HelmholtzZentrum münchen
German Research Center for Environmental Health

Assessment and prediction of ODE solver performance for biological processes

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HELMHOLTZ RESEARCH FOR GRAND CHALLENGES

Topics

- Theory:
  - Need for efficient ODE solver performance?
  - Mathematical approach
  - Bibliography

- Study:
  - Collection of ODE models
  - ODE settings

- Predictor model for solver performance

Theory

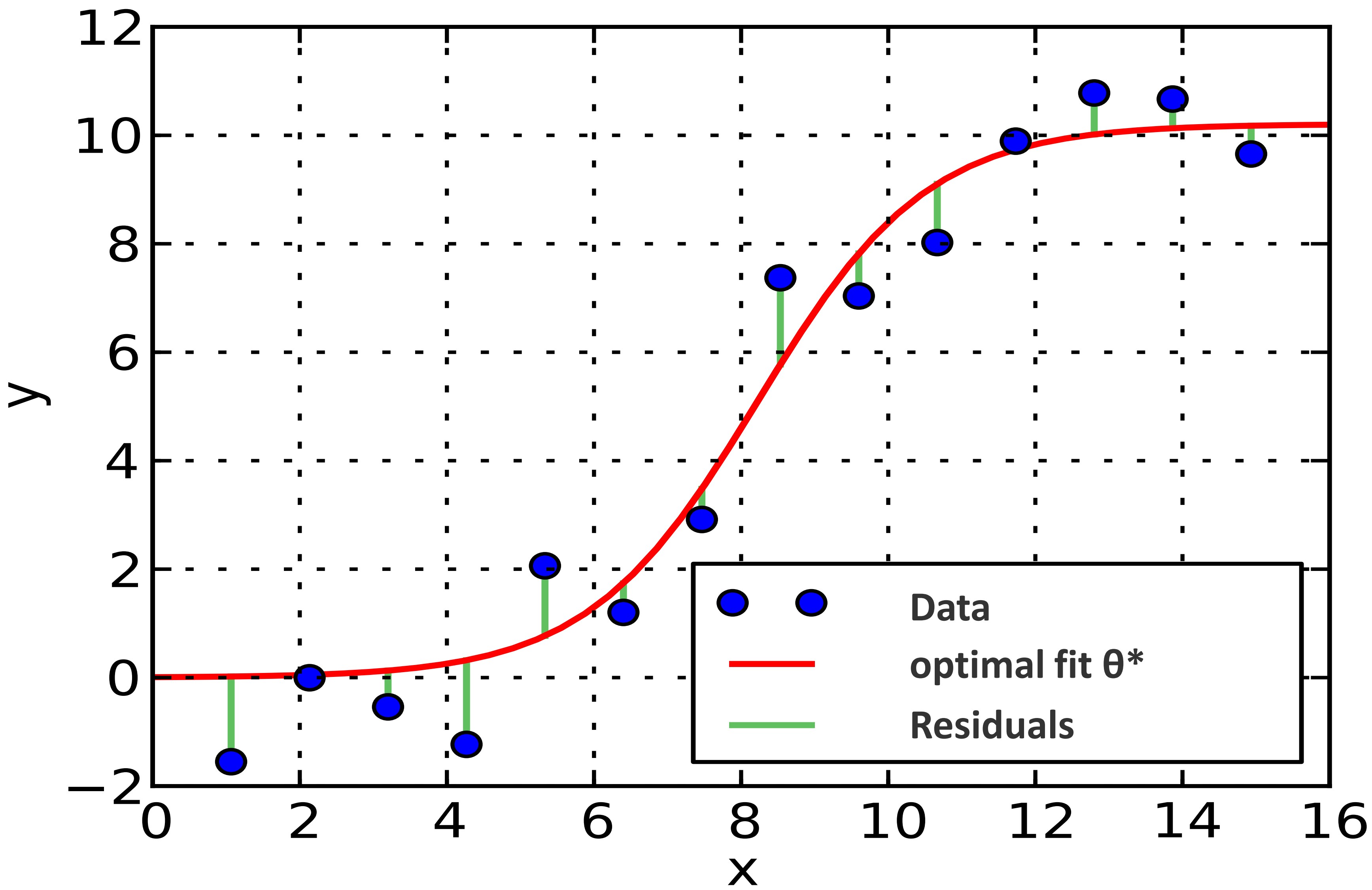
Why do we need efficient ODE solver performance?

- Simulate ODE lots of times

- Have: $\dot{x} = f(x, \theta)$, f is known, θ unknown
- Have: experimental data

=> Want: θ* (specific θ, where the **solution** of the equation fits data the best)

=> Use: optimisation method
e.g.: “Least squares“



12
10
8
6
4
2
0
−2
y
0
2
4
6
8
10
12
14
16
x
Data
optimal fit θ*
Residuals

Why do we need efficient ODE solver performance?

- Simulate ODE / system of ODEs lots of times

- Have: $\dot{x} = f(x, \theta)$, f is known, θ unknown
- Have: experimental data D

=> Want: θ* (specific θ, where the **solution** the equation fits data the best)

=> Method: Least squares

- Get: θ*(D) is optimal solution

Mathematical Approach

- Goal: Prediction of numerical behaviour
- Example: Adams(-Moulton) vs. BDF
- Application: **stiff** differential equations

Stiff Differential Equation

- Definition(1):

  The ODE is stiff, if **explicit** single step methods are **inefficient** in solving the ODE compared to **implicit** single step methods

- Definition(2):

  Let $y'(t) = A*y(t)$, A matrix

  let λ_j be the eigenvalues of A, let $\sigma \leq Re(\lambda_j) \leq \tau$

  Define the **stiffness-quotient:** $r_s = \sigma / \tau$

  Then the ODE is stiff, if: $\mathbf{Re(\lambda_j) < 0 \ \forall j}$ and $\mathbf{r_s \gg 1}$

Mathematical Approach

- Goal: Prediction of numerical behaviour
- Example: Adams(-Moulton) vs. BDF
- Application: **stiff** differential equations

- Used for: solving ODE by numerical integration
- Type: implicit
- Method: linear multistep
- IVP: $$\begin{cases} y'(t) = f(t, y(t)) \\ y(t_0) = y_0 \end{cases}$$

Adams - Moulton

- Approach: approximate $f(t_{n+1}, y_{n+1})$ by $q_{n,1}(t_{n+1})$
- General Formula for s steps:

$$y_{n+1} = y_n + h \sum_{k=0}^{s} b_k\, f(t_{n+1-k}, y_{n+1-k})$$

- Properties: - zero-stable for all s
  - **A-stable** until **s < 2**
  - not A(α)-stable
  - order of consistency: s + 1

=> Application: **non-stiff** differential equations

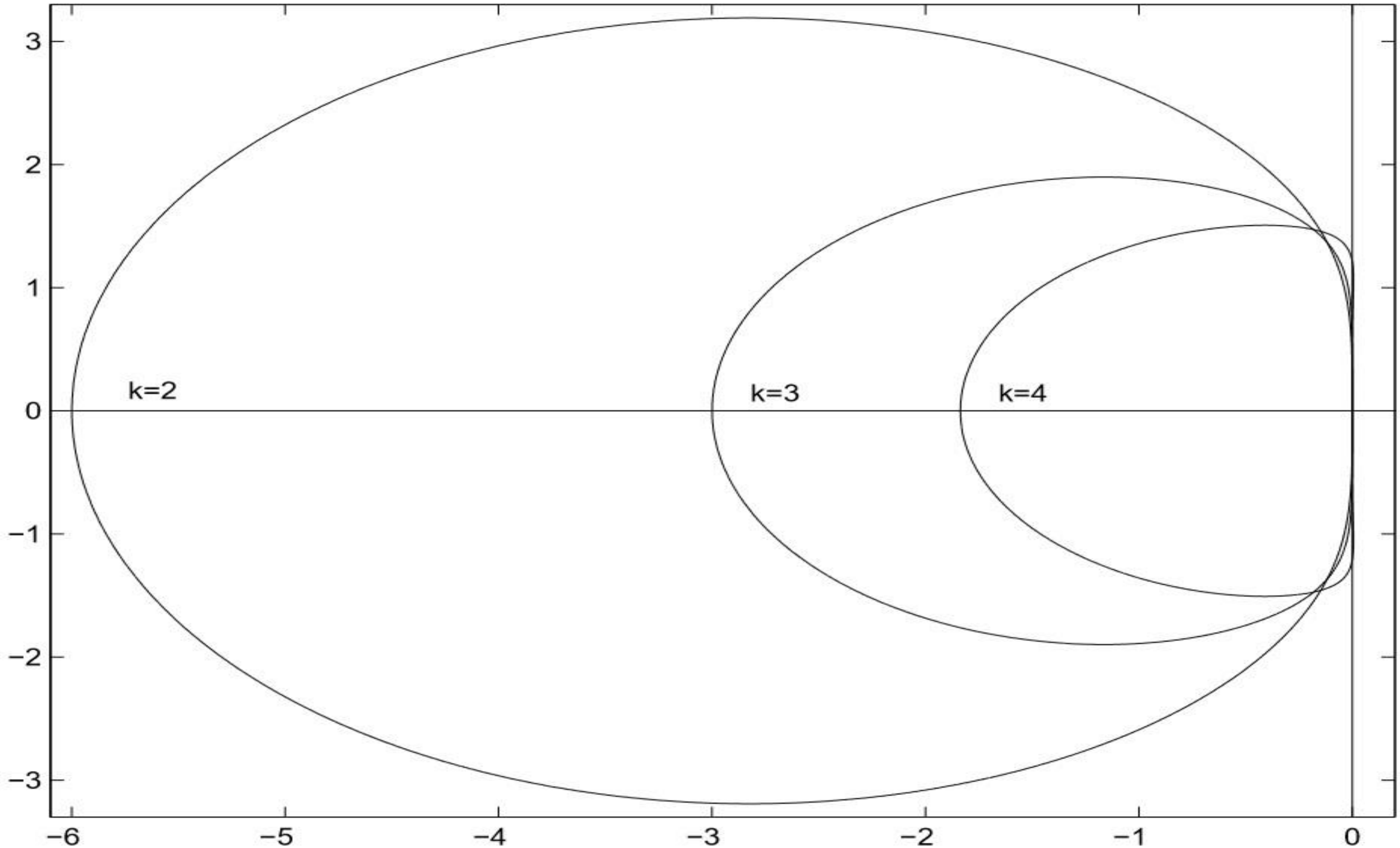
BDF

- Approach: approximate $f(t_{n+1} y_{n+1})$ by $p'_{n,1}(t_{n+1})$
- General Formula for s steps:

$$y_{n+1} = \sum_{k=0}^{s} a_k y_{n-k} + h\beta_{-1} f(t_{n+1}, y_{n+1})$$

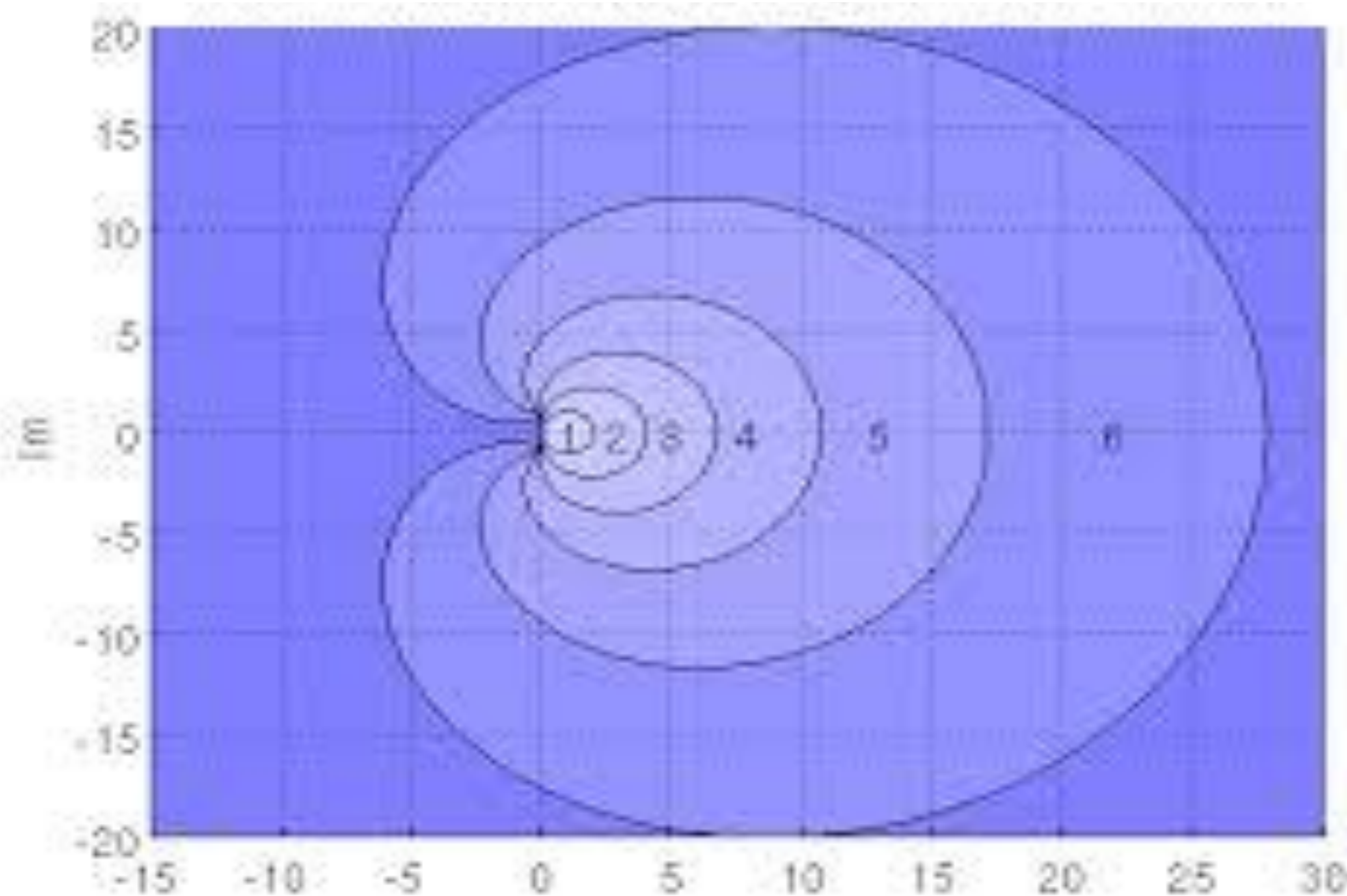
- Properties: - zero-stable until $s < 7$
  - **A-stable** until **s < 3**
  - A(α)-stable until $s < 7$
  - order of consistency: s

=> Application: **stiff** differential equations



Stabiliy region of the Adams-Moulton Method

Stabiliy region of the BDF Method



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Bibliography

- Quarteroni, Alfio et. al.: Numerische Mathematik 2, Springer, 2002 [1]
- Lambert, J.: Numerical Methods of ordinary differentiable systems, Wiley, 1991 [2]
- Hairer, Ernst, Wanner, Gerhard: Solving Ordinary Differential Equations II, Stiff problems, Springer, 1987 [3]

Study

Collection of ODE models

- JWS (+ Benchmark models + BioModels Database)

- JWS: 293 SEDML models with 710 SBML models

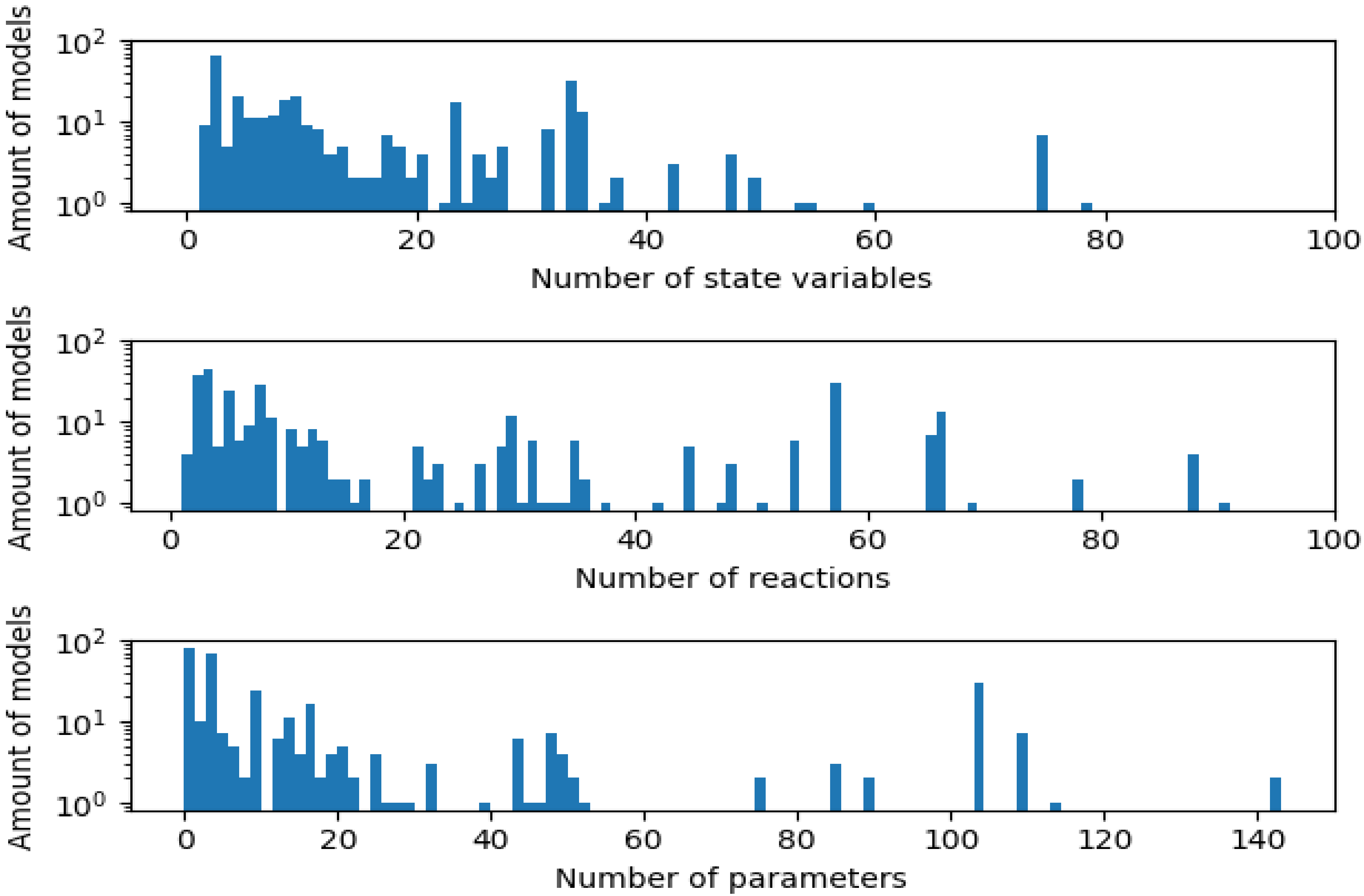
=> SBML to AMICI: 329 SBML models (~ 46%)

Time period / state variables / observables extracted from SEDML

=> Problem: - state variables < 100

- reactions < 100
- parameters < 150

- Benchmark + BioModels Database:
  - Models with high number of state variables
  - E.g.: Smallbone2013
  - State variables ~ 400
  - Parameters ~ 3000

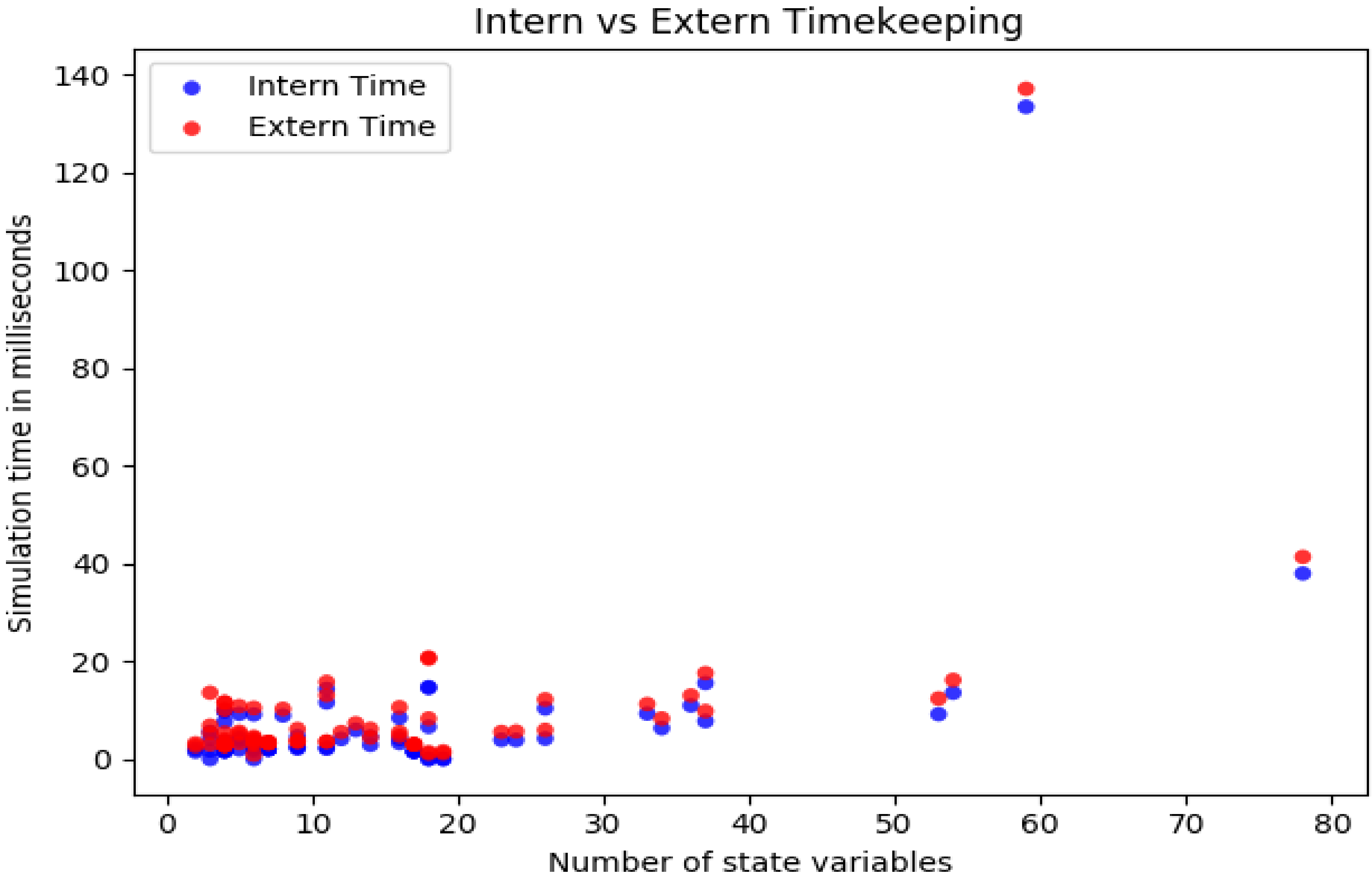


Amount of models
10^2
10^1
10^0
0
20
40
60
80
100
Number of state variables
Amount of models
10^2
10^1
10^0
0
20
40
60
80
100
Number of reactions
Amount of models
10^2
10^1
10^0
0
20
40
60
80
100
120
140
Number of parameters

ODE settings

- absolute / relative tolerances: combinations of 1e-6,… , 1e-16
- linear solver: Dense, KLU, GMRES, BICGSTAB, SPTFQMR
- (non-linear solver): Newton-type, functional
- solver algorithm: Adams-Moulton, **BDF**

- Additional properties:
  - Compare time difference: built-in timing vs external timing
  - Repeat 100 times + take median
    => to omit single "out-of-order" values
  - Type of right-hand-site $f(x, \theta)$: **stiff**, polynomial


Intern vs Extern Timekeeping
Intern Time
Extern Time
Simulation time in milliseconds
0
20
40
60
80
100
120
140
0
10
20
30
40
50
60
70
80
Number of state variables

Predictor model for solver performance

- Goal: predict most promising setting **before** simulation

- Method: - study as original investigation
  - (linear) Regression for key data
  - collect key data of new models
  [stiff, polynomial, state variables, parameters]

- Output: most promising numerical setting
  [atol, rtol, linear solver, solver algorithm]

=> Run simulation and check for correctness

Any Questions?