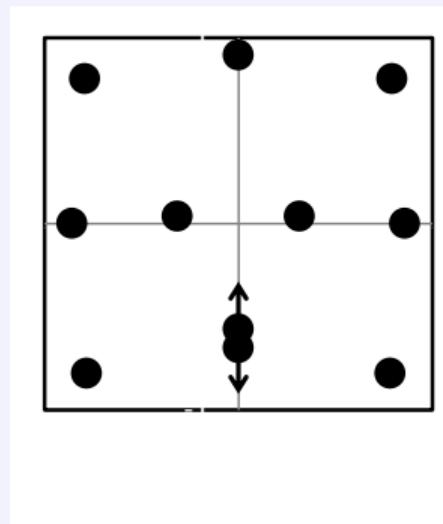
EXIT -- optimal solution found

No. of iterations	5318	Objective value	1.0266084830E-03
No. of major iterations	1	Linear objective	0.0000000000E+00
Penalty parameter	100.000000	Nonlinear objective	1.0266084830E-03
No. of calls to funobj	1489	No. of calls to funcon	0
No. of superbasics	2	No. of basic nonlinear	12614
No. of degenerate steps	3686	Percentage	69.31
Max x (scaled)	12400	Max pi (scaled)	662 1.5E+04
Max x	10269	Max pi	6083 3.4E+02
Max Prim inf(scaled)	7860	Max Dual inf(scaled)	9618 1.5E-21
Max Primal infeas	8602	Max Dual infeas	9618 4.8E-25

# Design of computer experiments

Selden Crary, indie-physicist, 2015

$n = 11$  points  $(x_i, y_i)$  on  $[-1, 1]$  square (one twin-point)



[d,n,p,theta1,theta2]=[2,11,2,0.128,0.069]

# Design of computer experiments

Selden Crary, indie-physicist, 2015

IMSPE-optimal designs (integrated mean-squared prediction error)

$$\min 1 - \text{trace}(L^{-1}R)$$

$L$  and  $R$ : symmetric matrices of order  $n + 1$   
with  $L$  increasingly ill-conditioned if points approach each other

2D, Gaussian covariance parameters  $\sigma, \theta_1, \theta_2$

$$L = \begin{bmatrix} 0 & \mathbf{1}^T \\ \mathbf{1} & V \end{bmatrix}, \quad R \propto \int_{-1}^1 \int_{-1}^1 \begin{bmatrix} 1 \\ v \end{bmatrix} \begin{bmatrix} 1 & v^T \end{bmatrix} dx dy$$

$$V_{ij} = \sigma^2 e^{-\theta_1(x_i-x_j)^2 - \theta_2(y_i-y_j)^2}, \quad v_i \text{ functions of } \exp(\cdot) \text{ and } \text{erf}(\cdot)$$

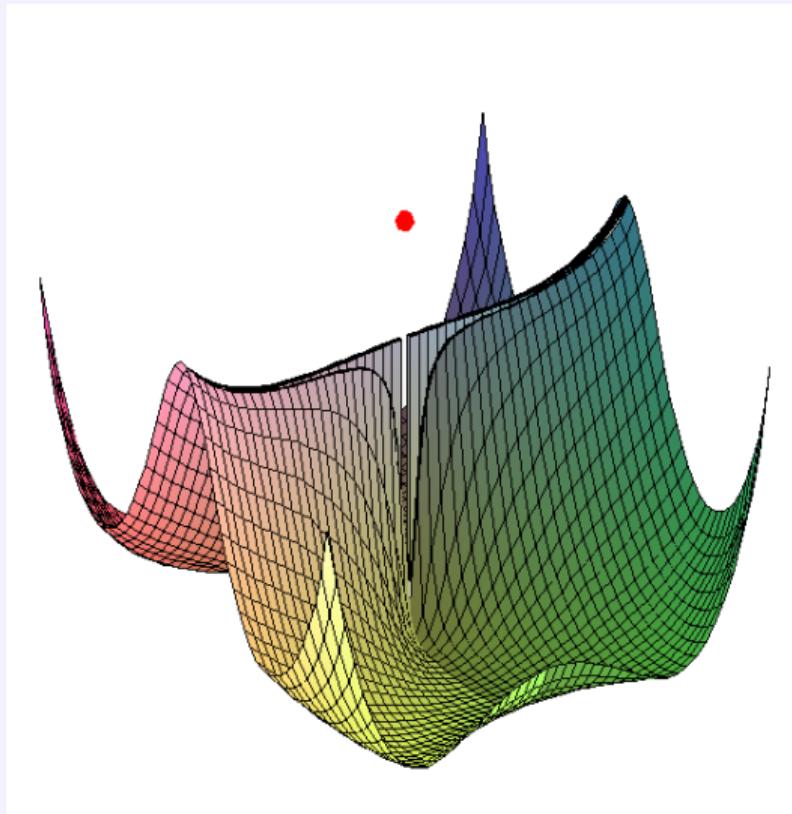
# Pagoda plot

Selden Crary, 2015

$C^\infty$  a.e.

"Post", not pole

Need multistarts



With Maple, Selden has found twin-points, triple-points, ... and a new class of rational functions (the Nu class)

Smooth sailing through the black-hole/white-hole event horizon

No string theory

No complex numbers in quantum mechanics

...

# IMSPE, 2D, $n = 11$ , $\theta = 0.128$ , $\theta_2 = 0.069$

Selden Crary

Quad MINOS      unconstrained optimization  $\in \mathbb{R}^{22}$  without gradients      6 secs

Itn	ph	pp	rg	step	objective	nobj	nsb	cond(H)
1	4	0	3.9E-05	1.0E+03	2.47305090E-05	57	22	4.5E+01
50	4	1	6.4E-07	6.2E+00	6.01181966E-06	1384	22	2.1E+04
100	3	1	-7.6E-08	1.1E+00	5.65611811E-06	2726	22	1.4E+05
150	4	1	8.5E-07	6.0E+00	5.11053080E-06	4102	22	8.2E+03
200	4	1	2.6E-08	1.1E-01	5.02762155E-06	5464	22	1.0E+07
239	4	1	1.1E-07	1.5E-06	5.02762154E-06	7478	22	1.0E+10
alfmax = 3.1E+04    pnorm = 1.5E-04    gnorm = 1.1E-07    g'p = -2.6E-15    numf = 15								

Search exit 7 -- too many functions.

EXIT -- optimal solution found

No. of iterations	239	Objective value	5.0276215358E-06
No. of calls to funobj	7538	Calls with mode=2 (f, known g)	244
Calls for forward differencing	4466	Calls for central differencing	1716
Max Primal infeas	0 0.0E+00	Max Dual infeas	2 1.1E-07 (usually 1.0E-15)

## IMSPE question

$$\min 1 - \text{trace}(L^{-1}R)$$

- Related to GEV problem  $Rv = \lambda Lv$ :  $\text{trace}(L^{-1}R) = \sum \lambda_i$
- $L, R$  real  $\Rightarrow$  trace is real
- $L, R$  symmetric but indefinite
- QZ algorithm ignores symmetry
- QZ avoids ill-conditioned  $L^{-1}$
- Will QZ compute real  $\lambda_i$ ?

# Conclusions

## Conclusions

Just as double-precision floating-point hardware revolutionized scientific computing in the 1960s, the advent of quad-precision data types (even in software) brings us to a new era of greatly improved reliability in optimization solvers.

- Exact simplex with rational arithmetic (e.g. Qsopt\_ex) can be warm-started, but is still too expensive on large problems.
- Iterative refinement of  $Bp = a$ ,  $B^T y = c$  is a sparing use of Quad, but doesn't help  $B = LU$  (with basis repair).  
Quad everywhere is the humane approach!
- Same difficulty with SoPlex80bit + refinement with rational arithmetic.  
Quad SoPlex is in the making!

## 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.
- Ding Ma and Michael Saunders (2015). *Solving multiscale linear programs using the simplex method in quadruple precision*, Proceedings of NAO-III, Muscat, Oman, Jan 2014, Springer.
- Ambros M. Gleixner (2015). *Exact and Fast Algorithms for Mixed-Integer Nonlinear Programming*, PhD thesis, ZIB, Technical University of Berlin.
- Selden Crary and Jan Stormann (2016). *Four-point, 2D, free-ranging, IMSPE-optimal, twin-point designs*, arxiv.org/abs/1510.01685.

## Special thanks

- George Dantzig, born 101+ years ago (8 Nov 1914)
- William Kahan (Berkeley), IEEE standard (including Quad), Boulder.pdf (2011)
- GCC, gfortran (GNU)
- Ronan Fleming, Ines Thiele (Luxembourg)
- Bernhard Palsson, Josh Lerman, Teddy O'Brien, Laurence Yang (UCSD)
- Philip Gill, Elizabeth Wong (UCSD)
- Ed Klotz (IBM CPLEX), Yuekai Sun, Jon Dattorro (Stanford), Selden Crary (Palo Alto)
- Dominique Orban, Annick Sartenaer

# FAQ

- 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? Yes for LPs
- How about AMPL? No, but should be feasible
- Is there a quadSNOPT? Yes, in f90 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 wish, but Kahan is pessimistic