4 Medical Akzo Nobel problem

4.1 General information

The problem consists of 2 partial differential equations. Semi-discretization of this system yields a stiff ODE. The parallel-IVP-algorithm group of CWI contributed this problem to the test set in collaboration with R. van der Hout from Akzo Nobel Central Research.

The software part of the problem is in the file medakzo.f available at [MM08].

4.2 Mathematical description of the problem

The problem is of the form

$$\frac{\mathrm{d}y}{\mathrm{d}t} = f(t,y), \quad y(0) = g, \tag{II.4.1}$$

with

$$y \in \mathbb{R}^{2N}, \quad 0 \le t \le 20.$$

Here, the integer N is a user-supplied parameter. The function f is given by

$$\begin{aligned} f_{2j-1} &= \alpha_j \frac{y_{2j+1} - y_{2j-3}}{2\Delta\zeta} + \beta_j \frac{y_{2j-3} - 2y_{2j-1} + y_{2j+1}}{(\Delta\zeta)^2} - k\, y_{2j-1} y_{2j}, \\ f_{2j} &= -k\, y_{2j} y_{2j-1}, \end{aligned}$$

where

$$\begin{aligned} \alpha_j &= \frac{2(j\Delta\zeta - 1)^3}{c^2}, \\ \beta_j &= \frac{(j\Delta\zeta - 1)^4}{c^2}. \end{aligned}$$

Here, j ranges from 1 to N, $\Delta\zeta = \frac{1}{N}$, $y_{-1}(t) = \phi(t)$, $y_{2N+1} = y_{2N-1}$ and $g \in \mathbb{R}^{2N}$ is given by

$$g = (0, v_0, 0, v_0, \ldots, 0, v_0)^{\mathrm{T}}.$$

The function ϕ is given by

$$\phi(t) = \begin{cases} 2 & \text{for} \quad t \in (0,5], \\ 0 & \text{for} \quad t \in (5,20]. \end{cases}$$

which means that f undergoes a discontinuity in time at $t = 5$. Suitable values for the parameters k, v_0 and c are 100, 1 and 4, respectively.

4.3 Origin of the problem

The Akzo Nobel research laboratories formulated this problem in their study of the penetration of radio-labeled antibodies into a tissue that has been infected by a tumor [Hou94]. This study was carried out for diagnostic as well as therapeutic purposes.

Let us consider a reaction diffusion system in one spatial dimension:

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} - kuv, \tag{II.4.2}$$

$$\frac{\partial v}{\partial t} = -kuv, \tag{II.4.3}$$

which originates from the chemical reaction

$$A + B \xrightarrow{k} C.$$

Here A, the radio-labeled antibody, reacts with substrate B, the tissue with the tumor, and k denotes the rate constant. The concentrations of A and B are denoted by u and v, respectively. In the derivation of the equations (II.4.2) and (II.4.3) it was assumed that the reaction is governed by mass action kinetics and in addition that the chemical A is mobile while B is immobile.

Consider a clean semi-infinite slab, in which the substrate B is uniformly distributed. When the slab is exposed at its surface to the chemical A, this chemical starts to penetrate into the slab.

To model this penetration, the equations (II.4.2) and (II.4.3) are considered in the strip

$$S_T = \{(x,t) : 0 < x < \infty,\ 0 < t < T\} \quad \text{for some } T,$$

along with the following initial and boundary conditions:

$$u(x,0) = 0, \quad v(x,0) = v_0 \quad \text{for } x > 0,$$

where v_0 is a constant, and

$$u(0,t) = \phi(t) \quad \text{for } 0 < t < T.$$

In order to solve the problem numerically, we transform the variable x in such a way that the semi-infinite slab is transformed into a finite one. A suitable transformation is provided by the following special family of Möbius transformations:

$$\zeta = \frac{x}{x+c}, \quad \text{with } c > 0.$$

Each transformation in this class transforms S_T into the slab:

$$\{(\zeta,t) : 0 < \zeta < 1,\ 0 < t < T\}.$$

In terms of ζ the problem now reads:

$$\frac{\partial u}{\partial t} = \frac{(\zeta-1)^4}{c^2}\frac{\partial^2 u}{\partial \zeta^2} + \frac{2(\zeta-1)^3}{c^2}\frac{\partial u}{\partial \zeta} - kuv, \tag{II.4.4}$$

$$\frac{\partial v}{\partial t} = -kuv, \tag{II.4.5}$$

with initial conditions

$$u(\zeta,0) = 0, \quad v(\zeta,0) = v_0 \quad \text{for } \zeta > 0, \tag{II.4.6}$$

and boundary conditions

$$u(0,t) = \phi(t), \quad \frac{\partial u}{\partial \zeta}(1,t) = 0 \quad \text{for } 0 < t < T. \tag{II.4.7}$$

The last boundary condition is derived from $\frac{\partial u}{\partial x}(\infty,t) = 0$.

The system consisting of (II.4.4), (II.4.5), (II.4.6) and (II.4.7) will be written as a system of ordinary differential equations by using the method of lines, i.e. by discretizing the spatial derivatives. We use the uniform grid $\{\zeta_j\}_{j=1,\ldots,N}$ defined by:

$$\zeta_j = j \cdot \Delta\zeta, \quad j = 1,\ldots,N, \quad \Delta\zeta = \frac{1}{N}.$$

Let u_j and v_j denote the approximations of $u(\zeta_j, t)$ and $v(\zeta_j, t)$, respectively. Obviously, u_j and v_j are functions of t. In terms of the function u_j, our choices for the discretization of the spatial first and second order derivatives read

$$\frac{\partial u_j}{\partial \zeta} = \frac{u_{j+1} - u_{j-1}}{2\Delta\zeta} \quad \text{and} \quad \frac{\partial^2 u_j}{\partial \zeta^2} = \frac{u_{j-1} - 2u_j + u_{j+1}}{(\Delta\zeta)^2},$$

respectively, where $j = 1, \ldots, N$. Suitable values for u_0 and u_{N+1} are obtained from the boundary conditions. They are given by $u_0 = \phi(t)$ and $u_{N+1} = u_N$.

Defining $y(t)$ by $y = (u_1, v_1, u_2, v_2, \ldots, u_N, v_N)^{\mathrm{T}}$, and choosing $T = 20$, this semi-discretized problem is precisely the ODE (II.4.1).

To give an idea of the solution to the PDE (II.4.4)–(II.4.7), Figure II.4.1 plots u and v as function of x and t. We nicely see that injection of chemical A (locally) destroys B.

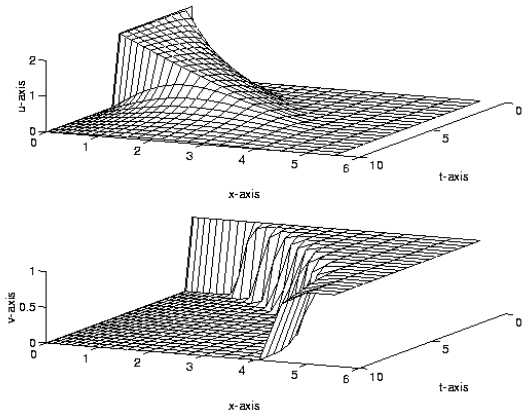

FIGURE II.4.1: *u and v as function of time and space.*

4.4 Numerical solution of the problem

The numerical experiments were done for the case $N = 200$. In Table II.4.1 we give the value of some components of the reference solution at the end of the integration interval. These components correspond to the values of u and v in $x = 1$, 2.4, 4.0 and 6.0. For the complete reference solution we refer to the Fortran subroutine `solut`. Figure II.4.2 plots the behavior of the solution components y_i for $i \in \{79, 80, 133, 134, 171, 172, 199, 200\}$, which correspond to approximations of the PDE solutions u and v on the grid lines $x = 1$, 2, 3 and 4. Table II.4.2 and Figures II.4.3–II.4.6 show the run

TABLE II.4.1: *Reference solution at the end of the integration interval.*

y_{79}	$0.2339942217046434 \cdot 10^{-3}$	y_{199}	$0.11737412926802 \cdot 10^{-3}$
y_{80}	$-0.1127916494884468 \cdot 10^{-141}$	y_{200}	$0.61908071460151 \cdot 10^{-5}$
y_{149}	$0.3595616017506735 \cdot 10^{-3}$	y_{239}	$0.68600948191191 \cdot 10^{-11}$
y_{150}	$0.1649638439865233 \cdot 10^{-86}$	y_{240}	0.99999973258552

TABLE II.4.2: *Run characteristics.*

solver	rtol	atol	h0	mescd	scd	steps	accept	#f	#Jac	#LU	CPU
BIMD	10^{-4}	10^{-4}	10^{-9}	4.94	4.92	110	110	1565	90	110	0.1932
	10^{-7}	10^{-7}	10^{-12}	8.19	8.13	125	125	3496	115	125	0.4451
DDASSL	10^{-4}	10^{-4}		3.41	3.35	381	373	550	46		0.1200
	10^{-7}	10^{-7}		5.69	5.69	1378	1369	1700	62		0.3972
GAMD	10^{-4}	10^{-4}	10^{-9}	5.03	5.01	66	66	2116	66	66	0.2235
	10^{-7}	10^{-7}	10^{-12}	7.79	7.78	104	104	4760	104	104	0.5290
MEBDFI	10^{-4}	10^{-4}	10^{-9}	3.95	3.94	375	361	1238	70	70	0.2235
	10^{-7}	10^{-7}	10^{-12}	7.44	7.43	826	803	2749	104	104	0.5046
PSIDE-1	10^{-4}	10^{-4}		5.16	5.00	118	83	1263	34	456	0.1776
	10^{-7}	10^{-7}		7.18	7.12	159	145	2838	109	624	0.3445
RADAU	10^{-4}	10^{-4}	10^{-9}	3.87	3.82	93	93	747	60	93	0.0859
	10^{-7}	10^{-7}	10^{-12}	6.93	6.92	100	100	1807	58	100	0.1972
VODE	10^{-4}	10^{-4}		2.84	2.84	364	359	506	10	62	0.0625
	10^{-7}	10^{-7}		5.62	5.61	1036	1023	1217	19	101	0.1571

characteristics, and the work-precision diagrams, respectively. The reference solution was computed on the Cray C90, using PSIDE with Cray double precision and atol = rtol = 10^{-10}. For the work-precision diagrams, we used: rtol = $10^{-(4+m/8)}$, $m = 0, 1, \ldots, 40$; atol = rtol; h0 = $10^{-5} \cdot$ rtol for BIMD, GAMD, MEBDFDAE, MEBDFI, RADAU and RADAU5. Since some solution components are zero, all scd values presented here denote absolute precision.

References

[Hou94] R. van der Hout, 1994. Private communication.

[MM08] F. Mazzia and C. Magherini. *Test Set for Initial Value Problem Solvers, release 2.4.* Department of Mathematics, University of Bari and INdAM, Research Unit of Bari, February 2008. Available at http://www.dm.uniba.it/~testset.

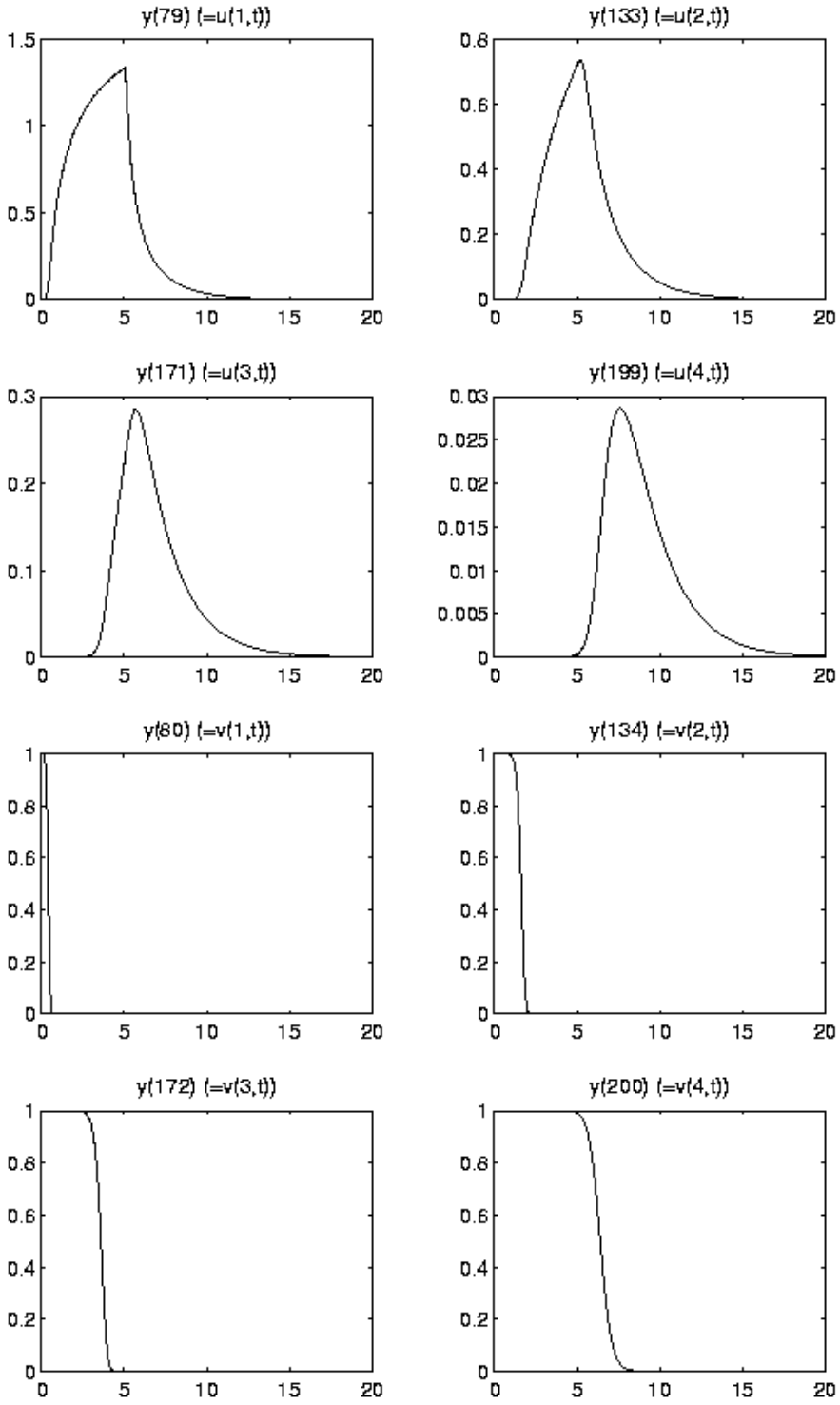

FIGURE II.4.2: *Behavior of some solution components over the integration interval.*

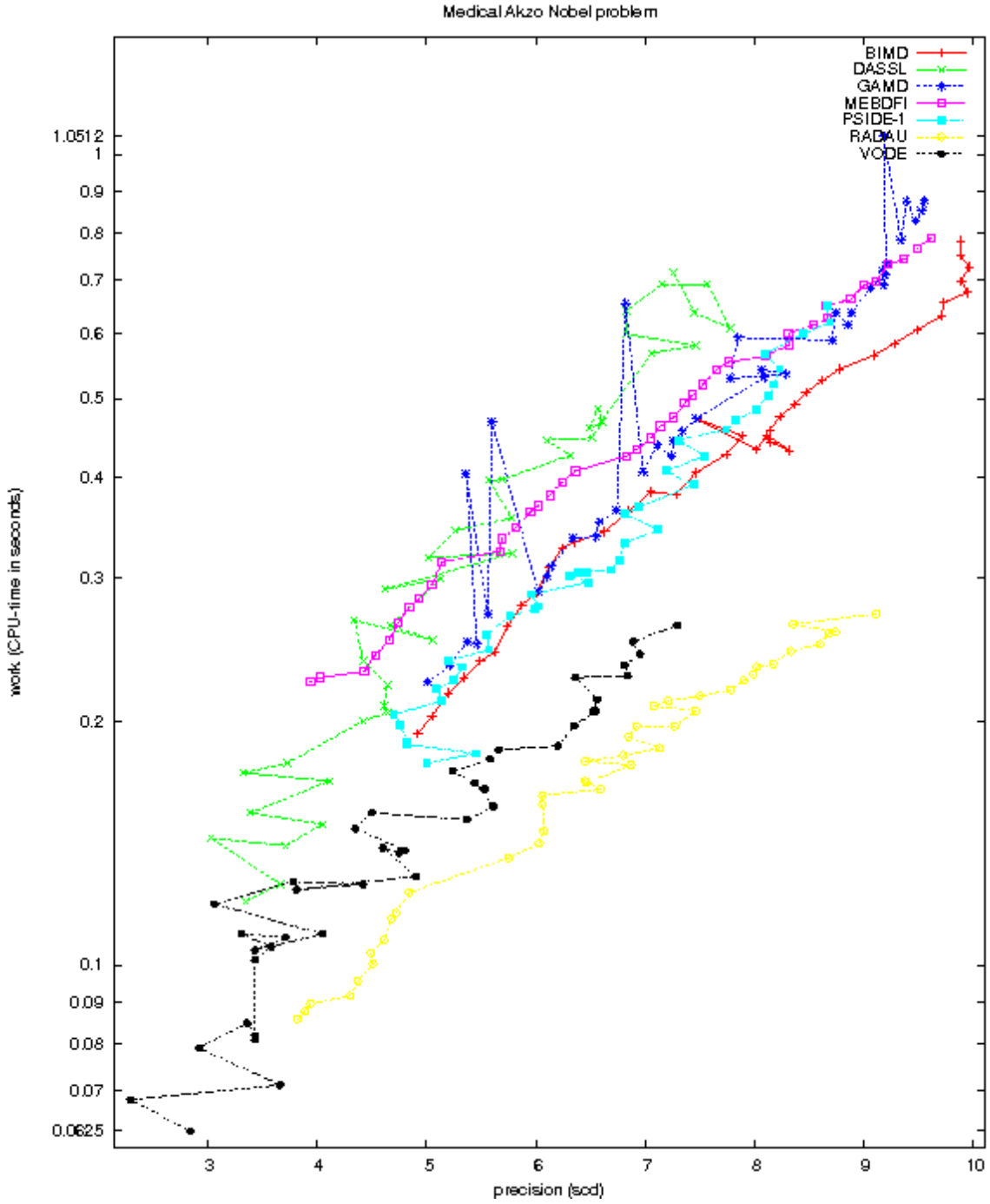

FIGURE II.4.3: *Work-precision diagram (scd versus CPU-time).*

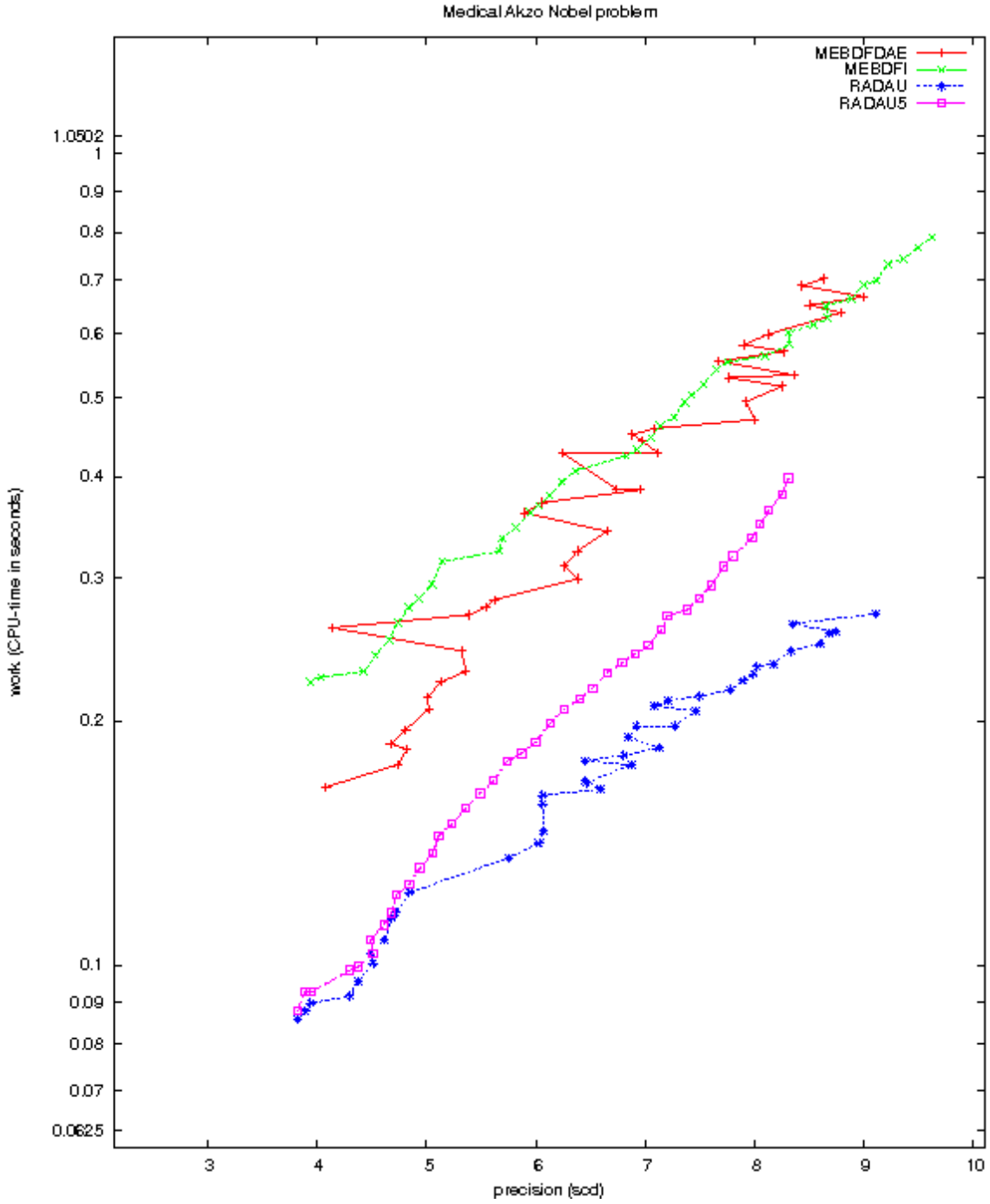

FIGURE II.4.4: *Work-precision diagram (scd versus CPU-time).*

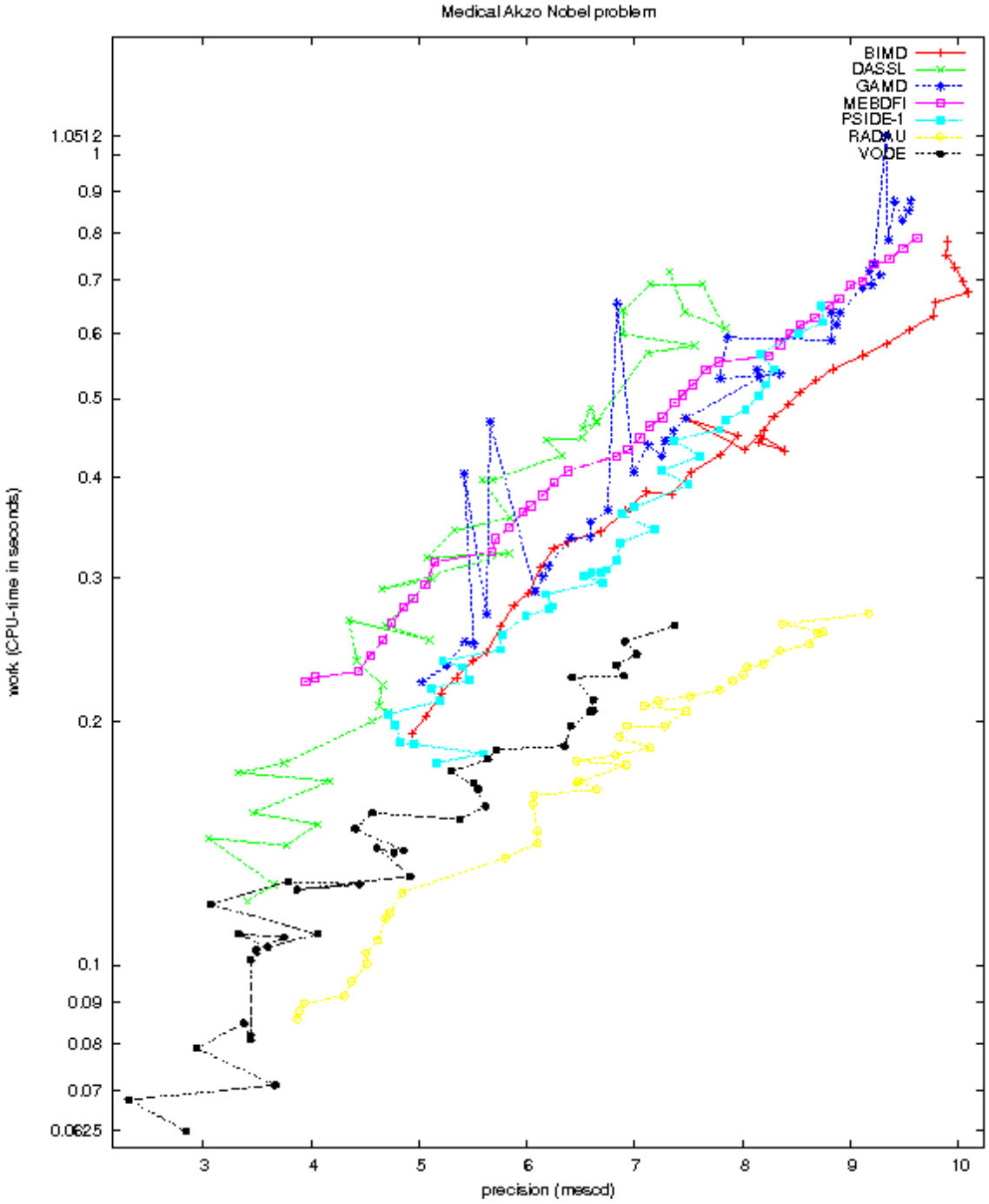

FIGURE II.4.5: *Work-precision diagram (mescd versus CPU-time).*

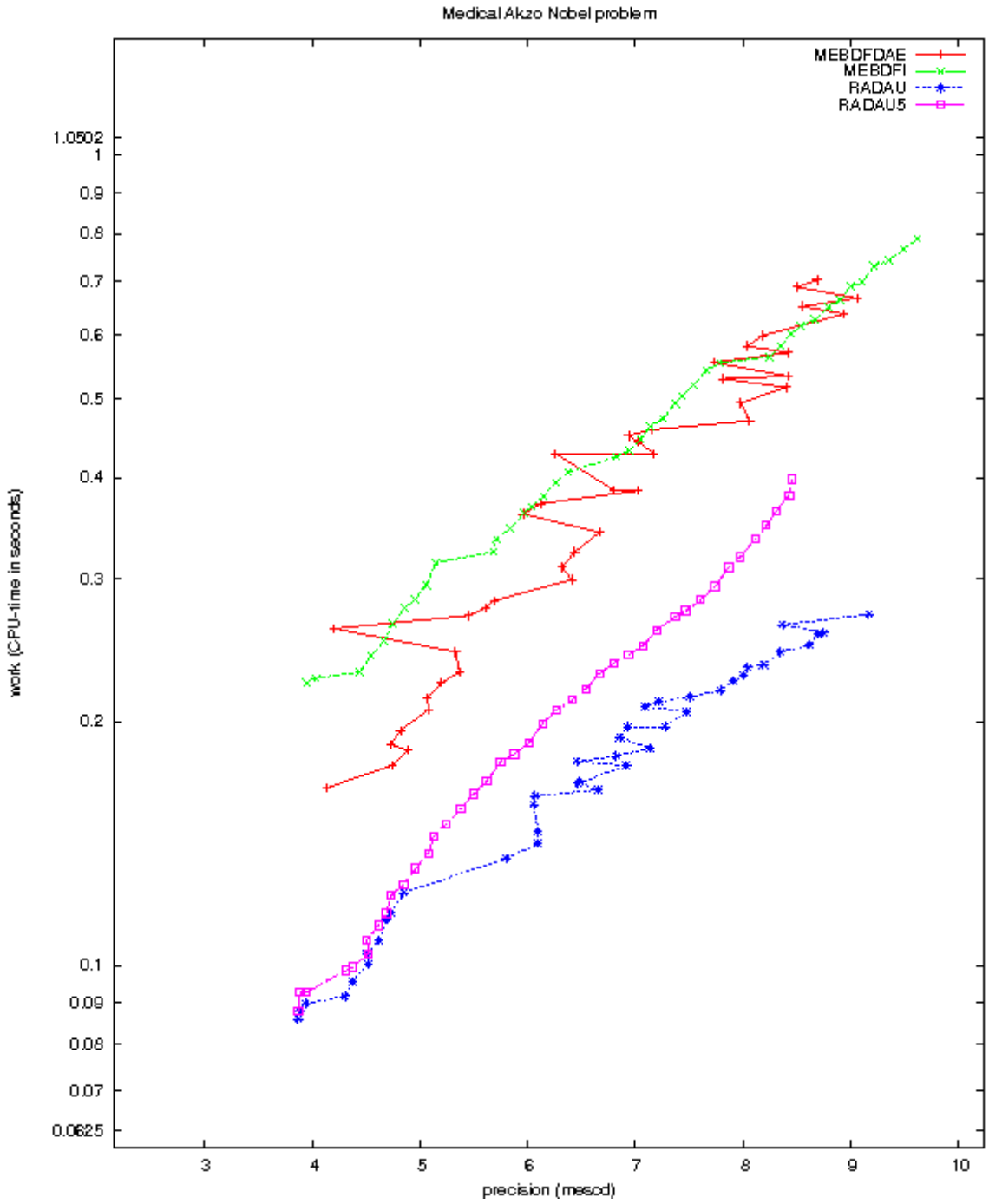

FIGURE II.4.6: *Work-precision diagram (mescd versus CPU-time).*