Time Dilation and Contraction for Programmable Analog Devices with Jaunt

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$$E = 6800 - ES$$

$$S = 4400 - ES$$

$$\partial ES/\partial t = 0.0001 \cdot E \cdot S - 0.01 \cdot ES$$

$$ES(0) = 0$$

Dynamical System

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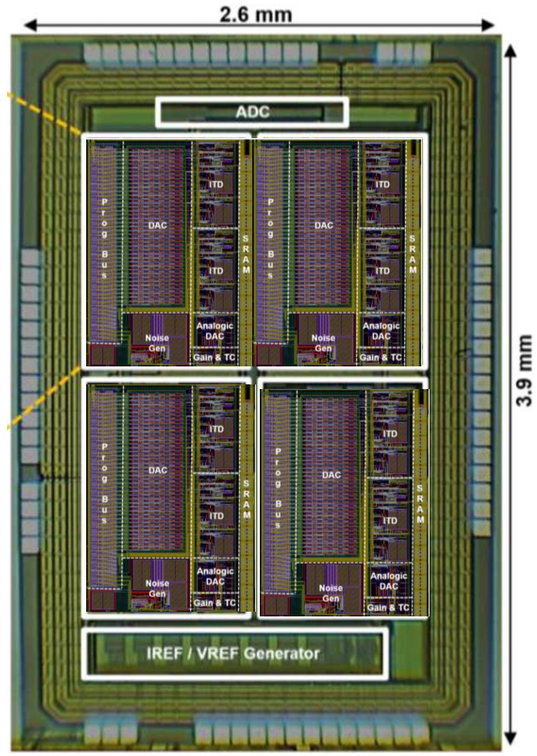
Dynamical System



Programmable Analog Devices

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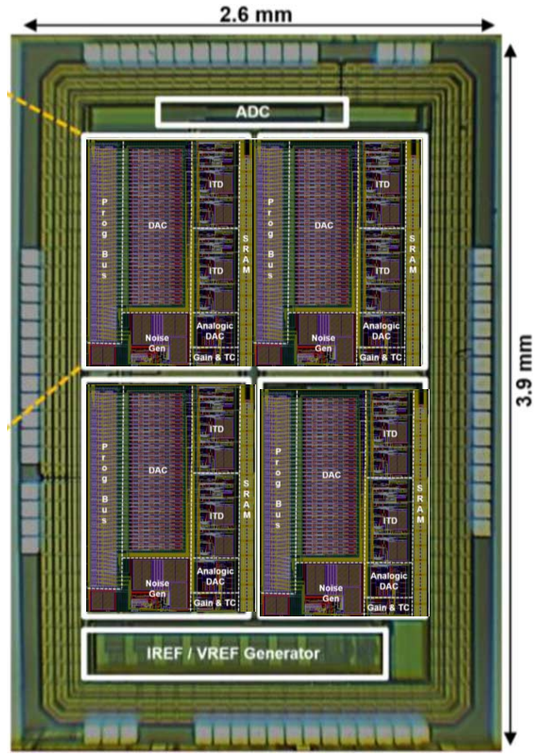


Programmable Analog Devices

With Physical Limitations

Change Dynamic Range of Variables
Change Speed of Simulation

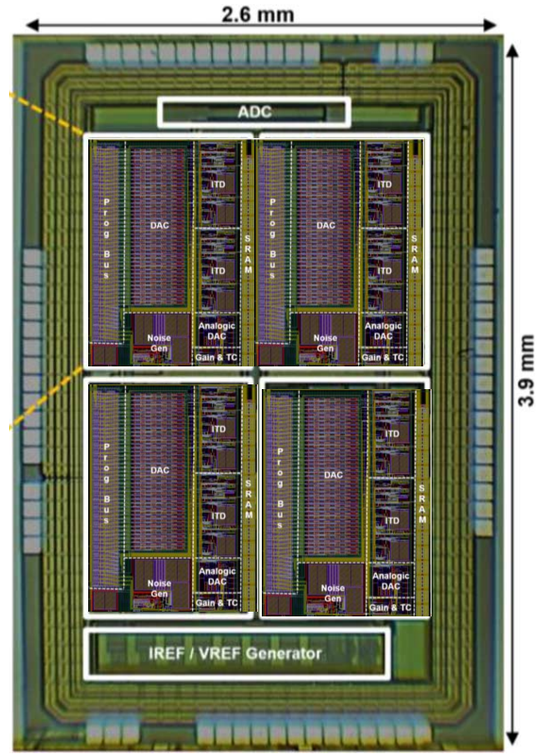
$$E = 6800 - ES$$

$$S = 4400 - ES$$

$$\partial ES/\partial t = 0.0001 \cdot E \cdot S - 0.01 \cdot ES$$

$$ES(0) = 0$$

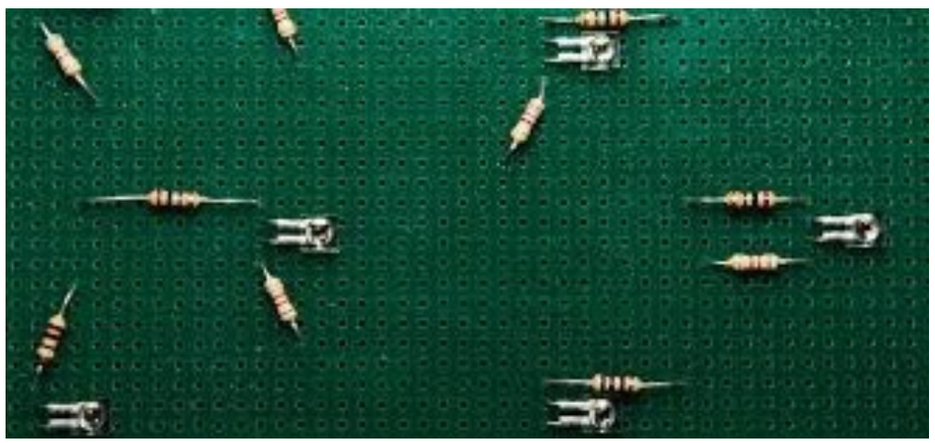
Dynamical System



Programmable Analog Devices

With Physical Limitations

Modeling the Physical World



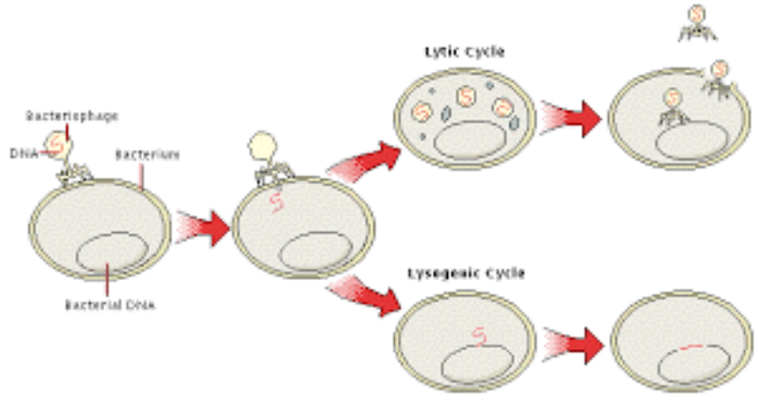
Dynamical Systems Model Biological Processes

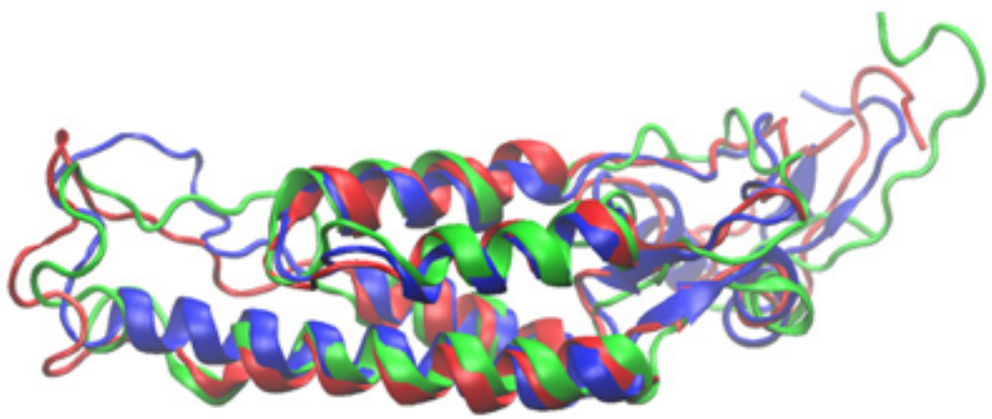
$$E = 6800 - ES$$

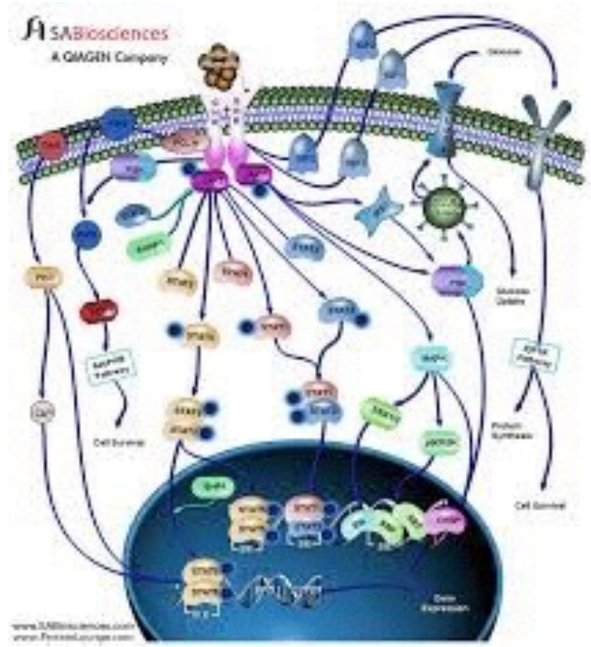
$$S = 4400 - ES$$

$$\partial ES/\partial t = 0.0001 \cdot E \cdot S - 0.01 \cdot ES$$

$$ES(0) = 0$$







Dynamical Systems

$$E = 6800 - ES$$

$$S = 4400 - ES$$

$$\partial ES/\partial t = 0.0001 \cdot E \cdot S - 0.01 \cdot ES$$

$$ES(0) = 0$$

- **state variables** that model physical quantities (E, S, ES)
- **differential equations** that specify continuous dynamics of *state variables* over time

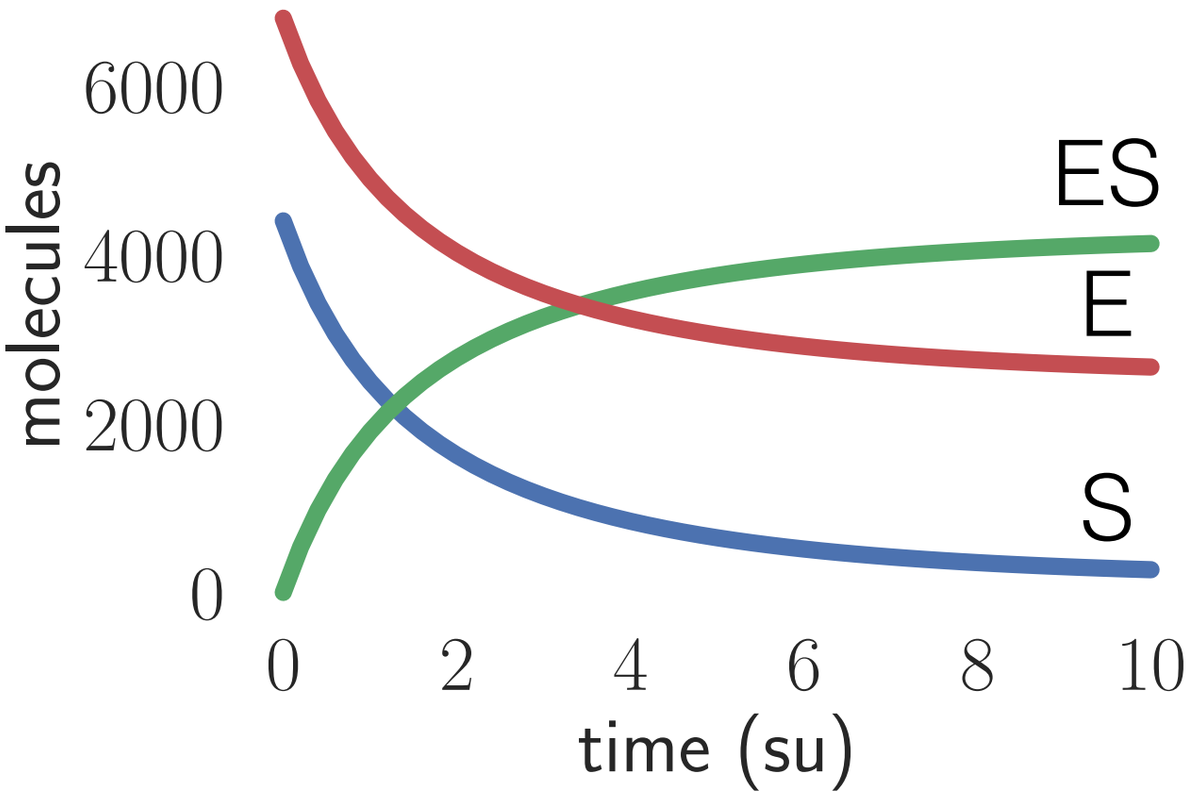
Goal: Simulate Dynamical System

$$E = 6800 - ES$$

$$S = 4400 - ES$$

$$\partial ES/\partial t = 0.0001 \cdot E \cdot S - 0.01 \cdot ES$$

$$ES(0) = 0$$



- Compute dynamics of state variables over time
- Plot concentrations of compounds over time

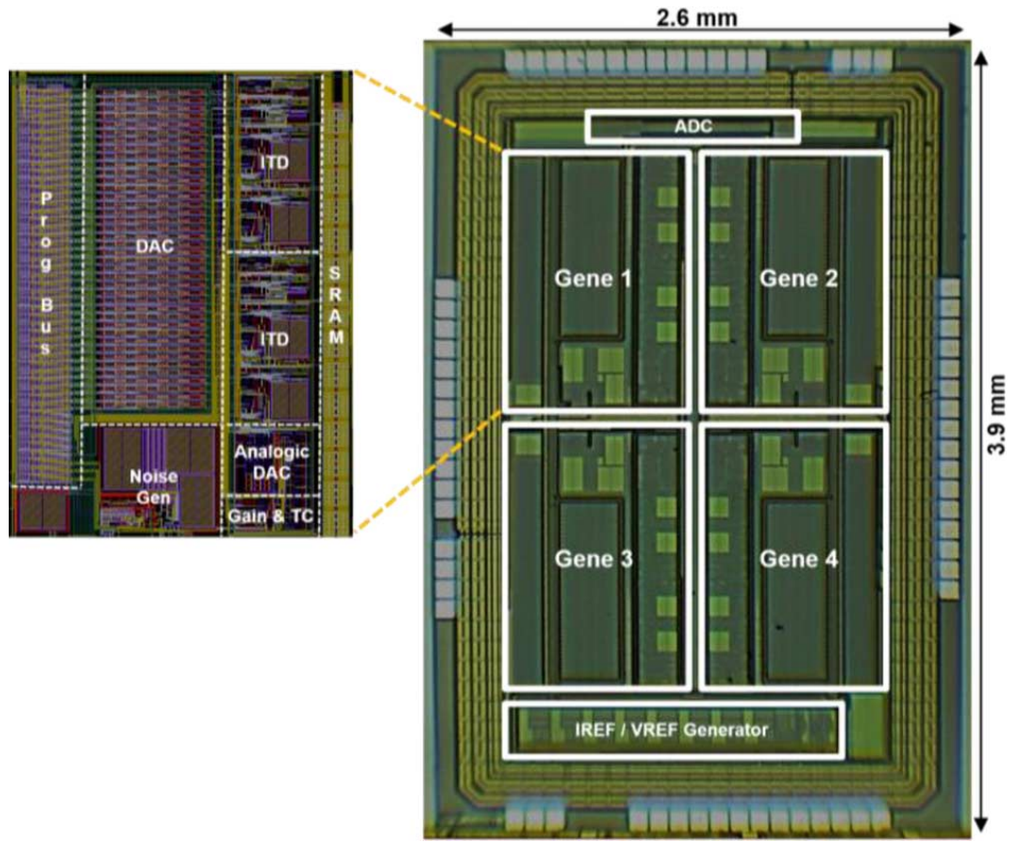
Analog Computing circa 1950

- **direct mapping**
  - variables → properties of wires
  - properties: voltage, current
  - dynamics → circuit dynamics
- **straightforward simulation**:
  - power up circuit
  - measure circuit properties over time
- **1970-2010**: *Age of Digital Computers*
  - Analog computers out of fashion

Telefunken RAT 700

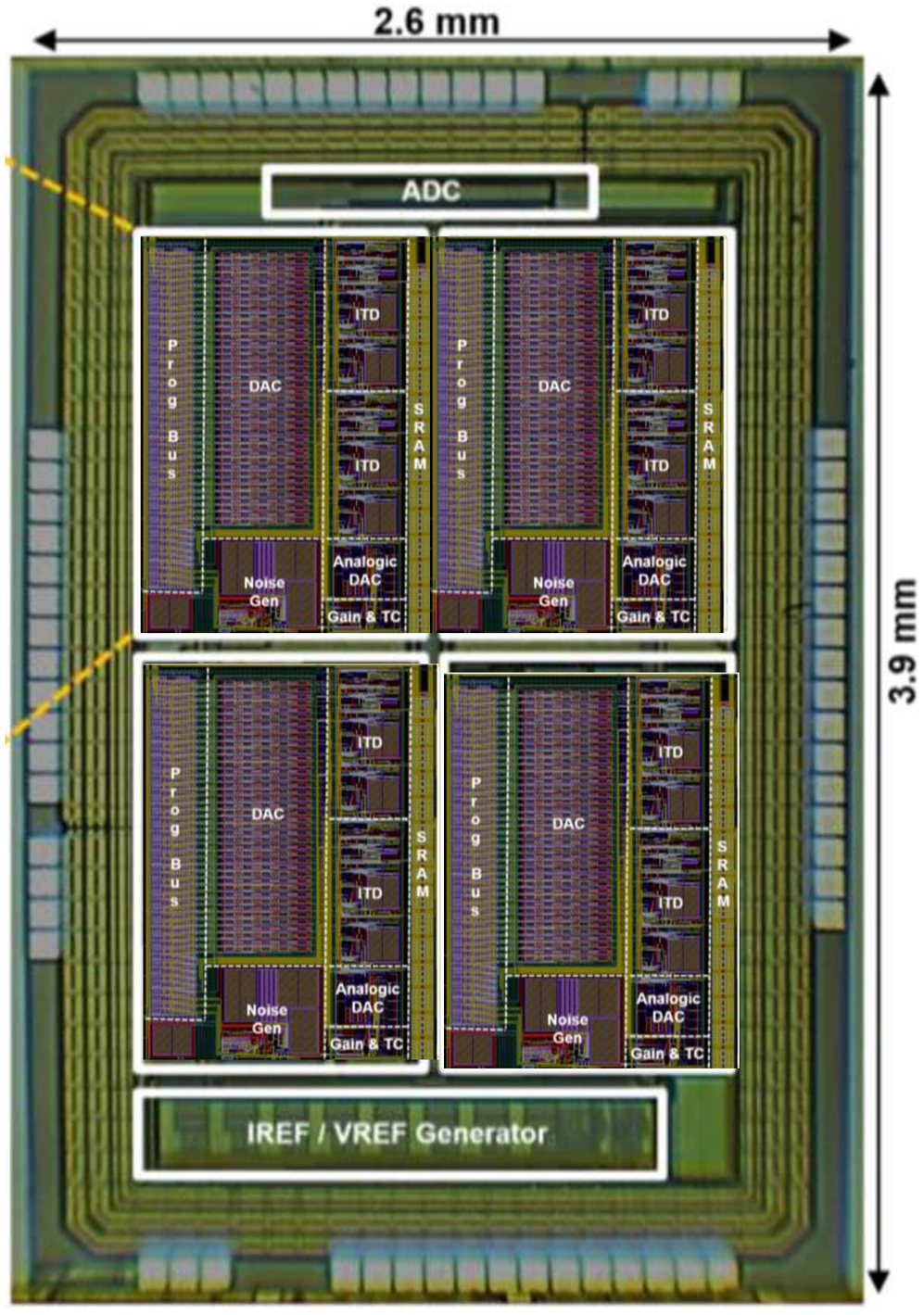
Programmable Analog Devices

- modernized hardware
  - modern semiconductor technology
- new capabilities
  - powerful, heavily optimized analog components
  - digital reprogrammability
  - exploit analog noise

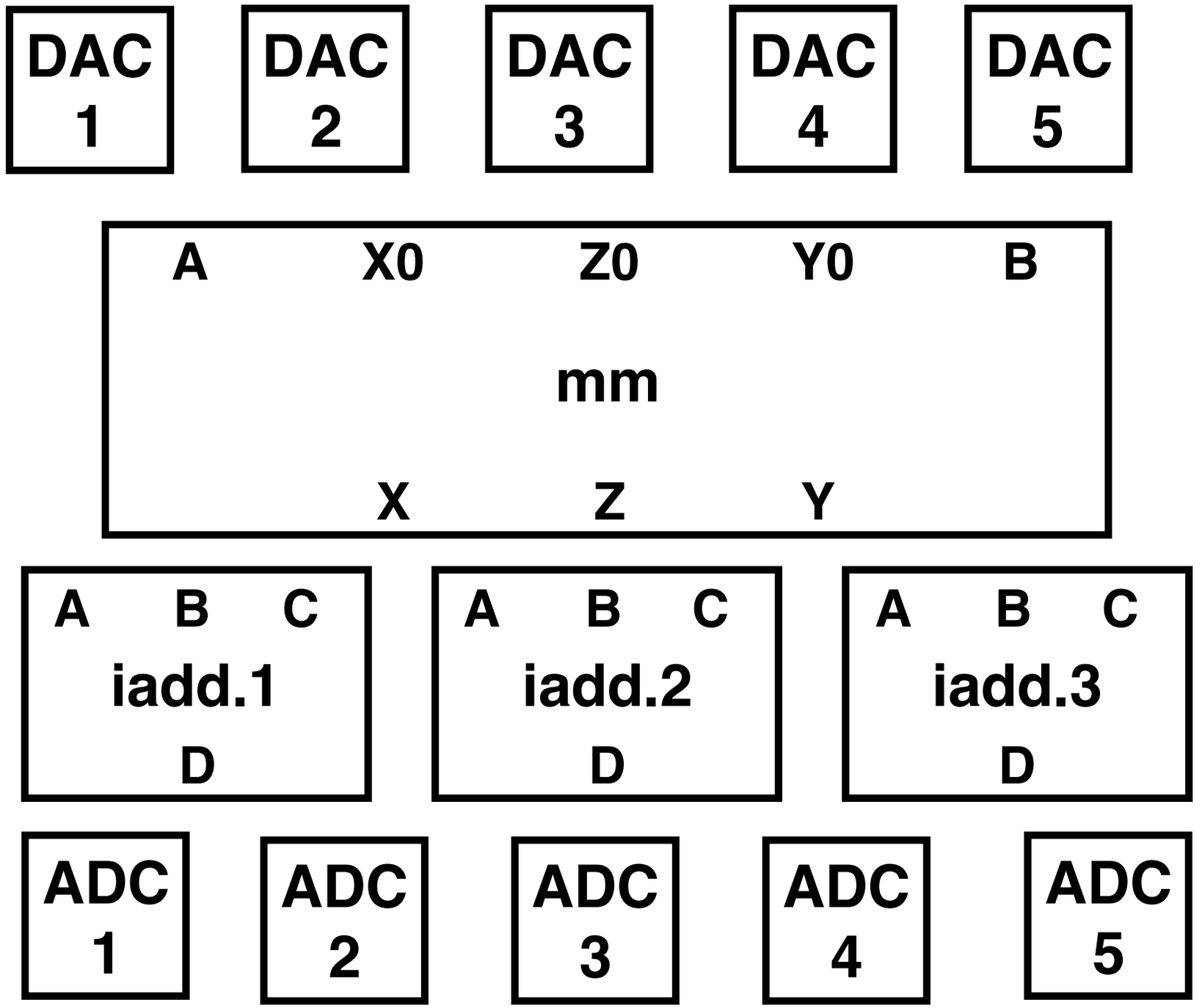


S. S. Woo, J. Kim, and R. Sarpeshkar. A cytomorphic chip for quantitative modeling of fundamental bio-molecular circuits. IEEE Trans. Biomed. Circuits and Systems, 9(4):527–542, 2015.

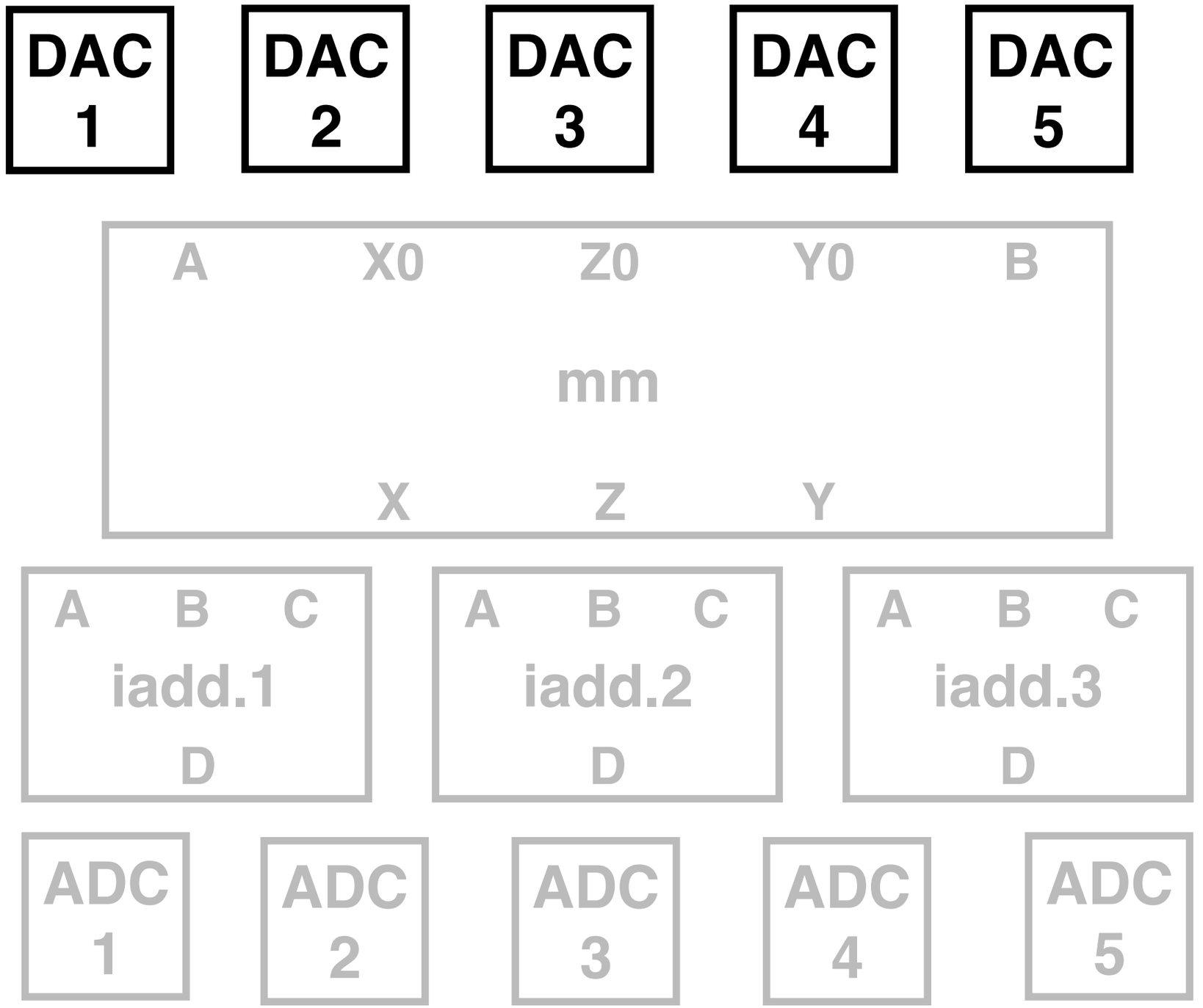
Analog Device



Analog Device



Analog Device



Analog Device

every 0.1 hu

DAC 1 | DAC 2 | DAC 3 | DAC 4 | DAC 5

A X0 Z0 Y0 B

mm

X Z Y

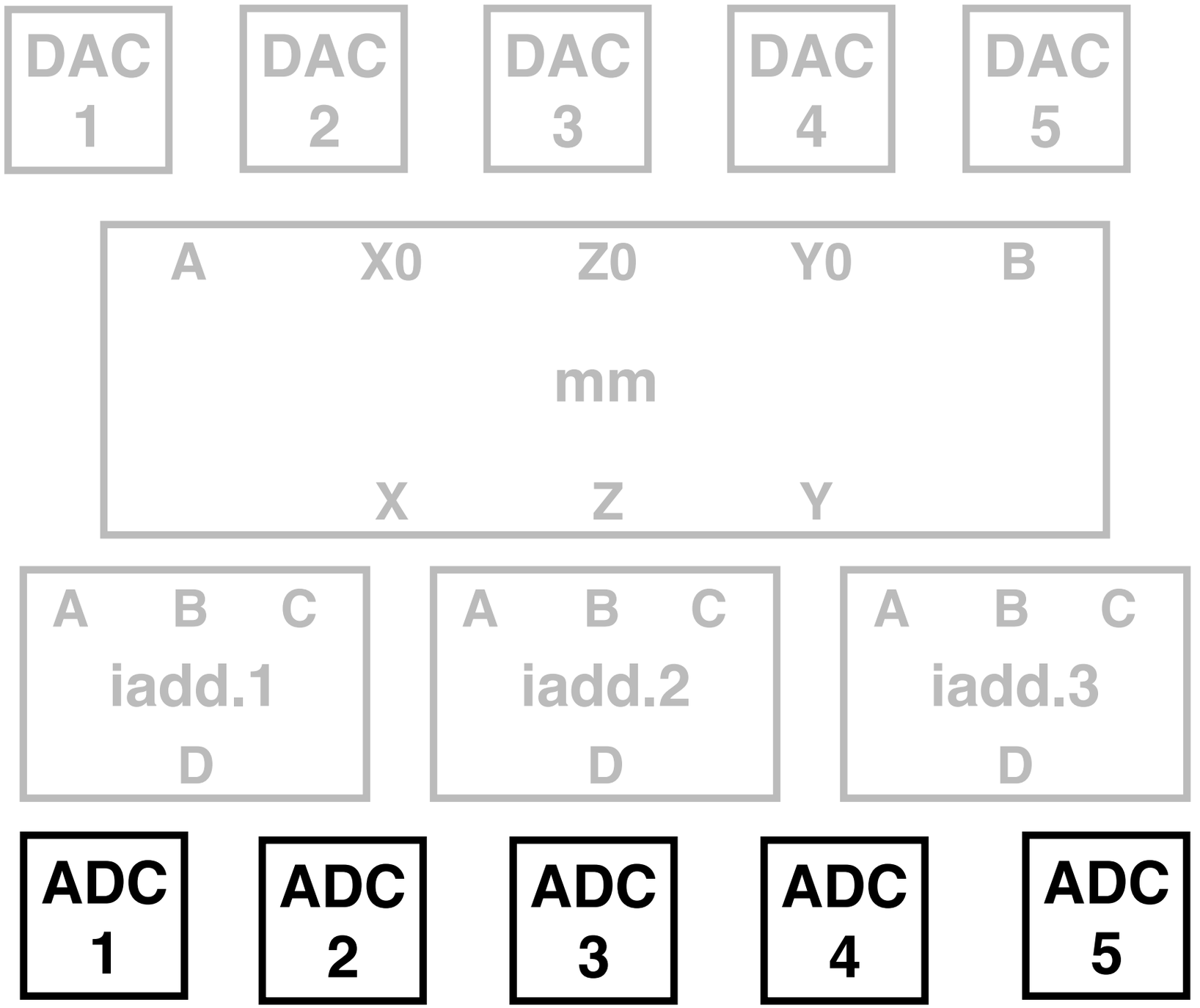
A B C iadd.1 D

A B C iadd.2 D

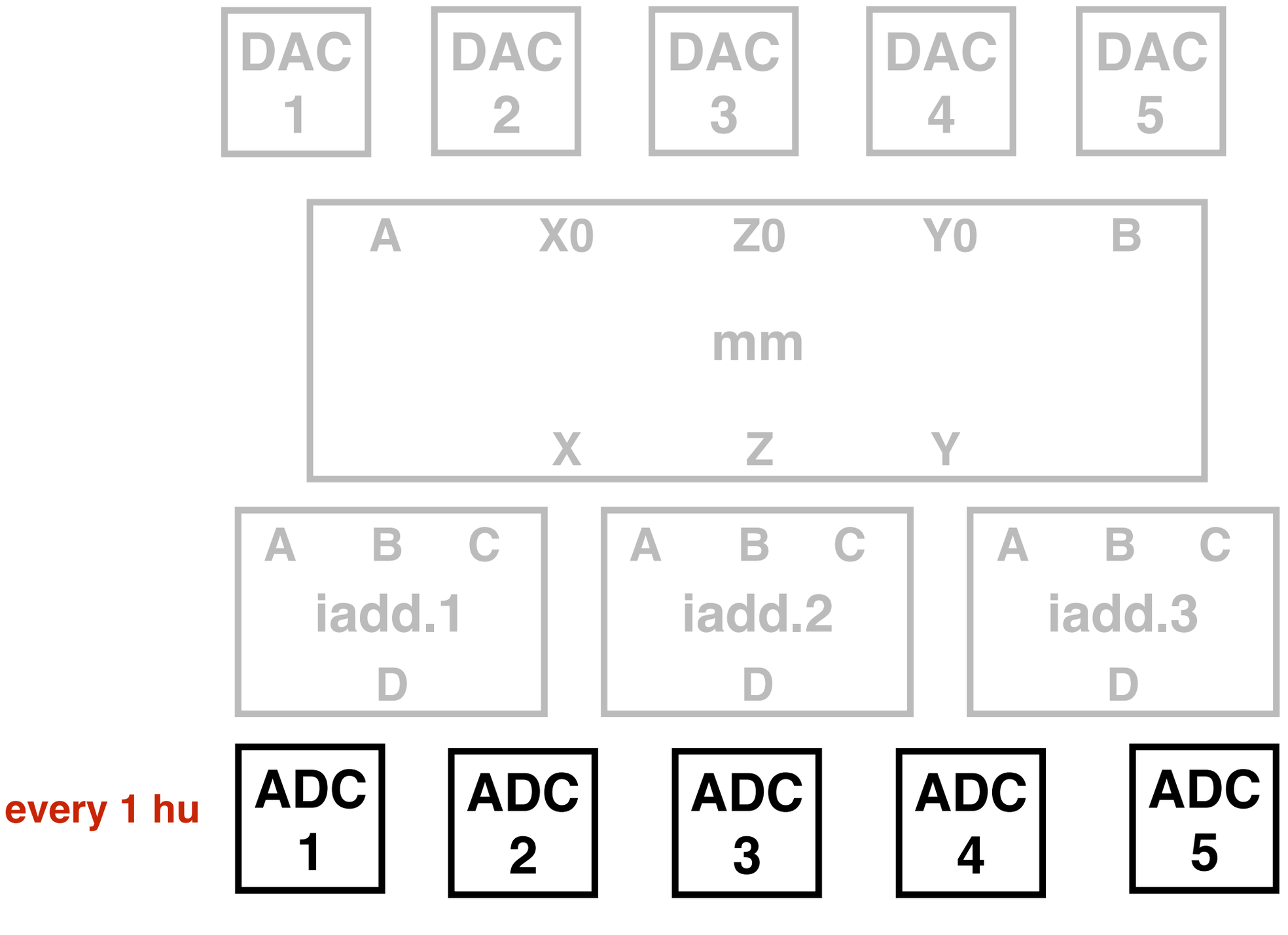
A B C iadd.3 D

ADC 1 | ADC 2 | ADC 3 | ADC 4 | ADC 5

Analog Device



Analog Device



Analog Device

DAC 1 | DAC 2 | DAC 3 | DAC 4 | DAC 5

A **X0** **Z0** **Y0** **B**

$Z = \int A \cdot X \cdot Y - B \cdot Z \, dt$ $X = X0 - Z$

$Z = Z0 \ @ \ t=0$ $Y = Y0 - Z$

X **Z** **Y**

A B C

$D = A+B-C$

D

A B C

$D = A+B-C$

D

A B C

$D = A+B-C$

D

ADC 1 | ADC 2 | ADC 3 | ADC 4 | ADC 5

Analog Device

DAC 1 | DAC 2 | DAC 3 | DAC 4 | DAC 5

A	X0	Z0	Y0	B
$[10^{-5},10^{-3}]$	[0,1000]	[0,600]	[0,1000]	$[10^{-4},1]$
	[0,1600]	[0,1600]	[0,1600]	
	X	Z	Y	

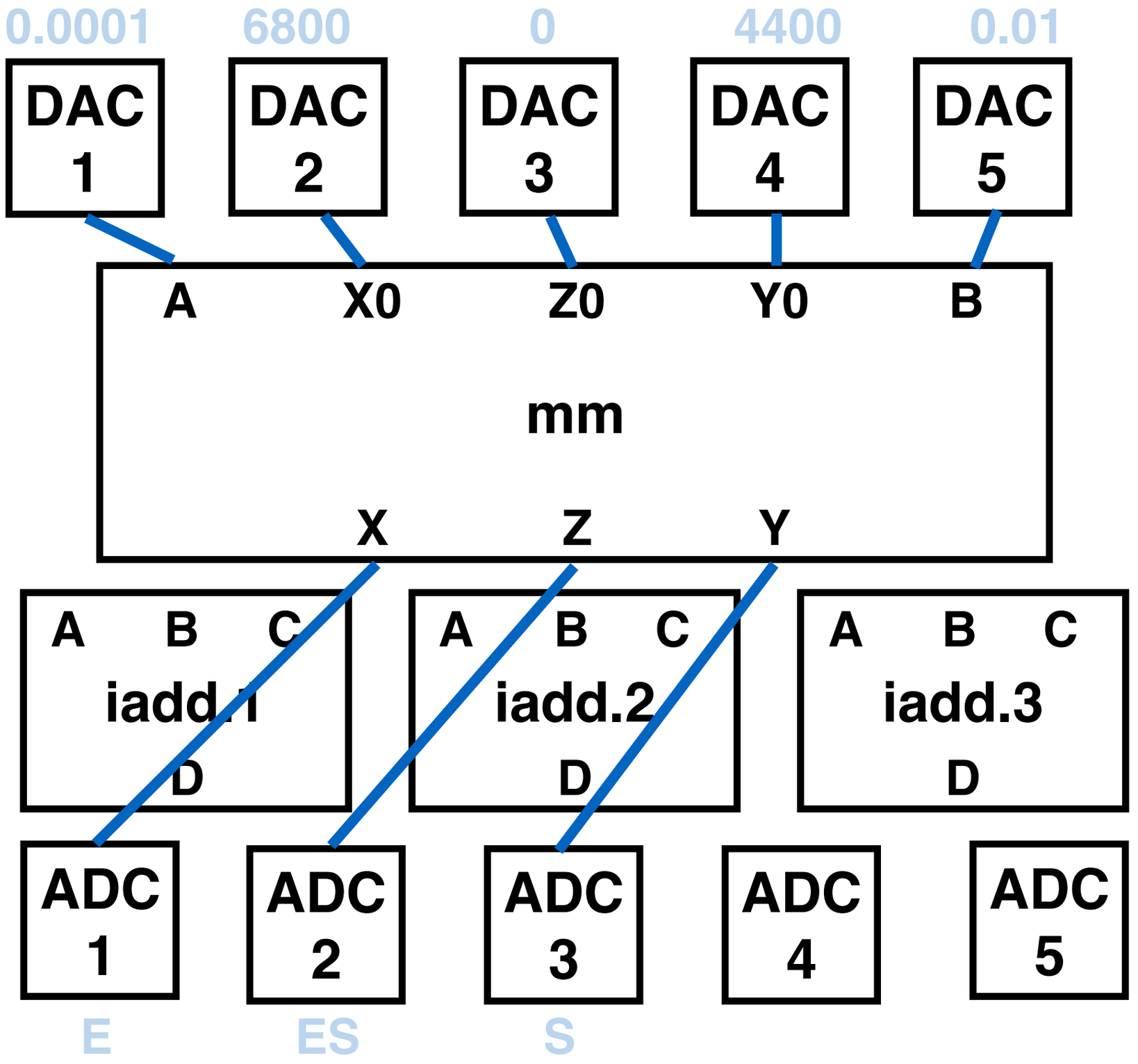
A	B	C	D
[0,5]	[0,5]	[0,5]	[0,10]

A	B	C	D
[0,5]	[0,5]	[0,5]	[0,10]

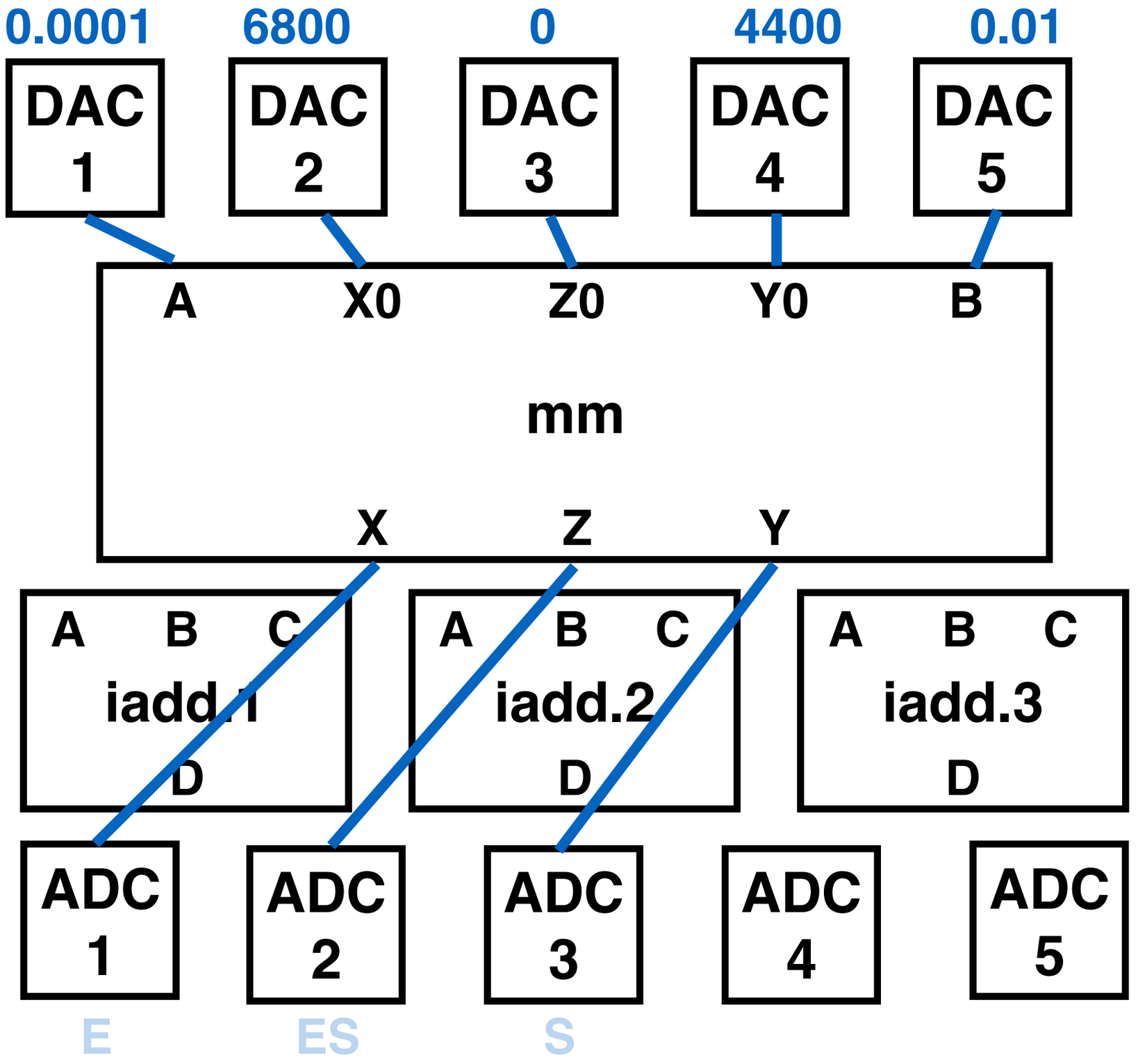
A	B	C	D
[0,5]	[0,5]	[0,5]	[0,10]

ADC 1 | ADC 2 | ADC 3 | ADC 4 | ADC 5

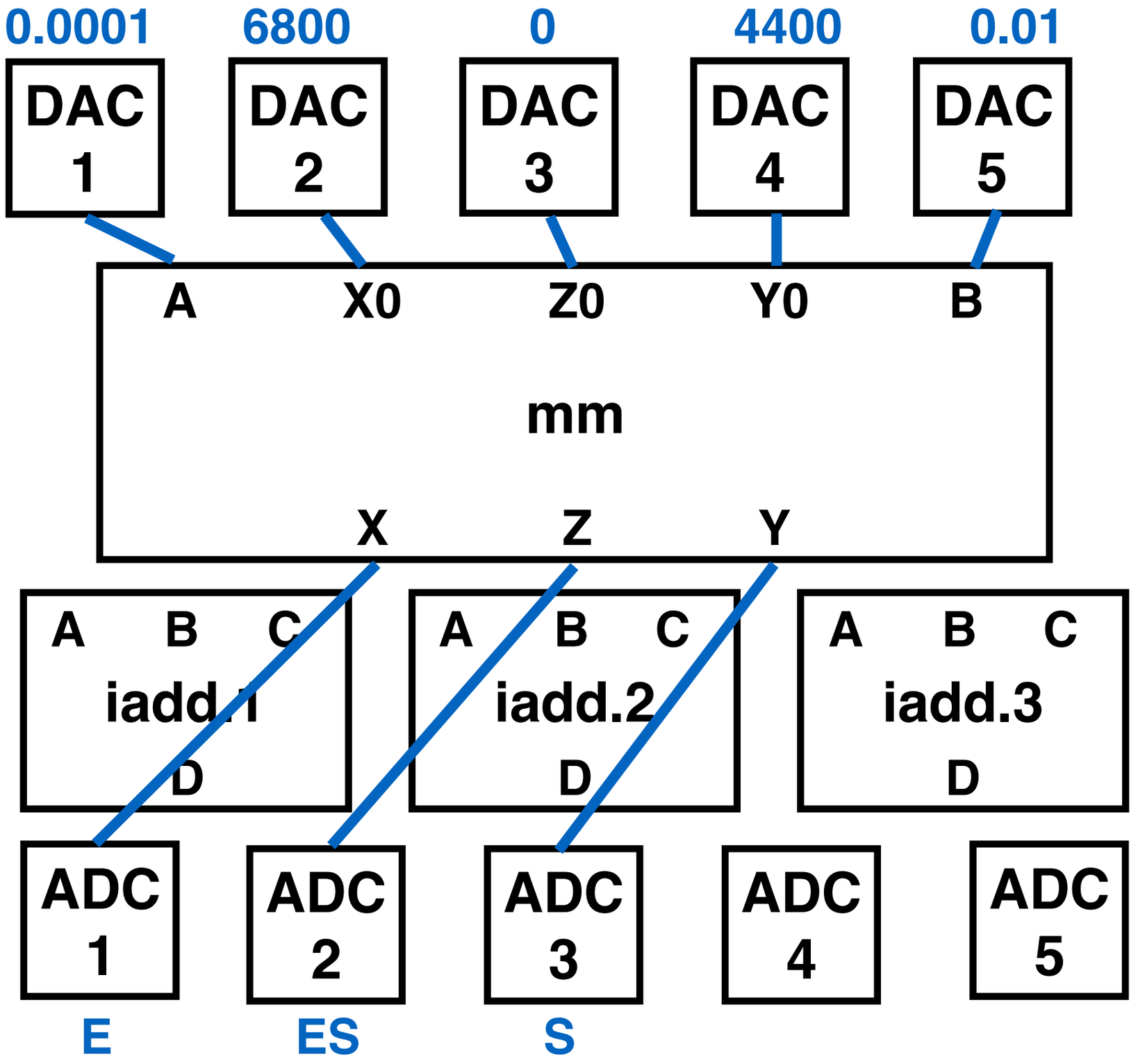
Configuring the Analog Device



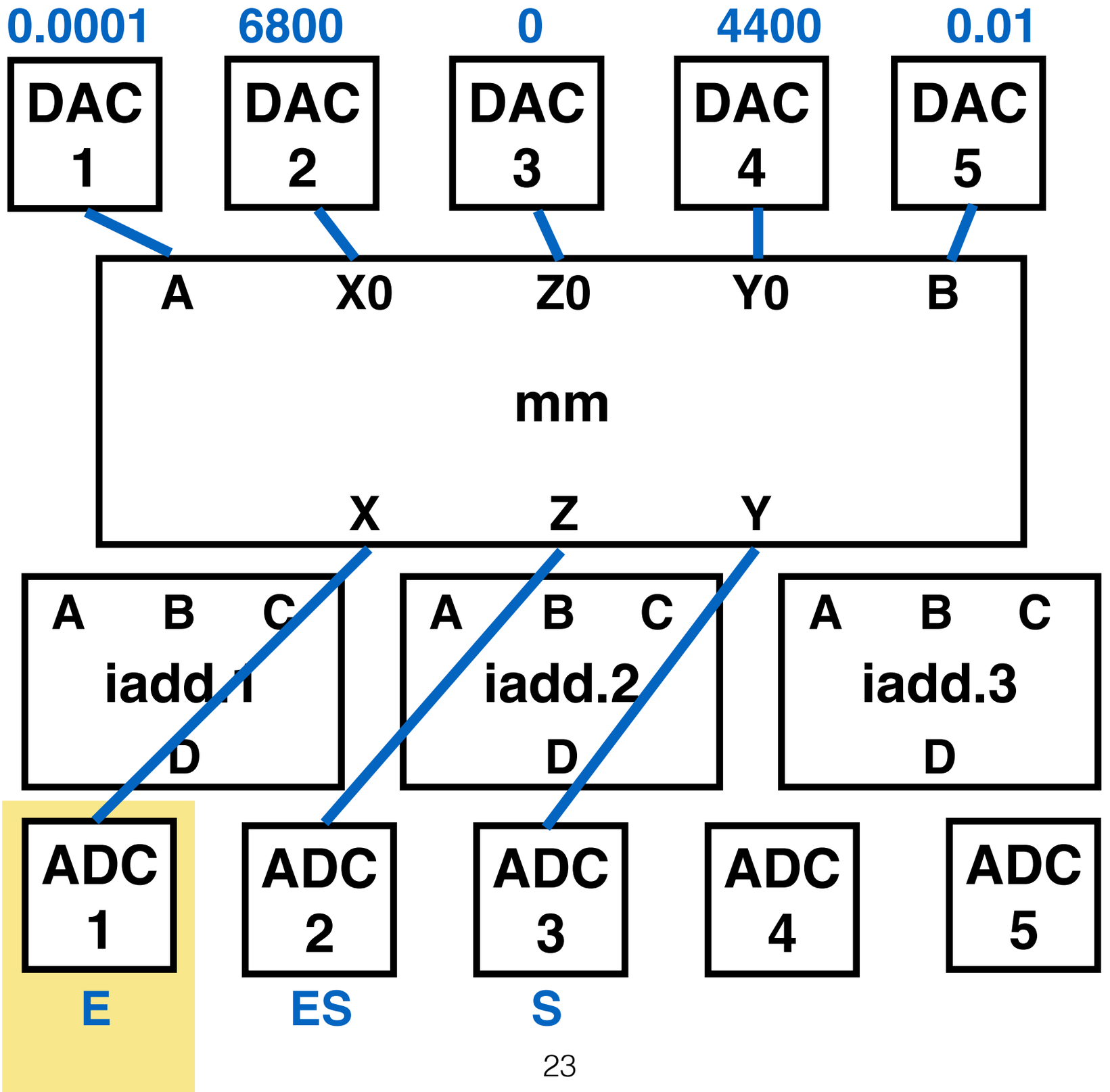
Configuring the Analog Device



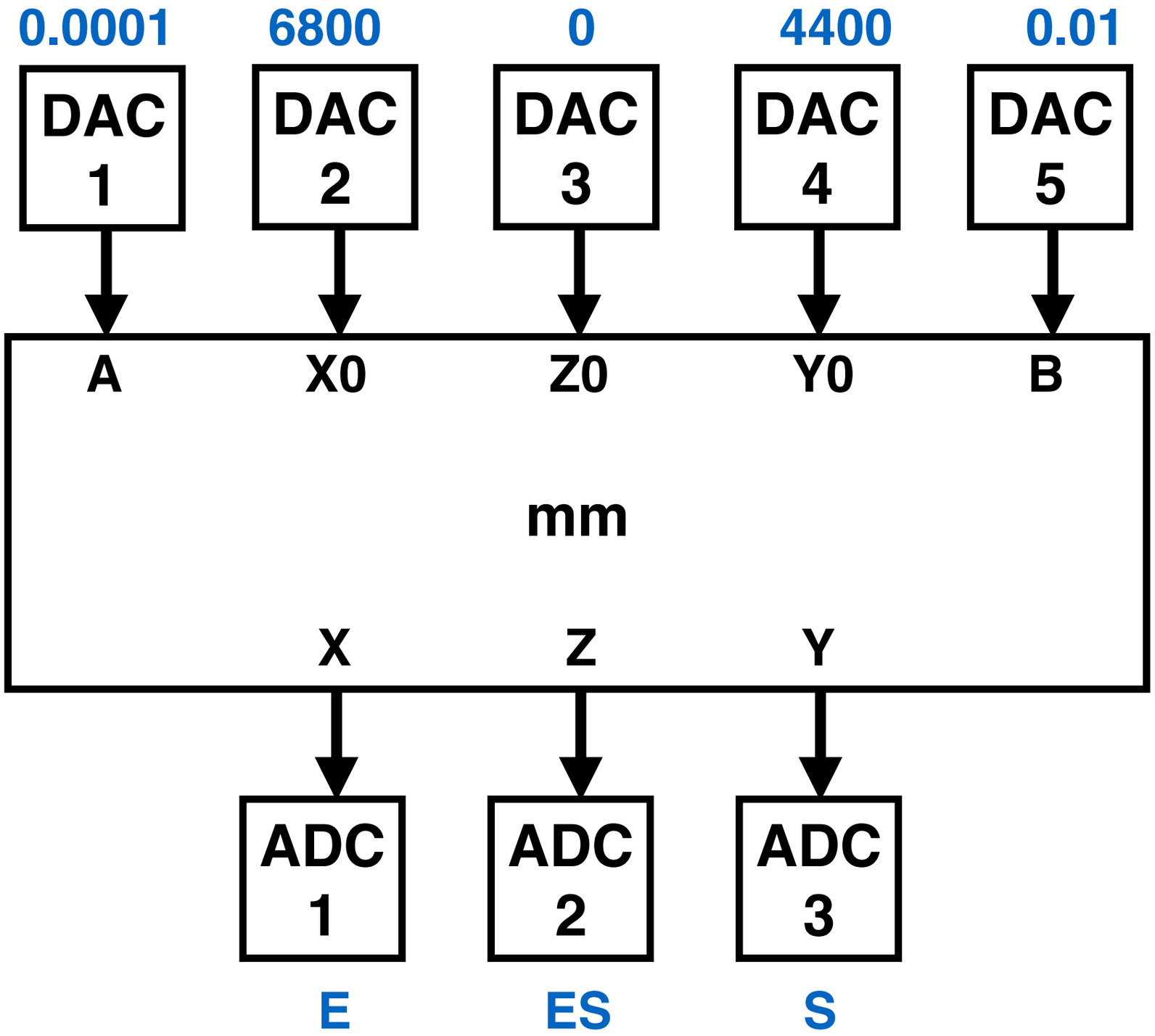
Configuring the Analog Device

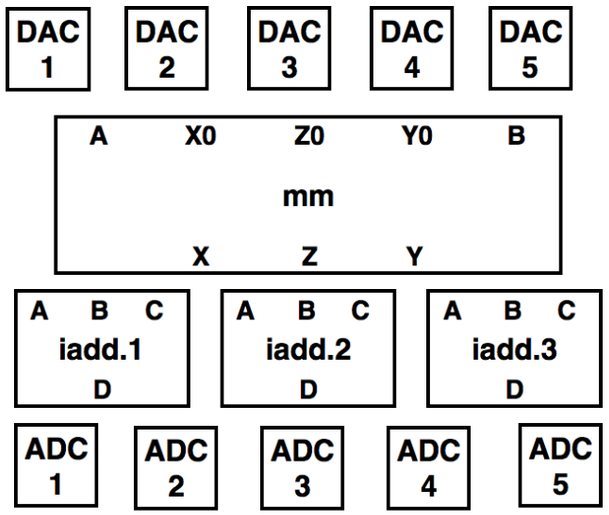


Configuring the Analog Device



Analog Device Configuration

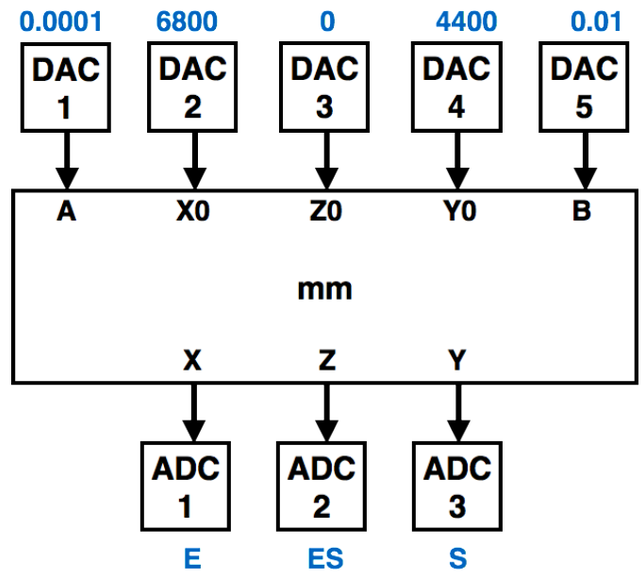




Analog Device Specification

$$E = 6800 - ES$$
$$S = 4400 - ES$$
$$\partial ES/\partial t = 0.0001 \cdot E \cdot$$
$$-0.01 \cdot ES$$
$$ES(0) = 0$$

Dynamical System



Analog Device Configuration

[1] Sara Achour, Rahul Sarpeshkar,and Martin C. Rinard. Configuration synthesis for programmable analog devices with Arco. PLDI 2016

does not consider

physical limitations of hardware

- operating range of ports

- sampling rates of DACs/ADCs

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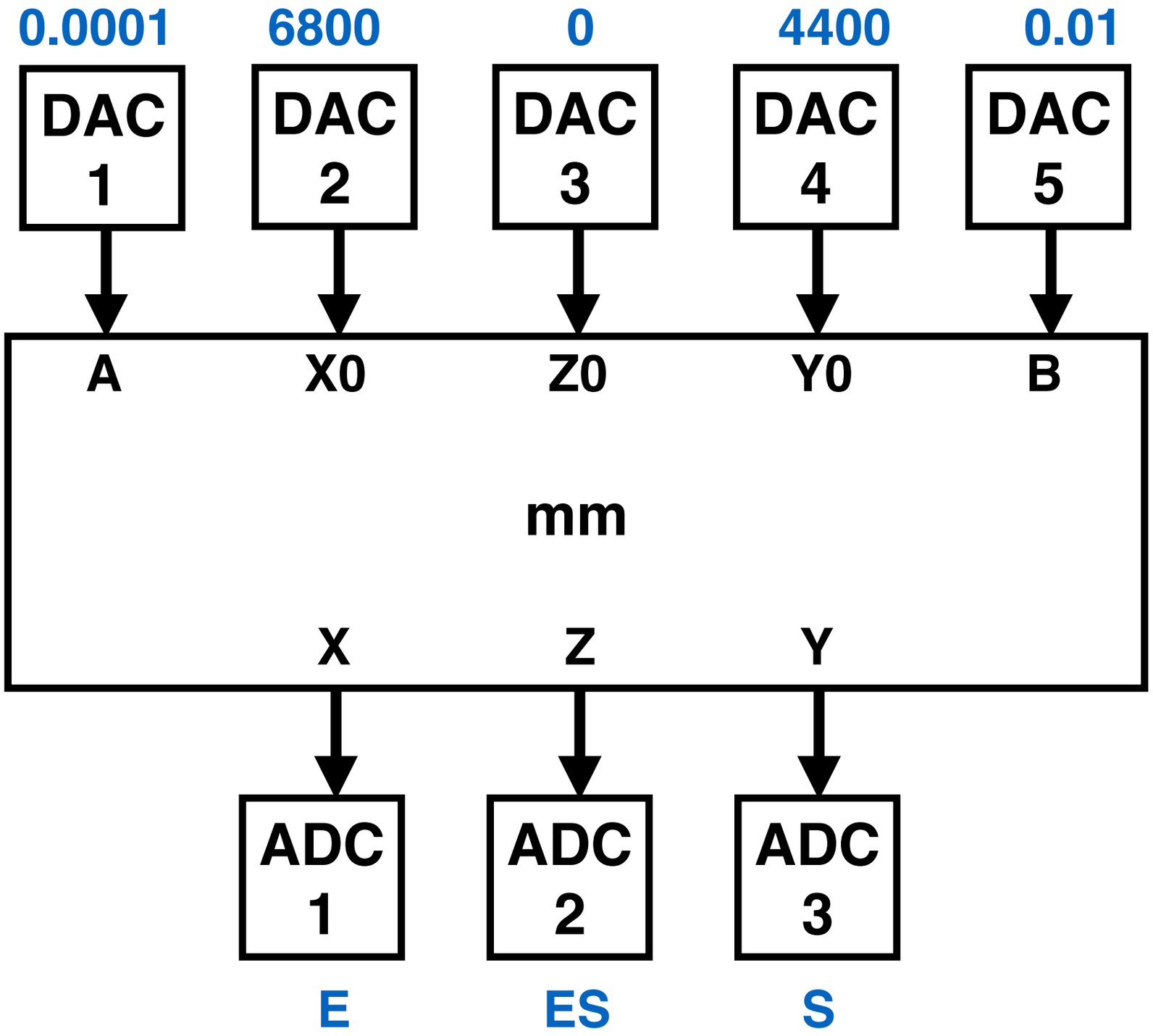
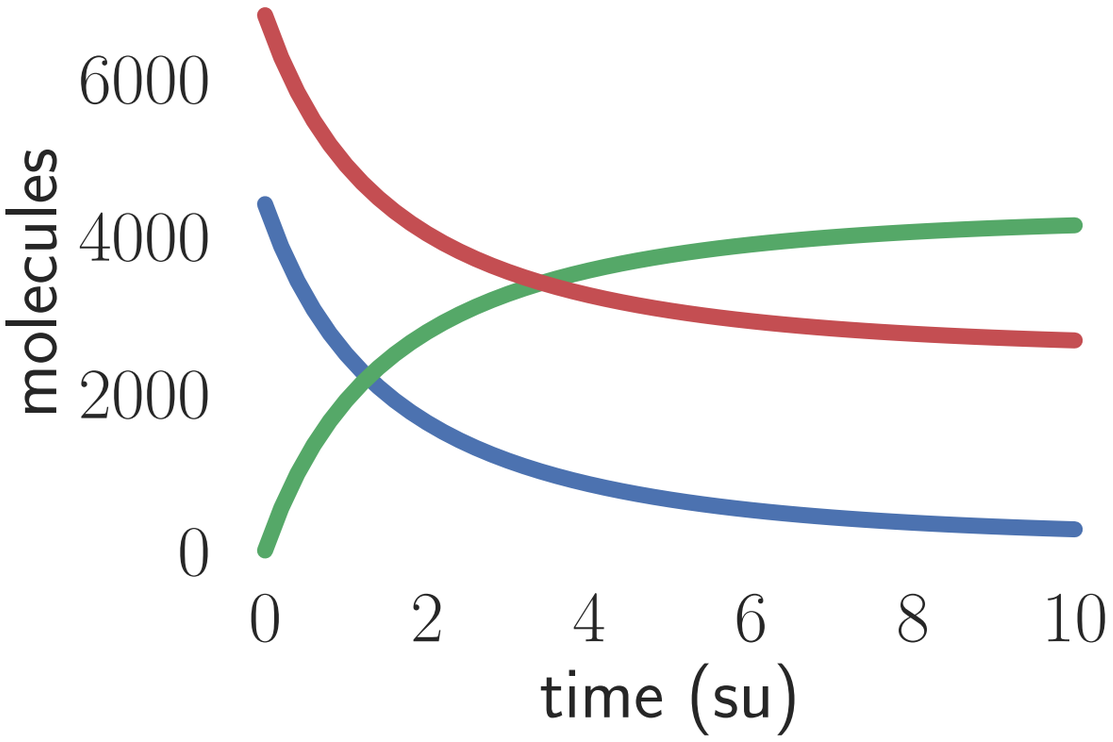
Analog Device Configuration

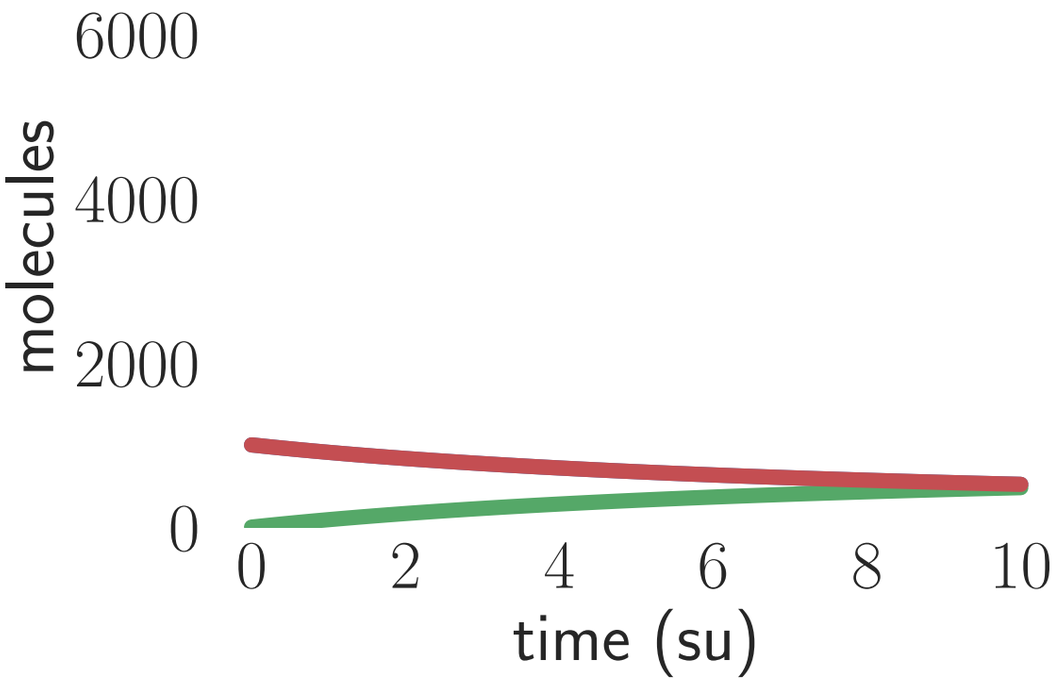


Execution on Analog Device

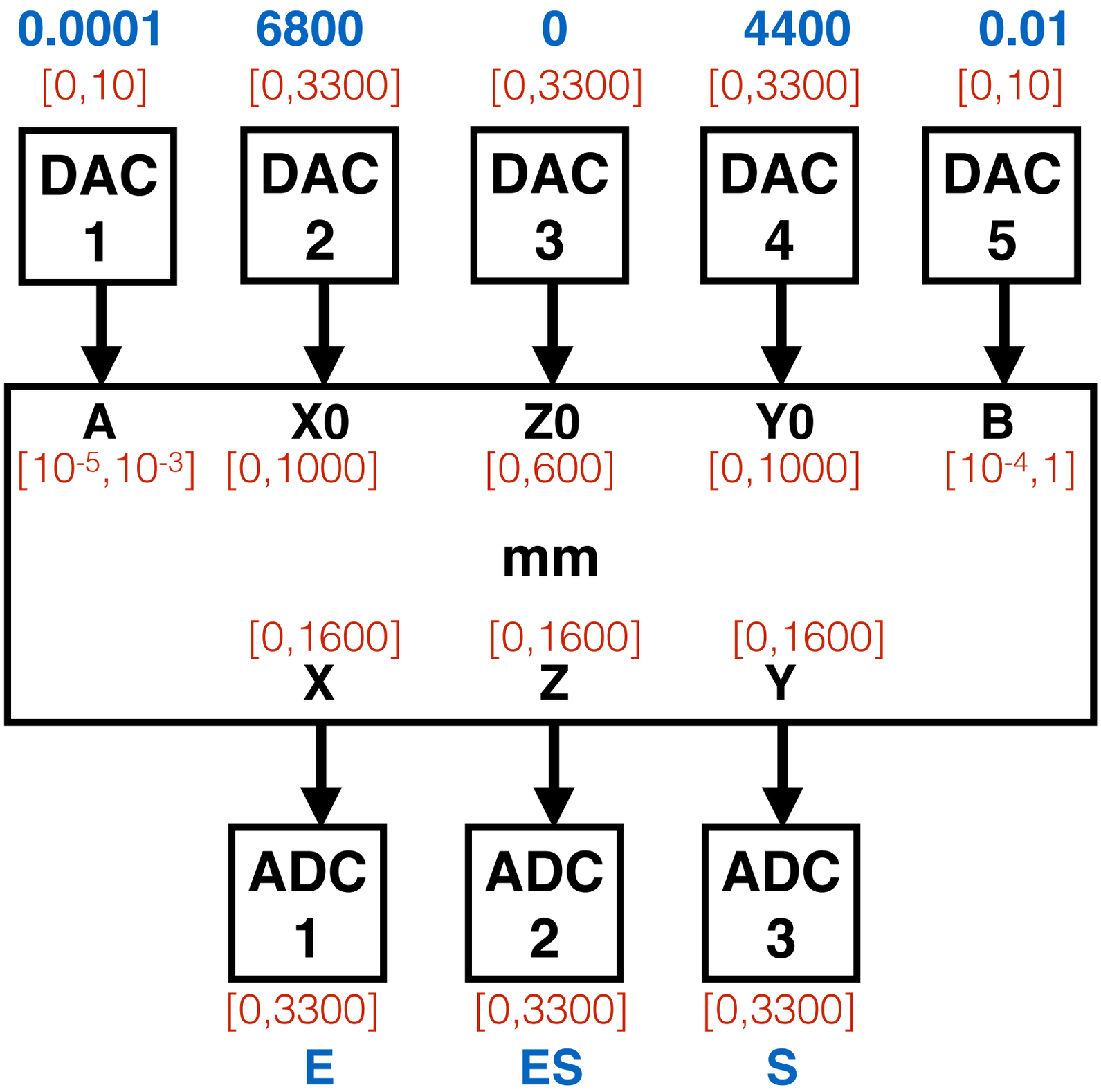
Expected



Actual



Analog Device has Physical Limitations



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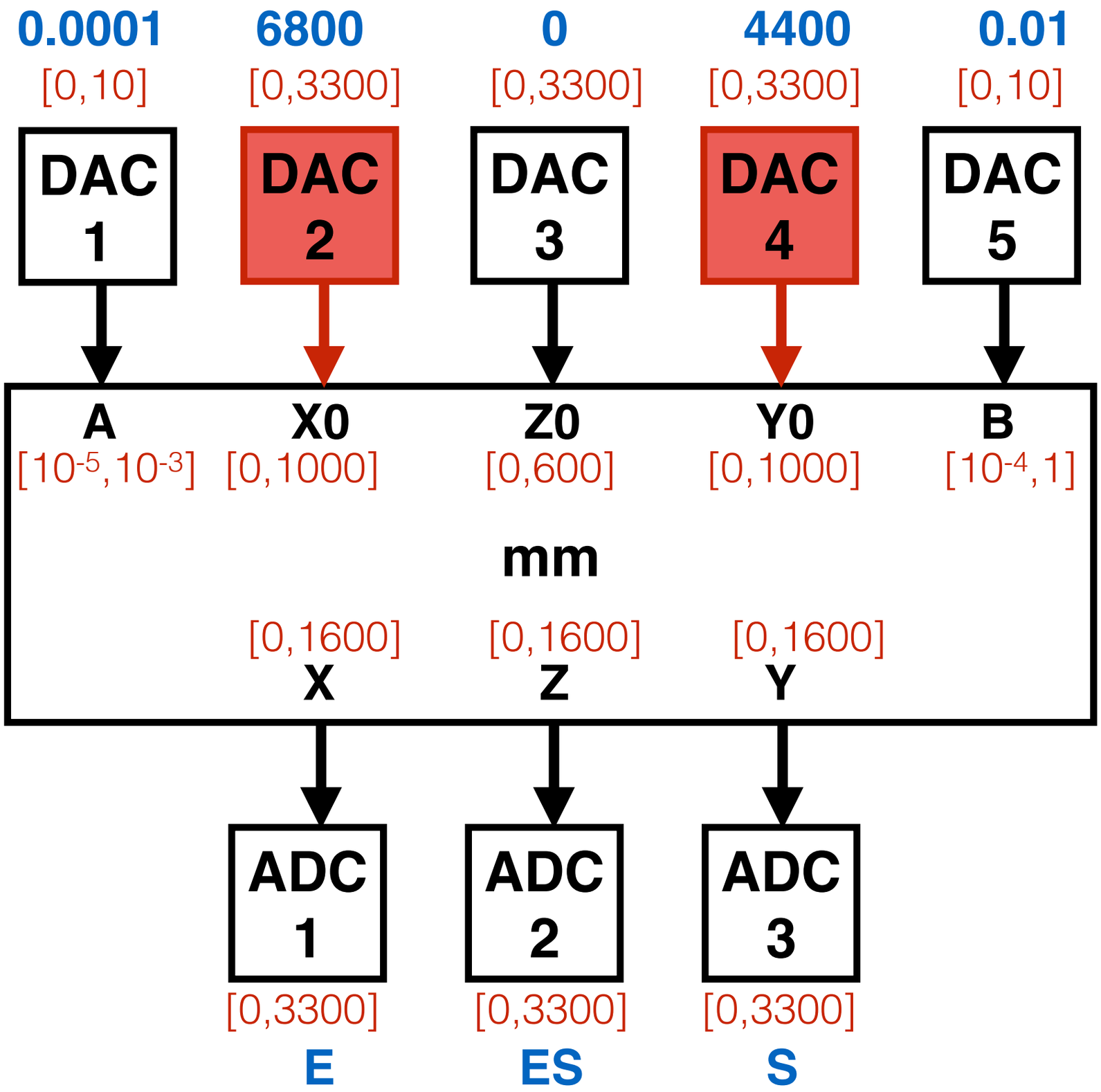
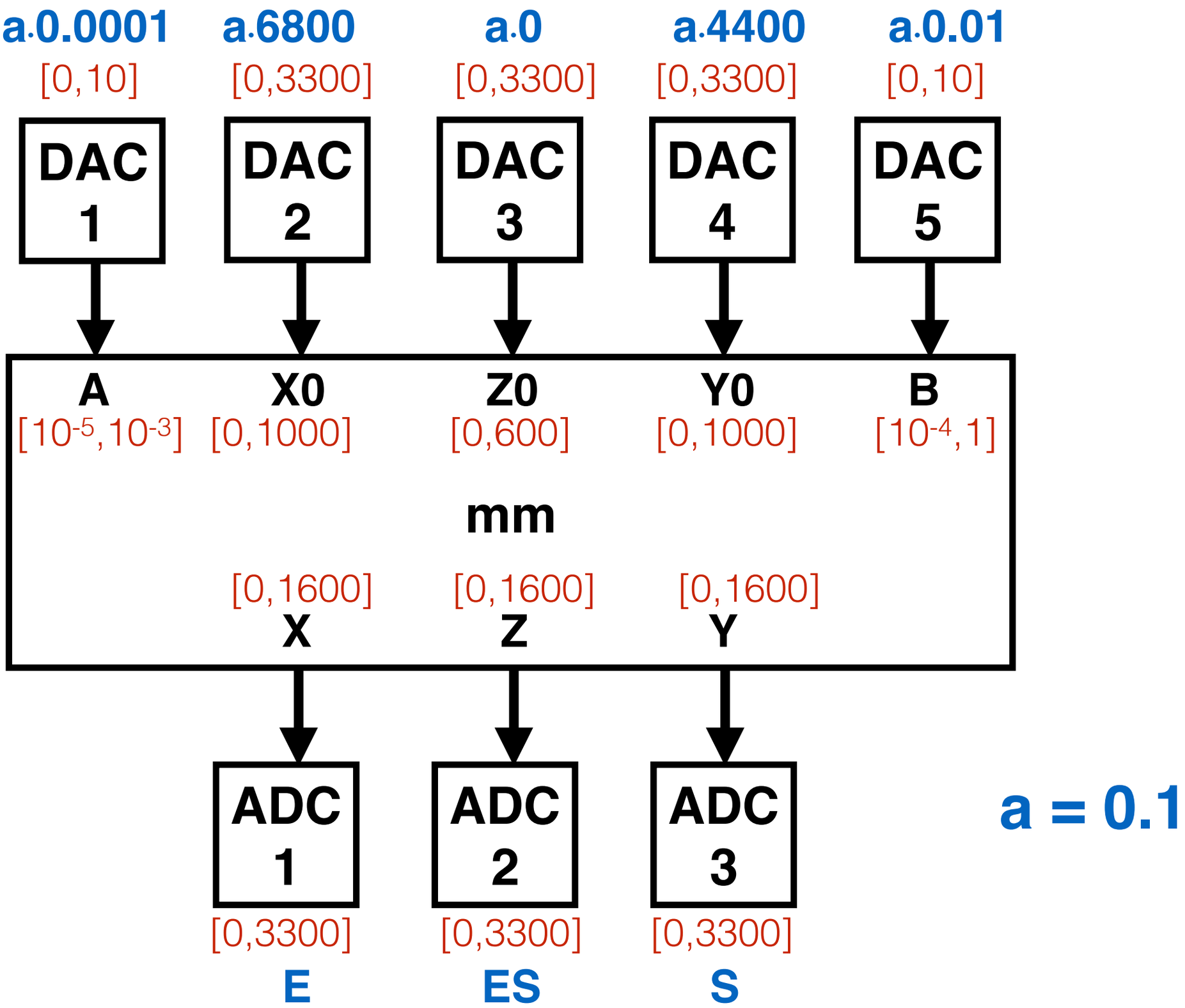
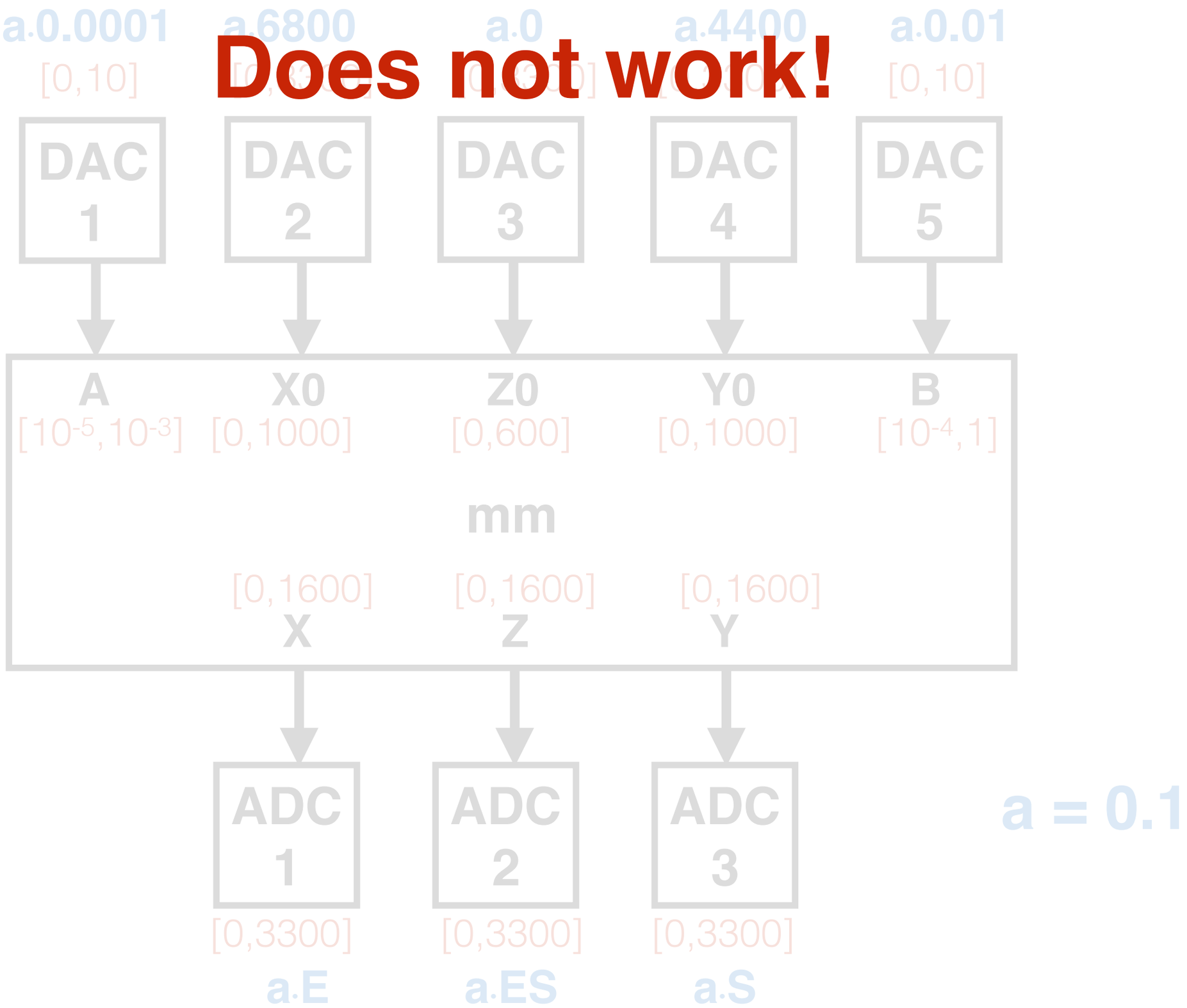


Uniformly scaling the configuration



Uniformly scaling the configuration

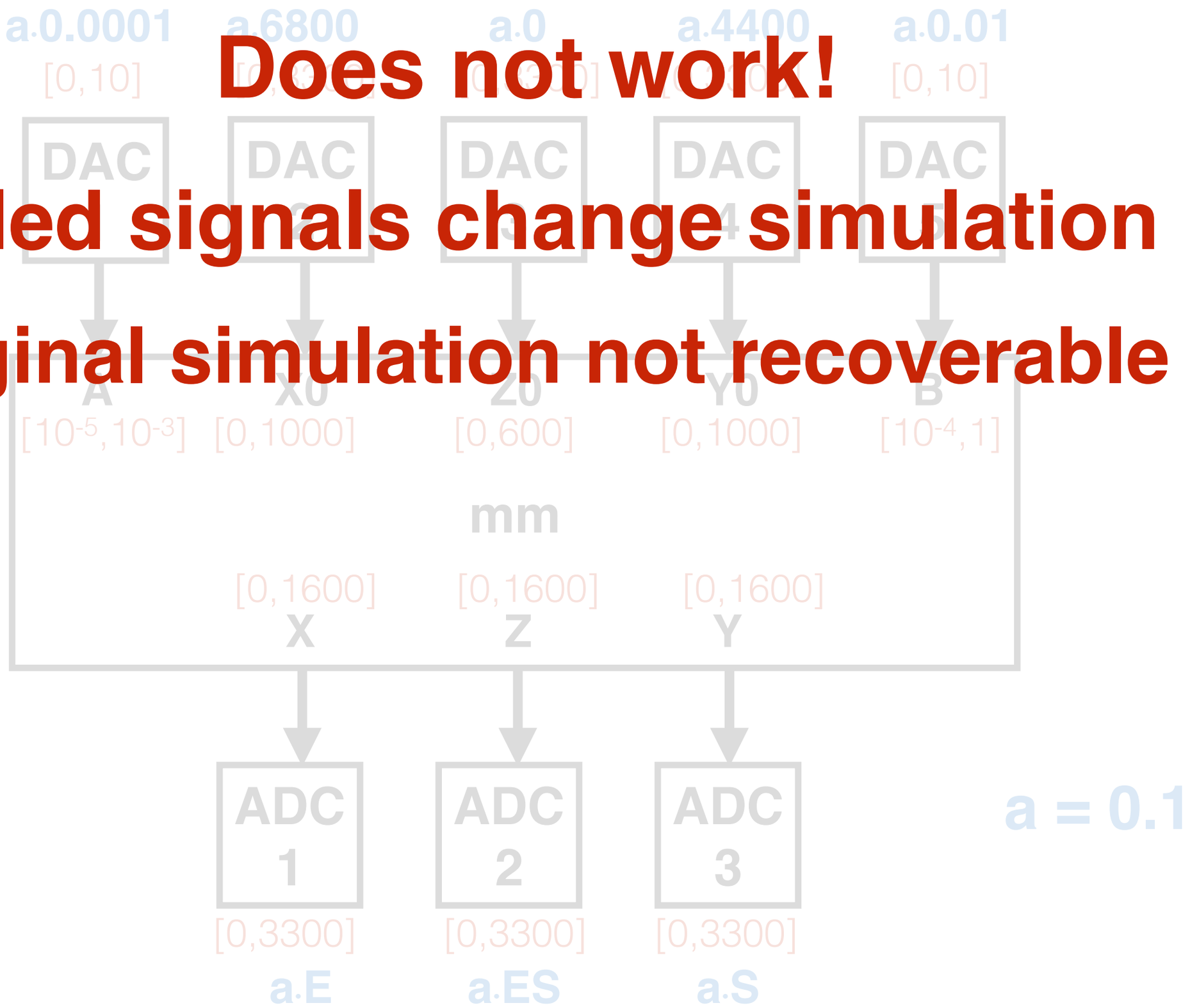


Uniformly scaling the configuration

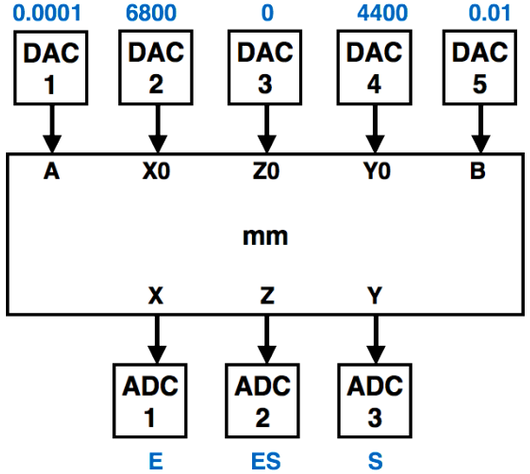
Does not work!

Scaled signals change simulation

Original simulation not recoverable

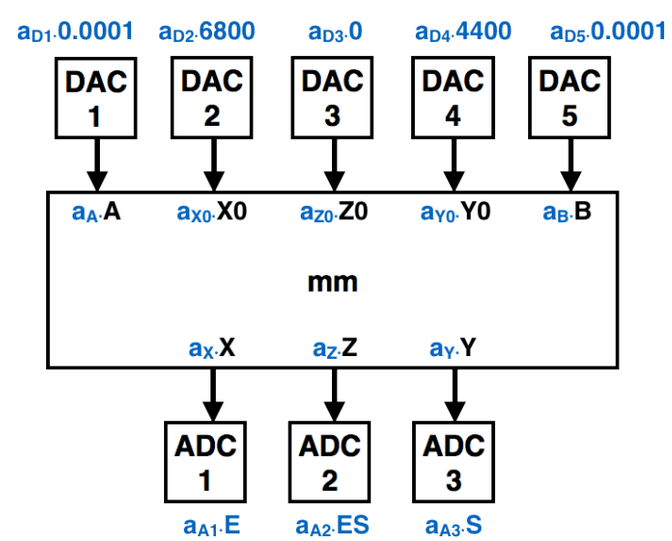


Analog Device Configuration



Jaunt

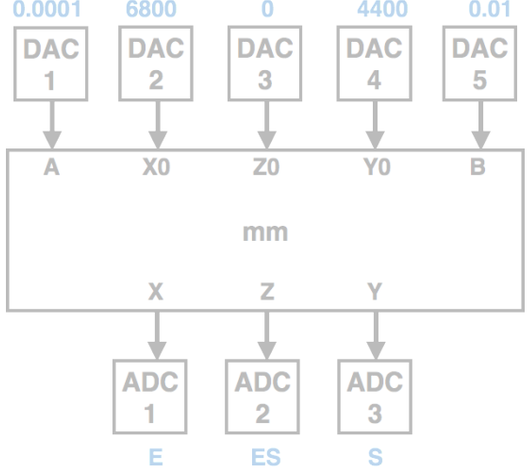
Scaled Analog Device Configuration



physically realizable: signals are within port operating ranges

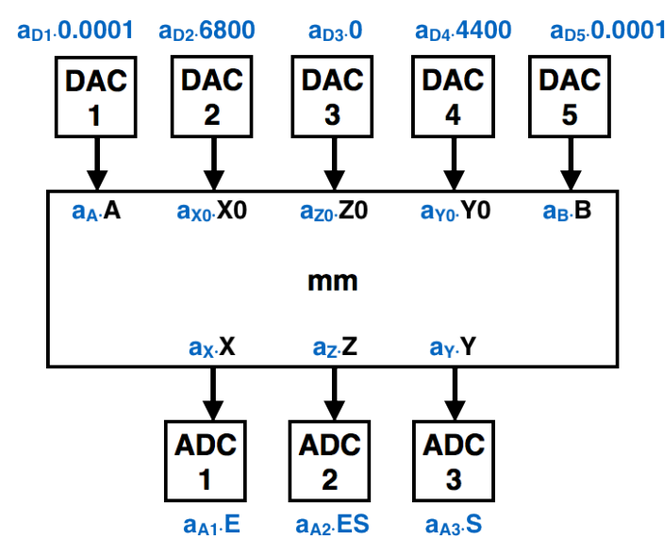
recoverable: recover original simulation at digital interface

Analog Device Configuration

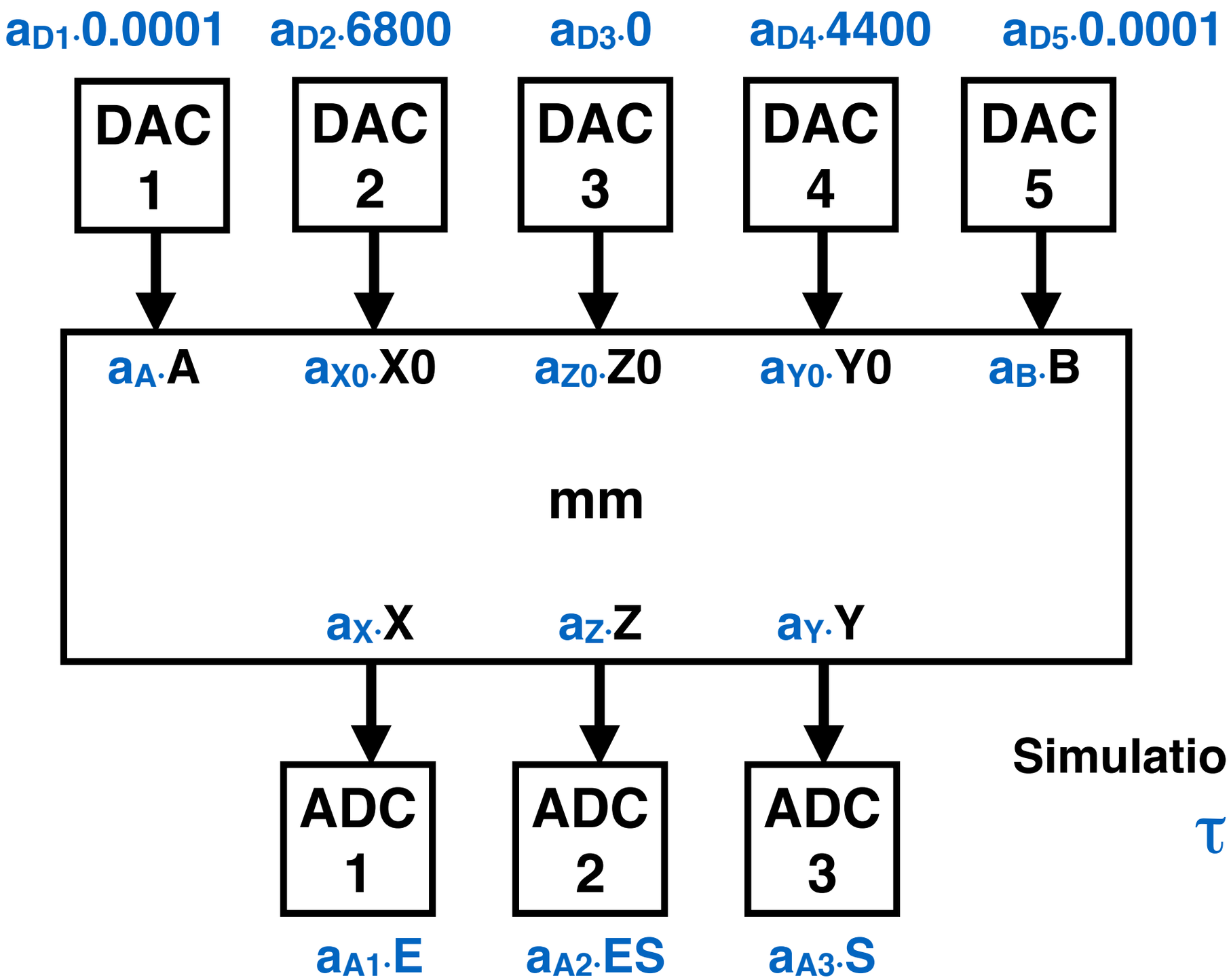


Jaunt

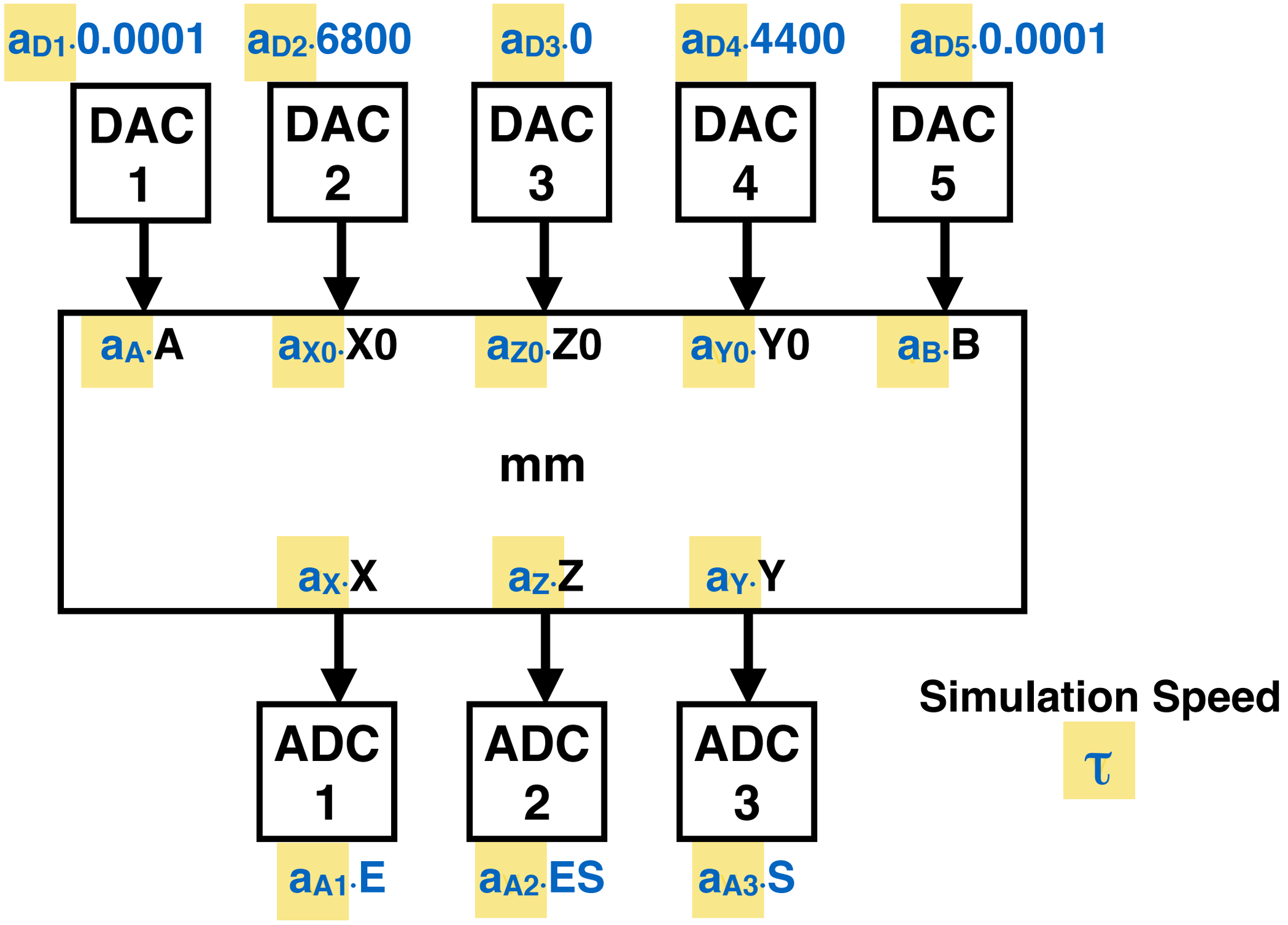
Scaled Analog Device Configuration



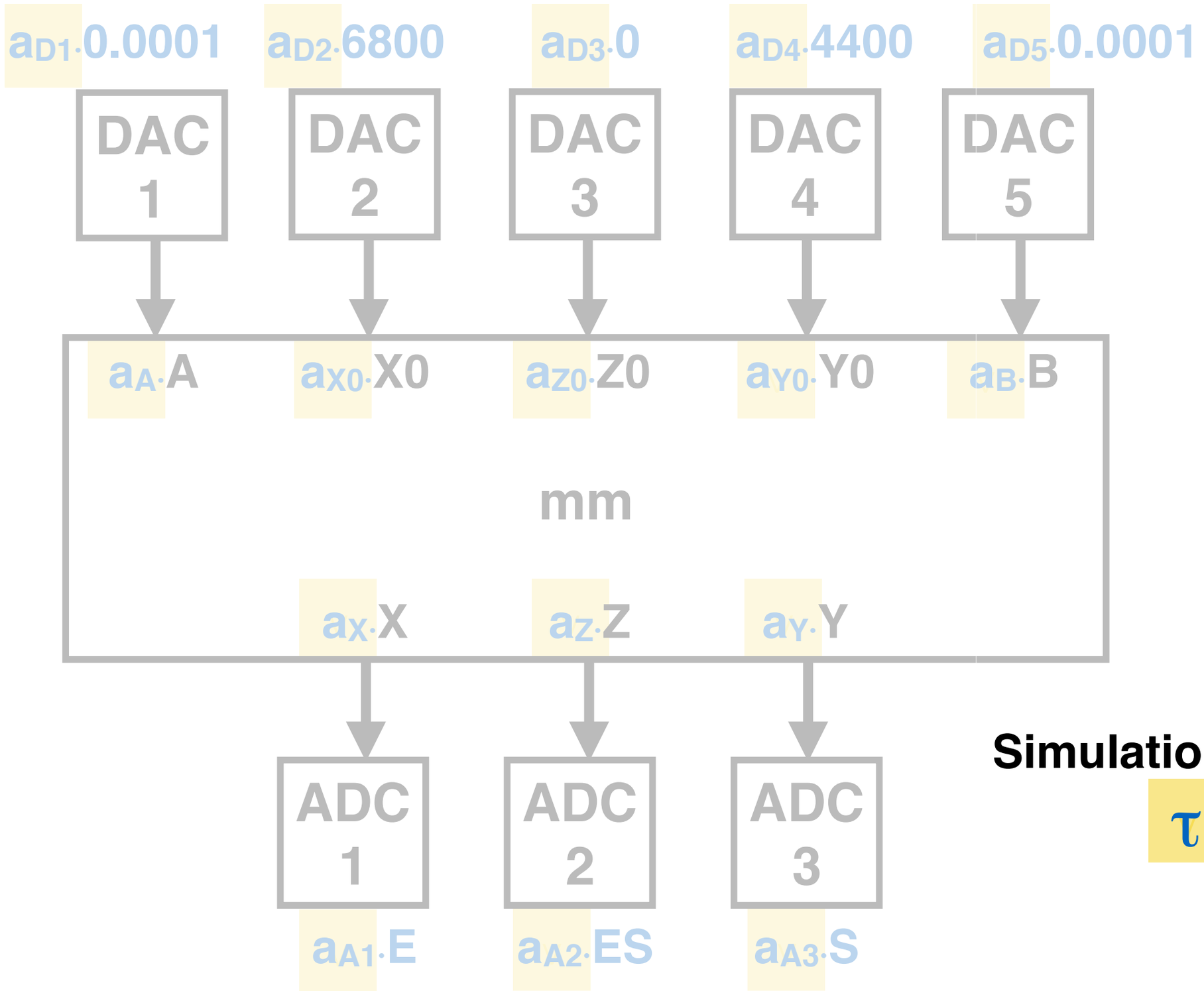
Scaled Configuration



Scaled Configuration



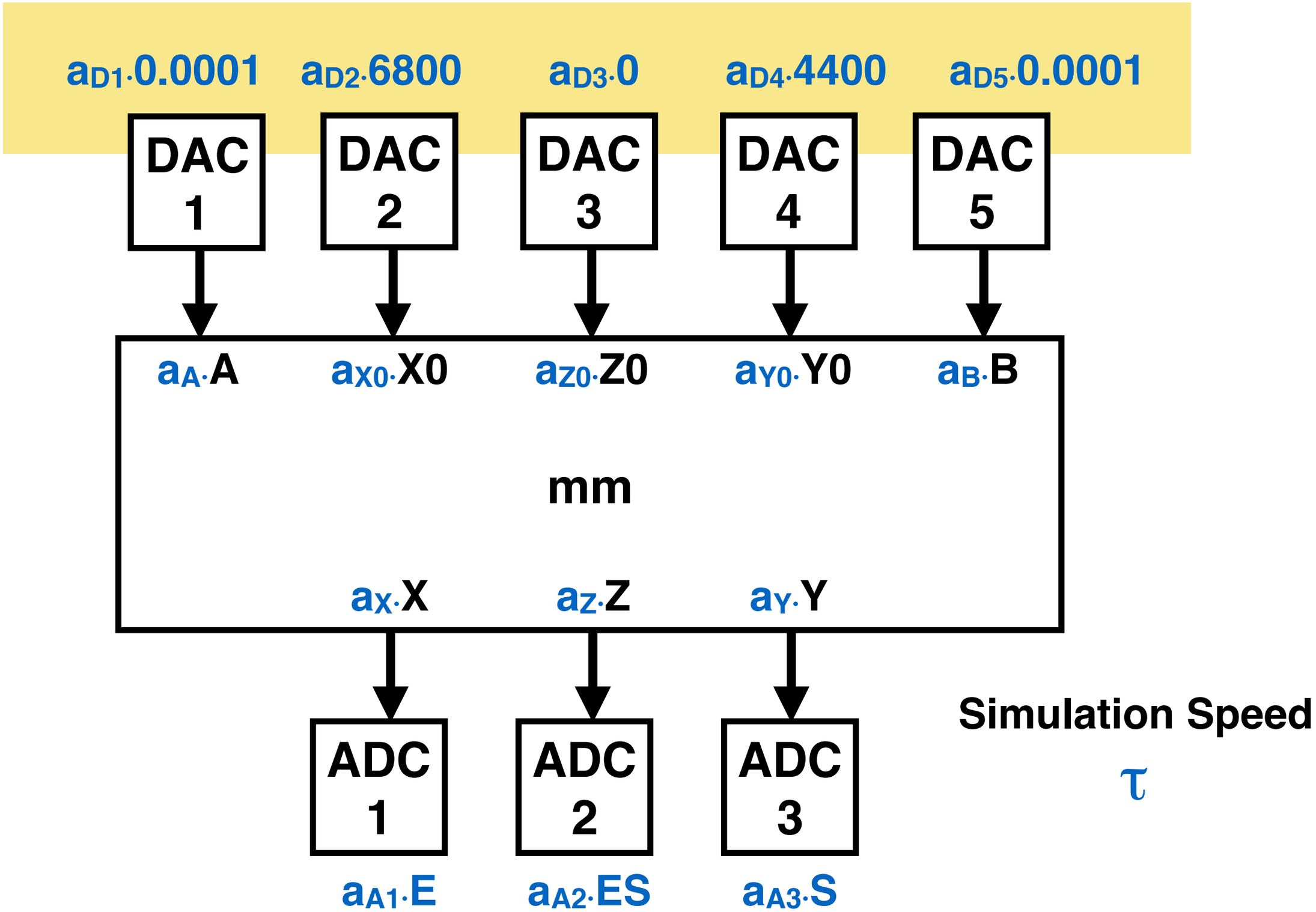
Time Scaling Factor, τ



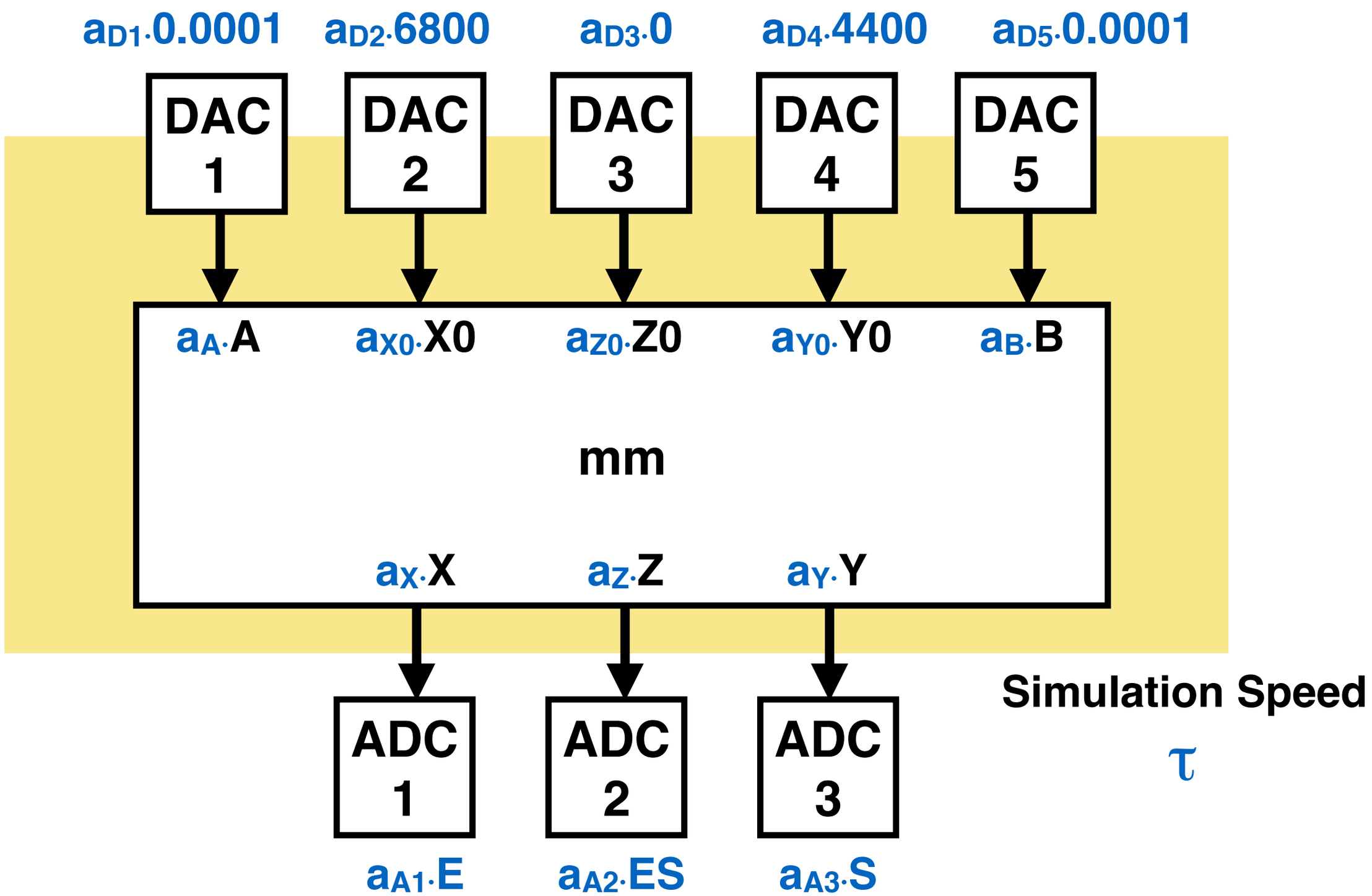
Simulation Speed

τ

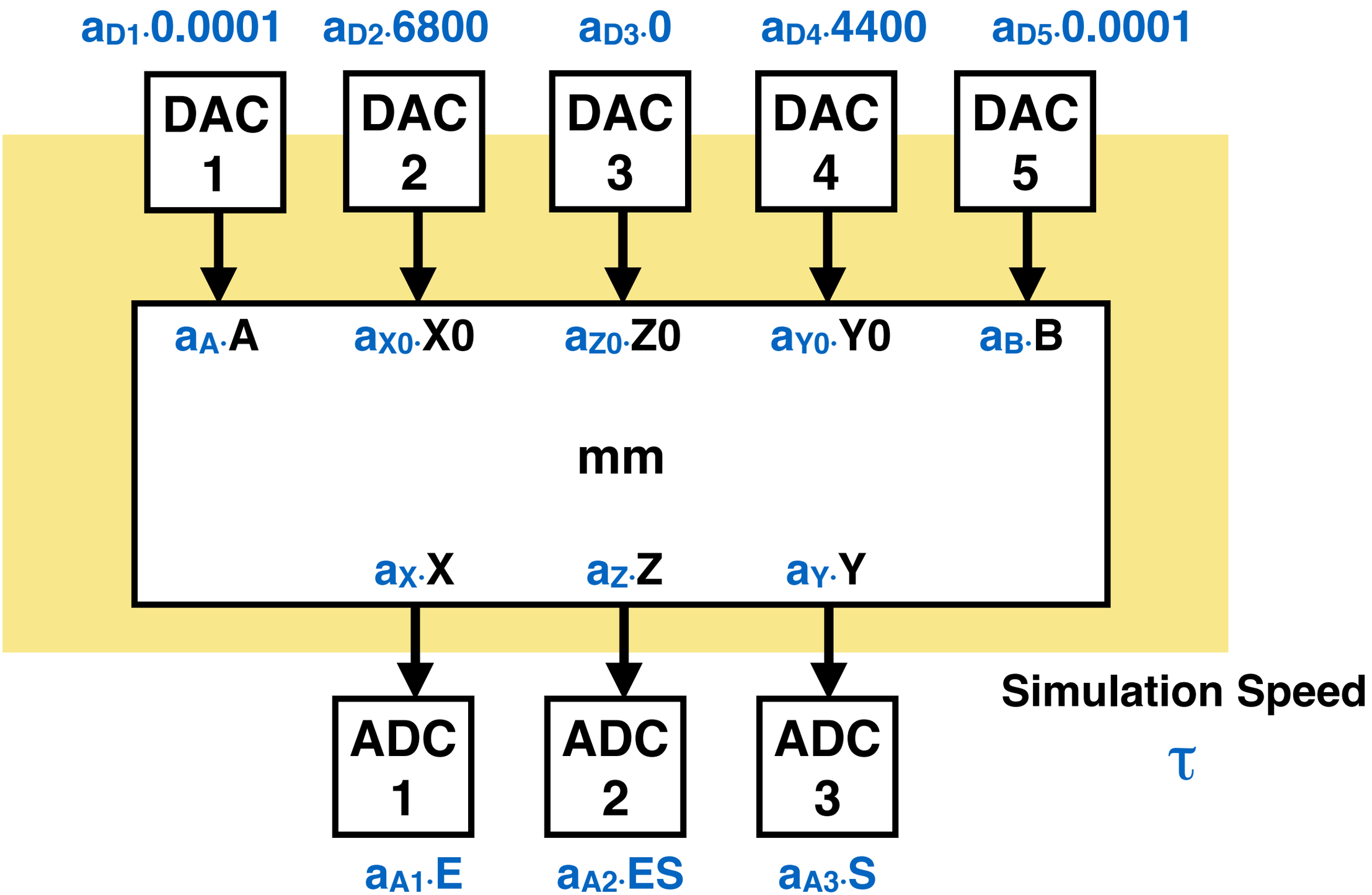
Multiply each DAC value by its scaling factor



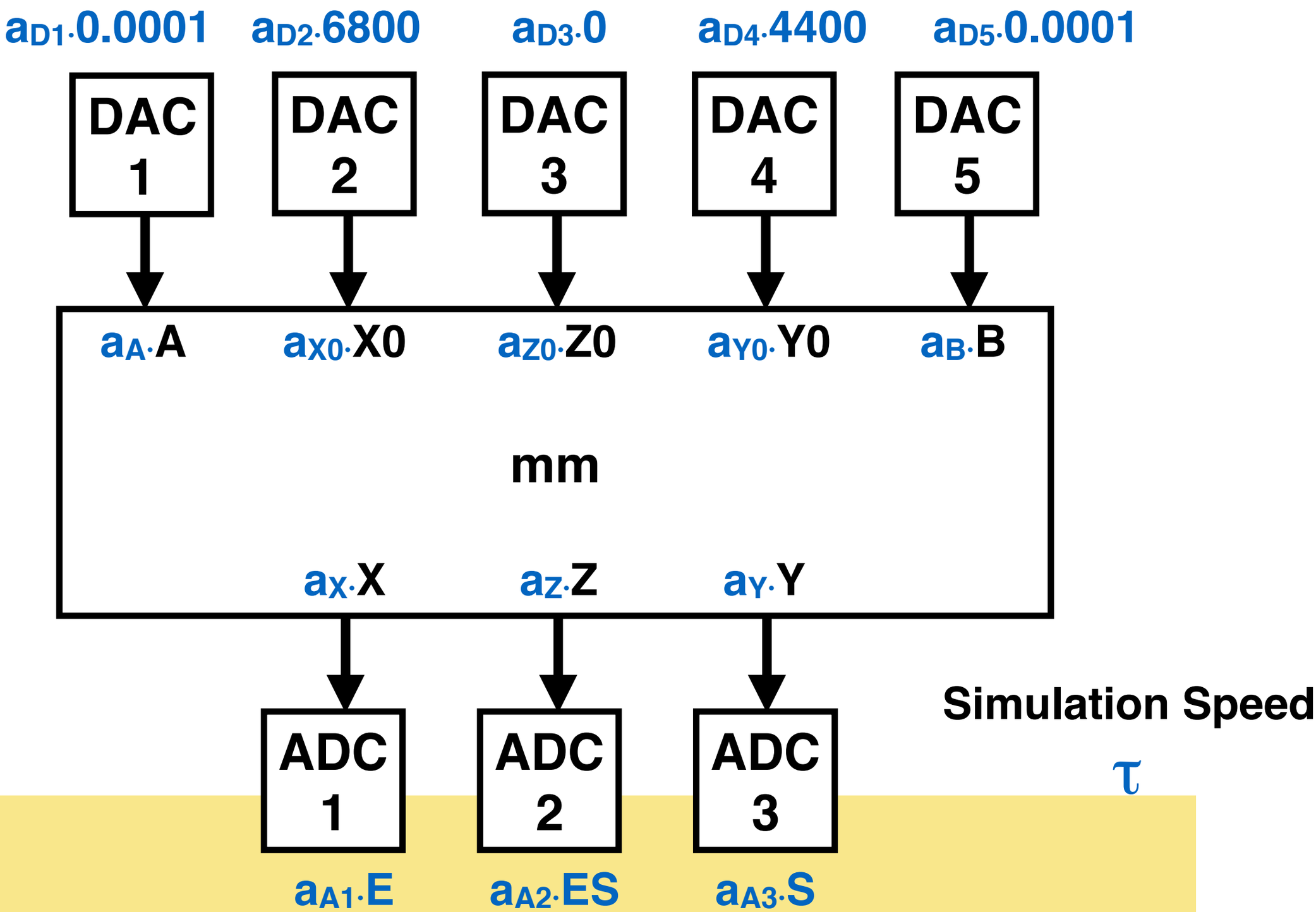
The scaled signals propagate through the analog device



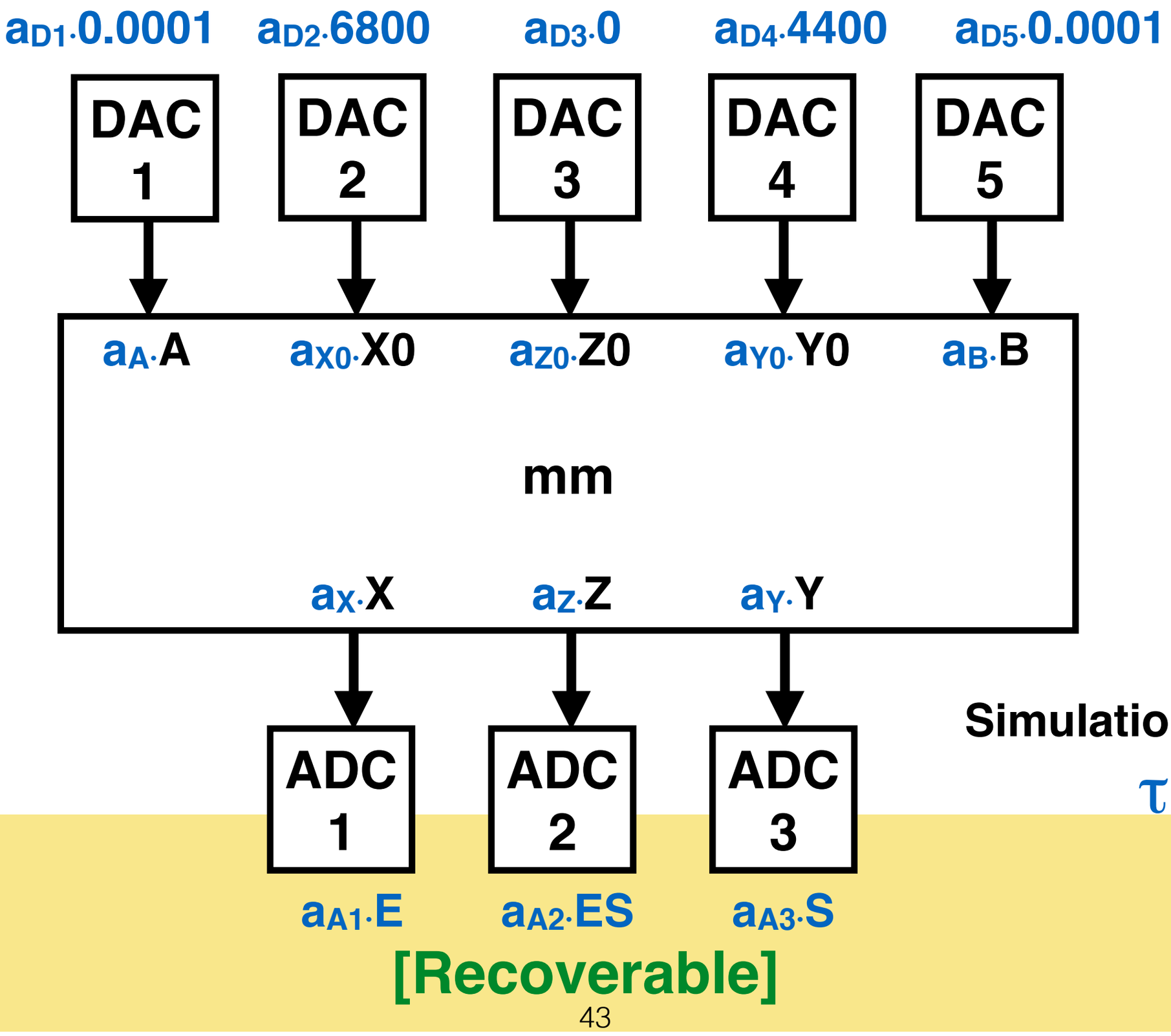
All of the internal signals fall in the port operating ranges



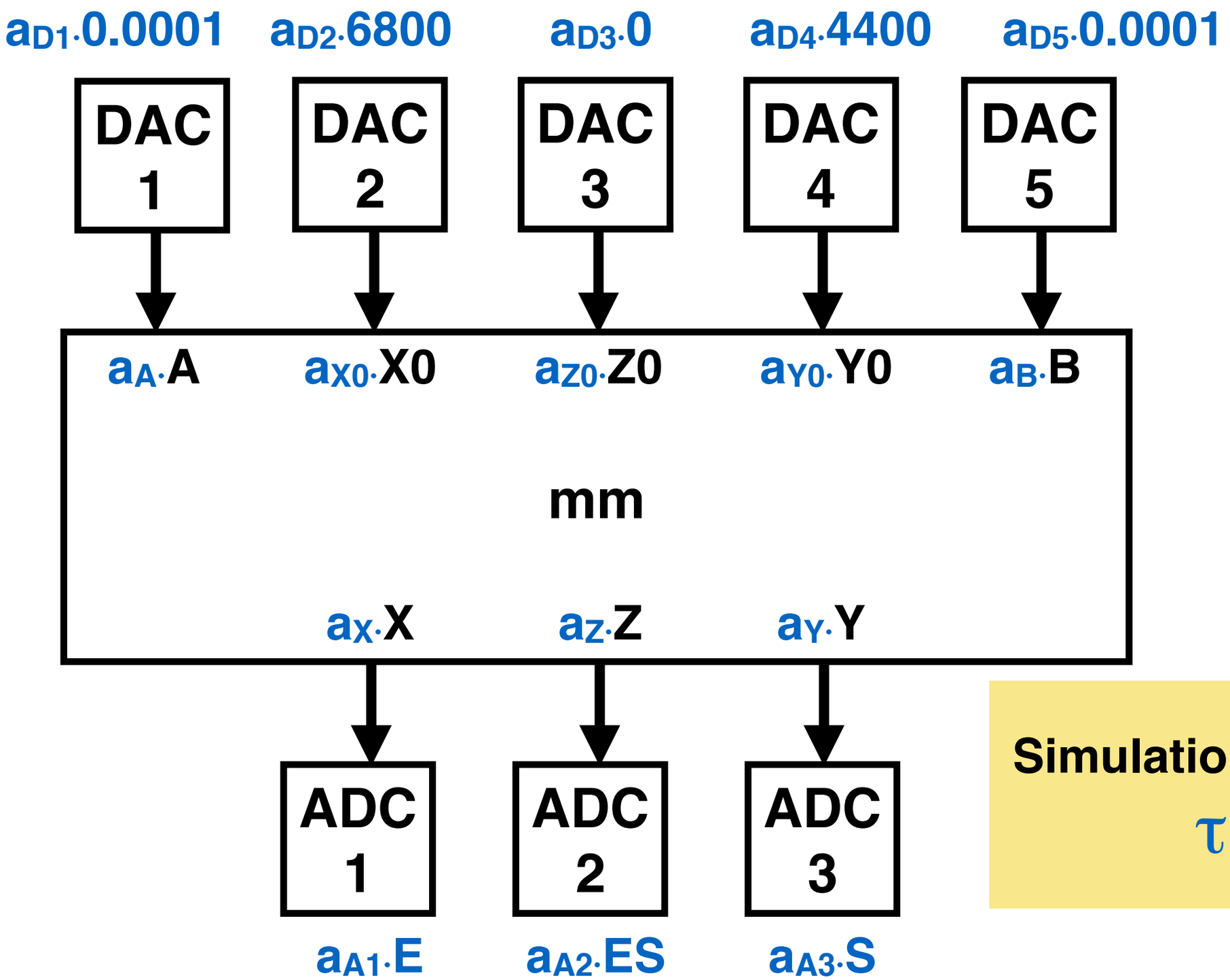
[Physically Realizable]


a_{D1}·0.0001
a_{D2}·6800
a_{D3}·0
a_{D4}·4400
a_{D5}·0.0001
DAC 1
DAC 2
DAC 3
DAC 4
DAC 5
a_A·A
a_{X0}·X0
a_{Z0}·Z0
a_{Y0}·Y0
a_B·B
mm
a_X·X
a_Z·Z
a_Y·Y
ADC 1
ADC 2
ADC 3
a_{A1}·E
a_{A2}·ES
a_{A3}·S
Simulation Speed
τ
[Recoverable]

Divide ADC samples by scaling factors



Multiply hardware time by τ



Simulation Speed

τ

[Recoverable]

Jaunt

- **<u>Objective</u>**: Find numerical assignments for scaling factors that produces fastest simulation

  - <u>Scaling Factors</u>: $\tau, a_{D1}, \ldots, a_{D5}, a_{A1}, \ldots, a_{A3}, a_{A}, \ldots, a_{Z}$

  - <u>Values</u>: real numbers > 0

Jaunt

- **Objective**: Find numerical assignments for scaling factors that produces fastest simulation

  - Scaling Factors: $\tau, a_{D1}, \ldots, a_{D5}, a_{A1}, \ldots, a_{A3}, a_{A}, \ldots, a_{Z}$

    - Values: real numbers > 0

- **Geometric Program**: Convex optimization problem

  - Device Configuration → Geometric Program

Geometric Program Generation

maximize T

subject to:

Operating Range Constraints

Sampling Constraints

} **physically realizable**

Connection Constraints

Factor Constraints

} **recoverable**

Geometric Program Generation

maximize τ

subject to:

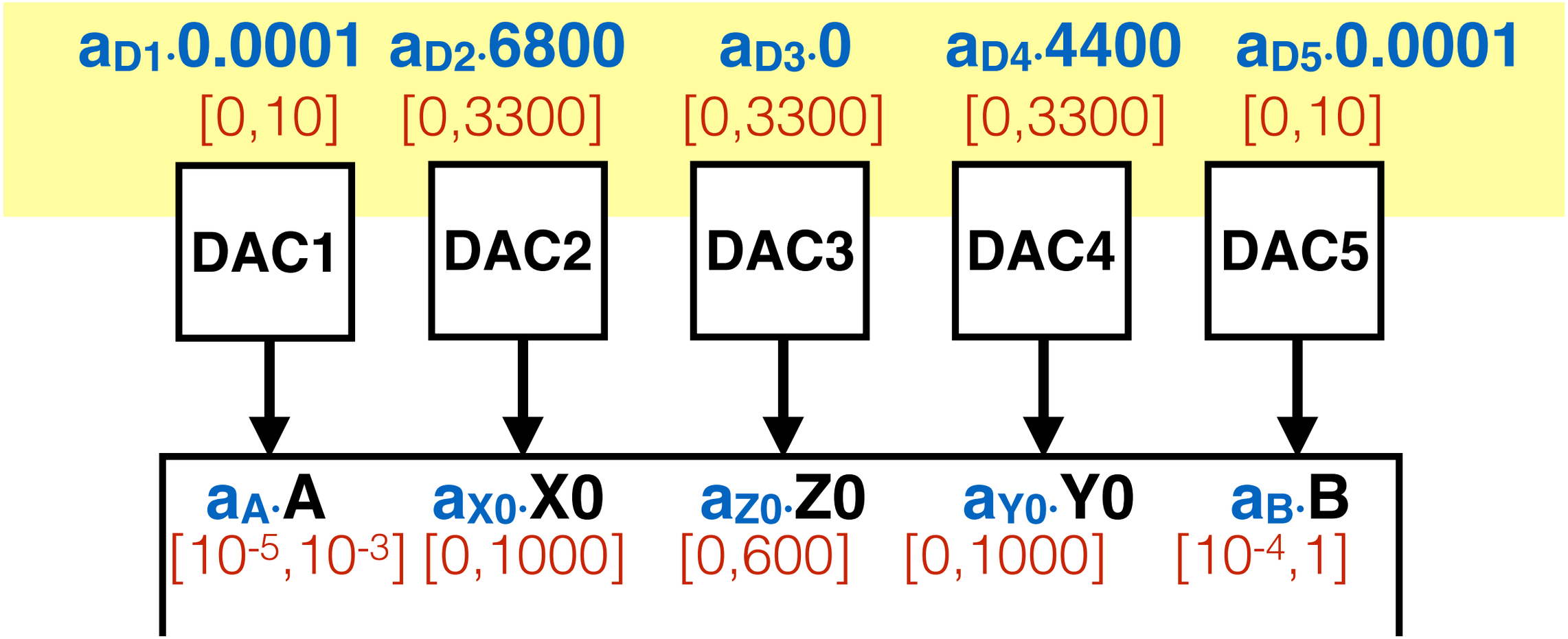
Operating Range Constraints } **physically realizable**

Sampling Constraints

Connection Constraints } **recoverable**

Factor Constraints

Operating Range Constraints



a_{D1}·0.0001 ∈ [0,10]

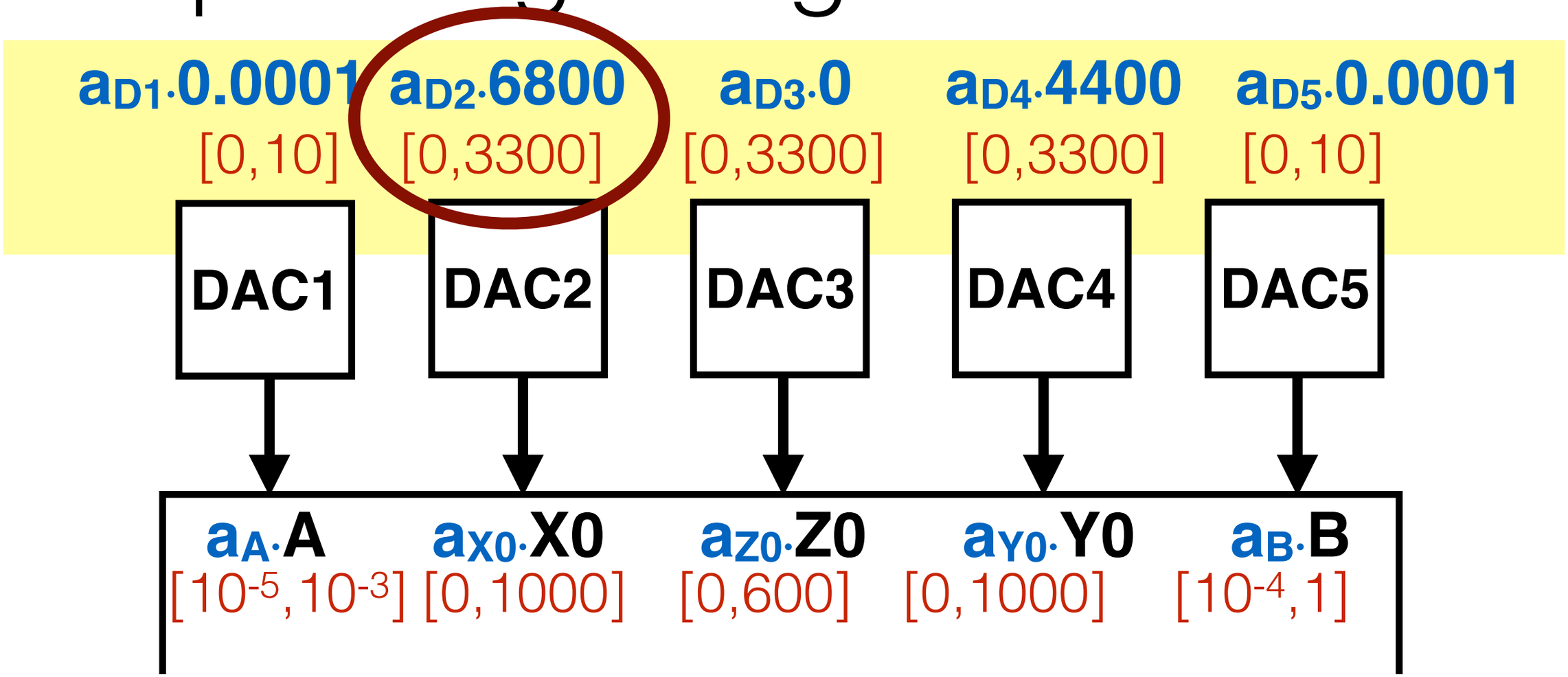
a_{D2}·6800 ∈ [0,3300]

a_{D3}·0 ∈ [0,3300]

a_{D4}·4400 ∈ [0,3300]

a_{D5}·0.0001 ∈ [0,10]

Operating Range Constraints



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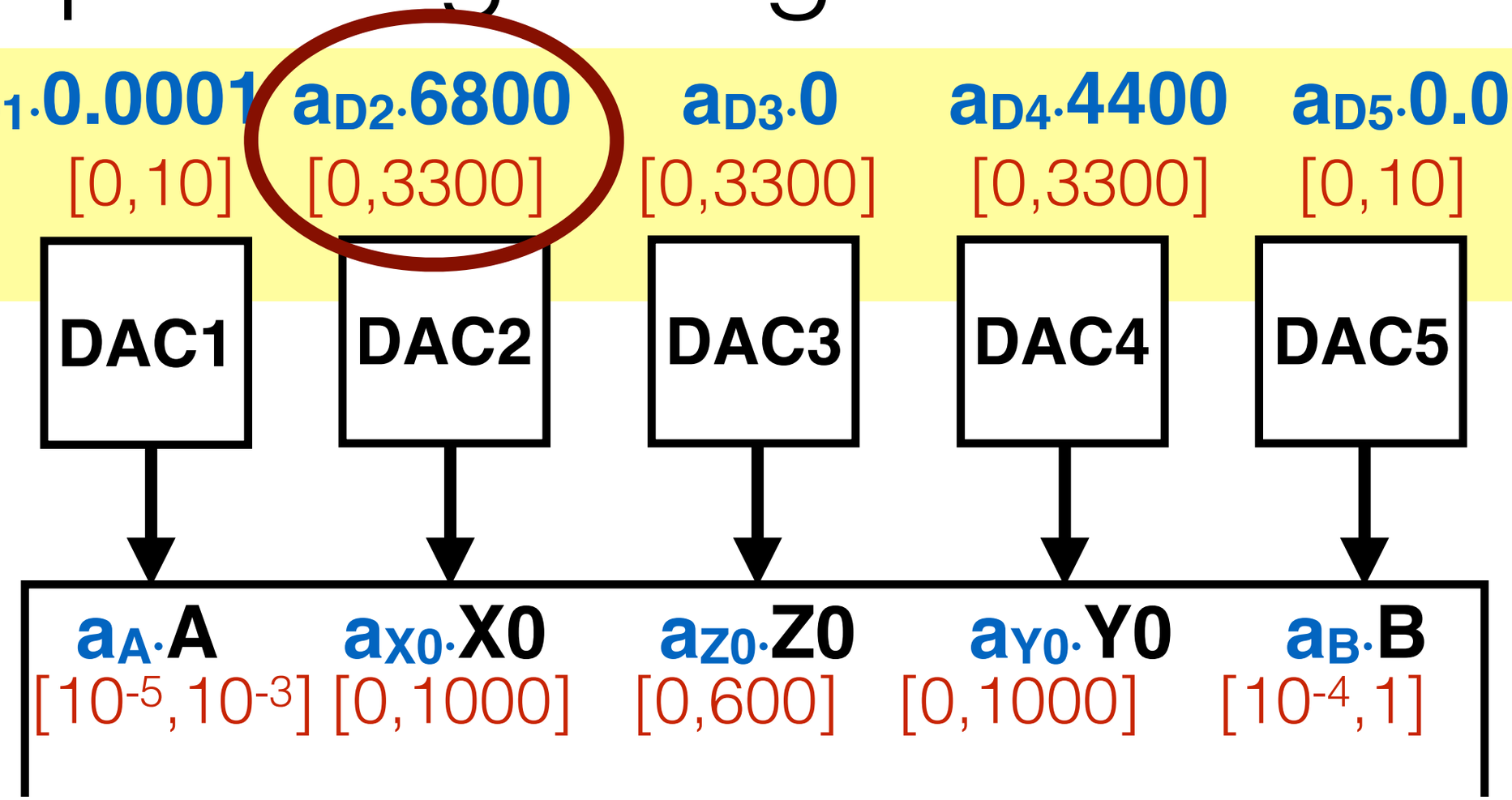
a_{D5}·0.0001 ∈ [0,10]

Operating Range Constraints



a_{D1}·0.0001 ∈ [0,10]

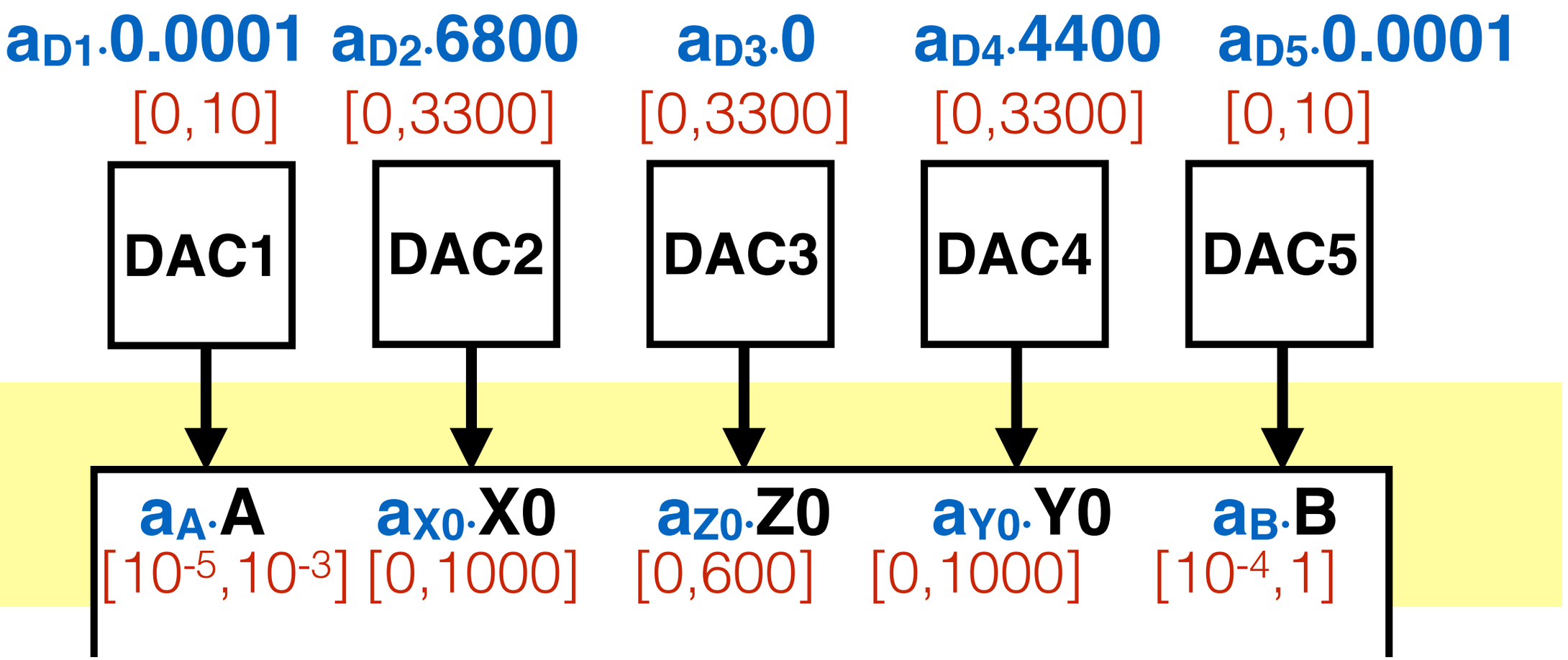
a_{D2}·6800 ∈ [0,3300]

a_{D3}·0 ∈ [0,3300]

a_{D4}·4400 ∈ [0,3300]

a_{D5}·0.0001 ∈ [0,10]

Operating Range Constraints



$a_A \cdot 0.0001 \in [10^{-5}, 10^{-3}]$

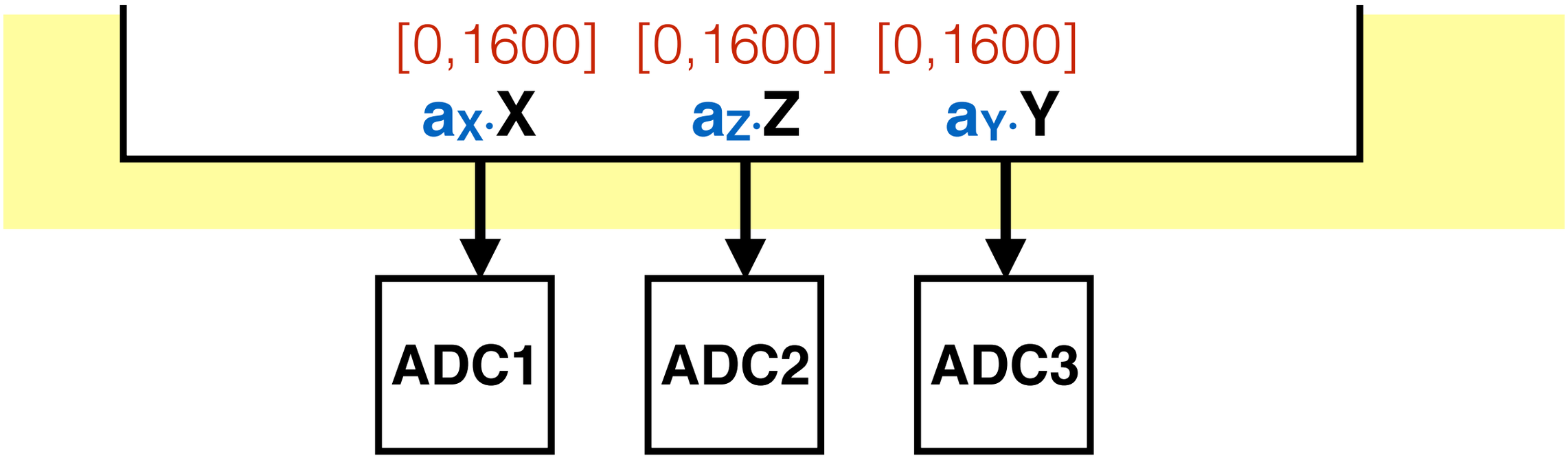
$a_{X0} \cdot 6800 \in [0,1000]$

$a_{Z0} \cdot 0 \in [0,600]$

$a_{Y0} \cdot 4400 \in [0,1000]$

$a_B \cdot 0.0001 \in [10^{-4}, 1]$

Operating Range Constraints



[0,3300] [0,3300] [0,3300]

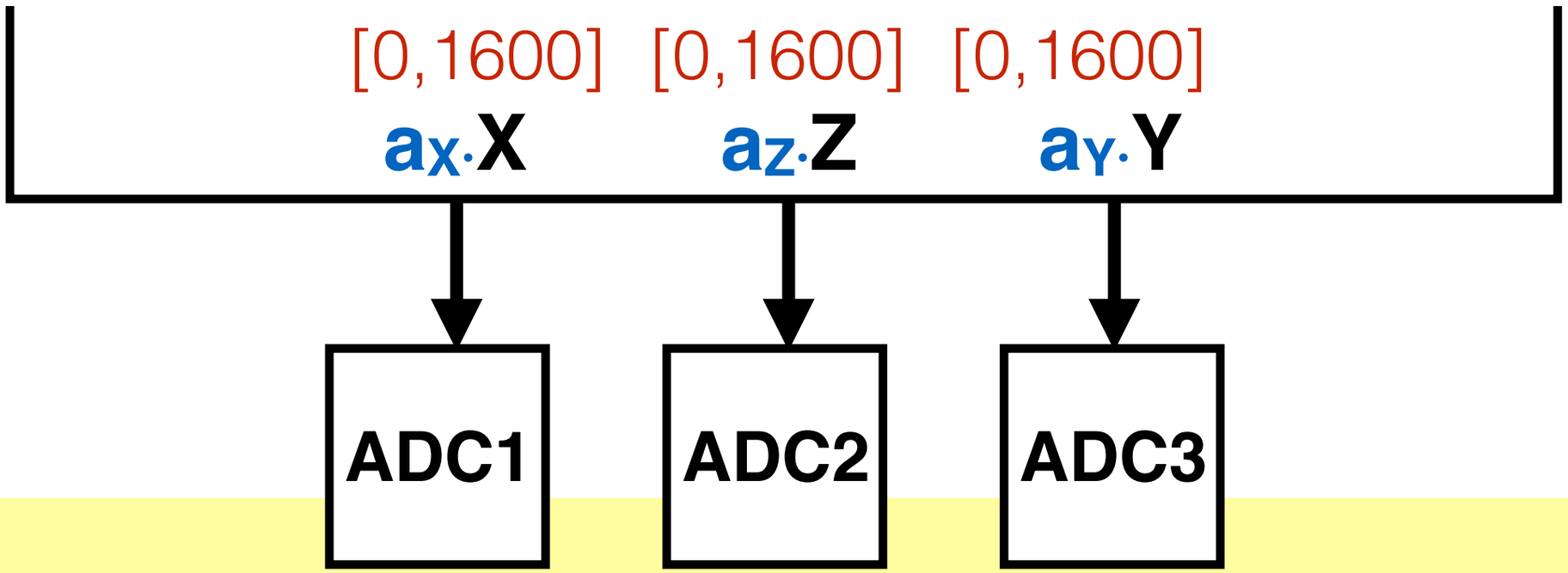
a_{A1}·E a_{A2}·ES a_{A3}·S

$a_X \cdot [0,6800] \subseteq [0,1600]$

$a_Z \cdot [0,4400] \subseteq [0,1600]$

$a_Y \cdot [0,4400] \subseteq [0,1600]$

Operating Range Constraints



[0,3300] [0,3300] [0,3300]

a_{A1}·E a_{A2}·ES a_{A3}·S

$$a_{A1}\cdot[0,6800] \subseteq [0,3300]$$

$$a_{A2}\cdot[0,4400] \subseteq [0,3300]$$

$$a_{A3}\cdot[0,4400] \subseteq [0,3300]$$

Geometric Program Generation

maximize τ

subject to:

Operating Range Constraints

Sampling Constraints

} **physically realizable**

Connection Constraints

Factor Constraints

} **recoverable**

Geometric Program Generation

maximize τ

subject to:

Operating Range Constraints

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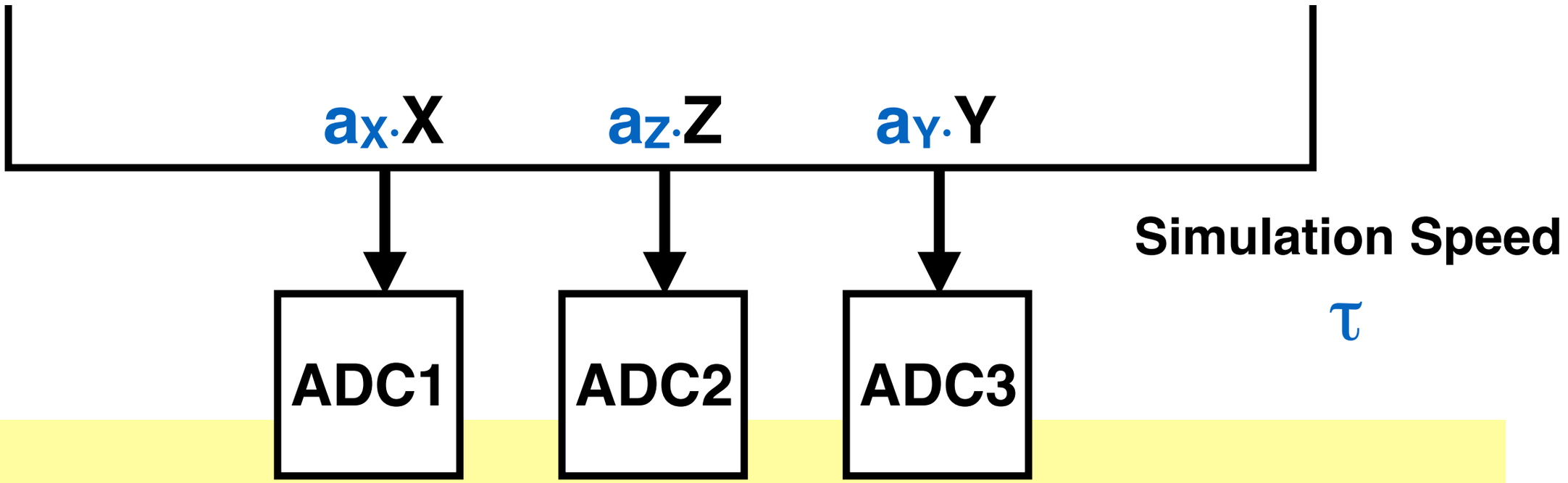
Factor Constraints

} **physically realizable**

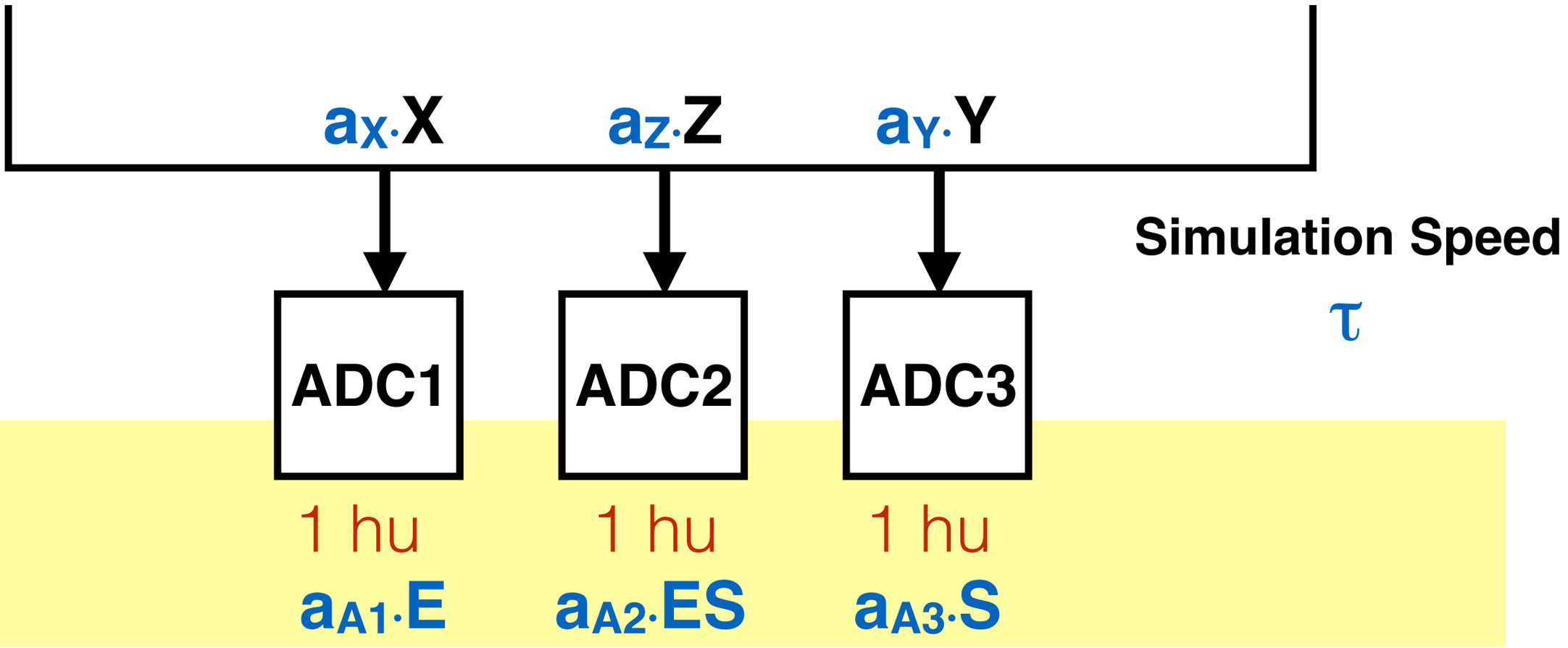
} **recoverable**

Sampling Constraints



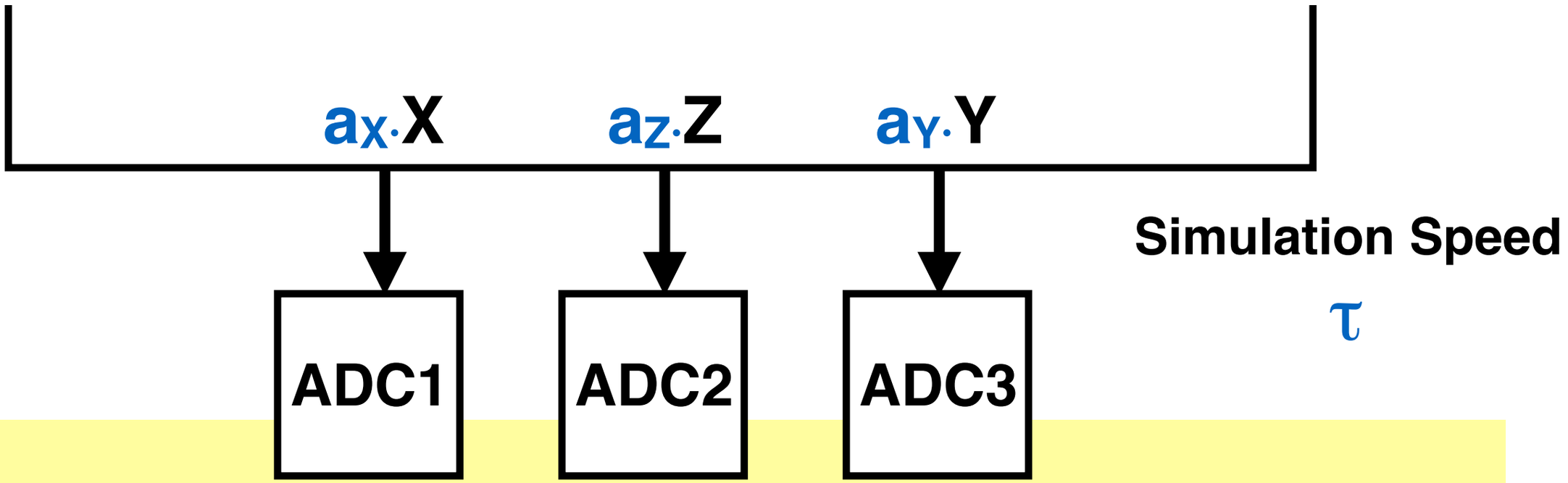
$$1\ \text{hu} \cdot \tau \leq 0.5\ \text{su}$$

Sampling Constraints



$$1\ \text{hu} \cdot \tau \leq 0.5\ \text{su} \qquad \tau\text{: hu} \rightarrow \text{su}$$

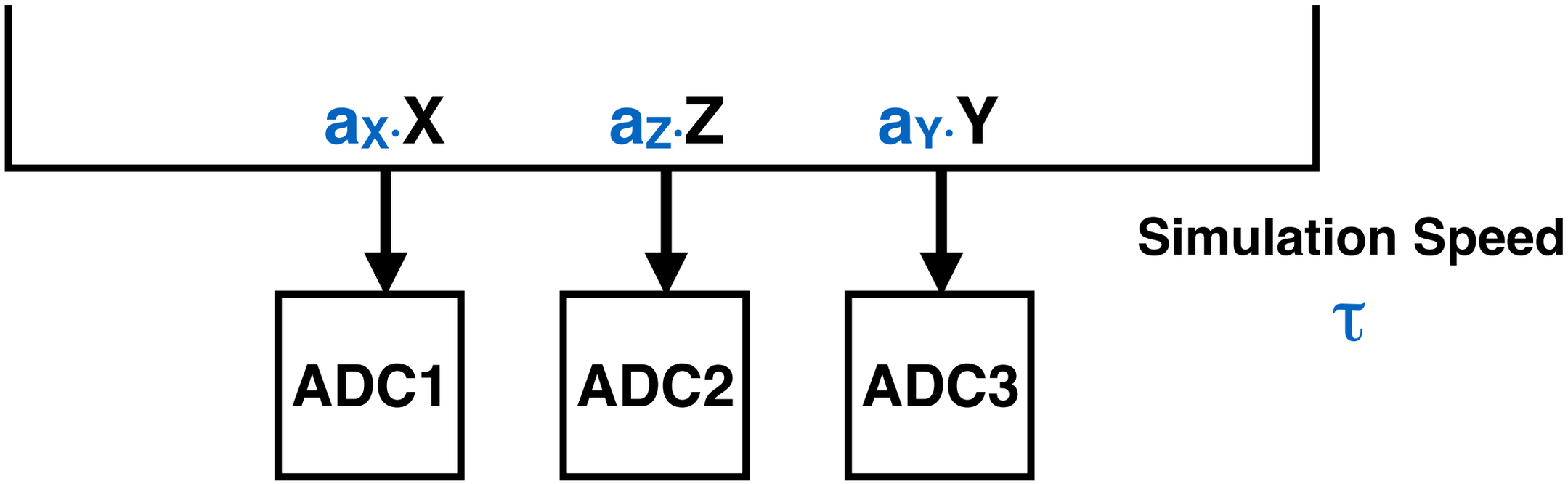
Sampling Constraints



$$1\ \text{hu} \cdot \tau \leq 0.5\ \text{su} \qquad \tau\text{: hu} \rightarrow \text{su}$$

time between simulation observations (su)

Sampling Constraints



$$1\ \text{hu} \cdot \tau \leq 0.5\ \text{su} \qquad \tau\text{: hu} \rightarrow \text{su}$$

user defined maximum time between samples

Limits simulation speed

Improves sample fidelity

Geometric Program Generation

maximize T

subject to:

Operating Range Constraints

Sampling Constraints

} **physically realizable**

Connection Constraints

Factor Constraints

} **recoverable**

Geometric Program Generation

maximize τ

subject to:

Operating Range Constraints

Sampling Constraints

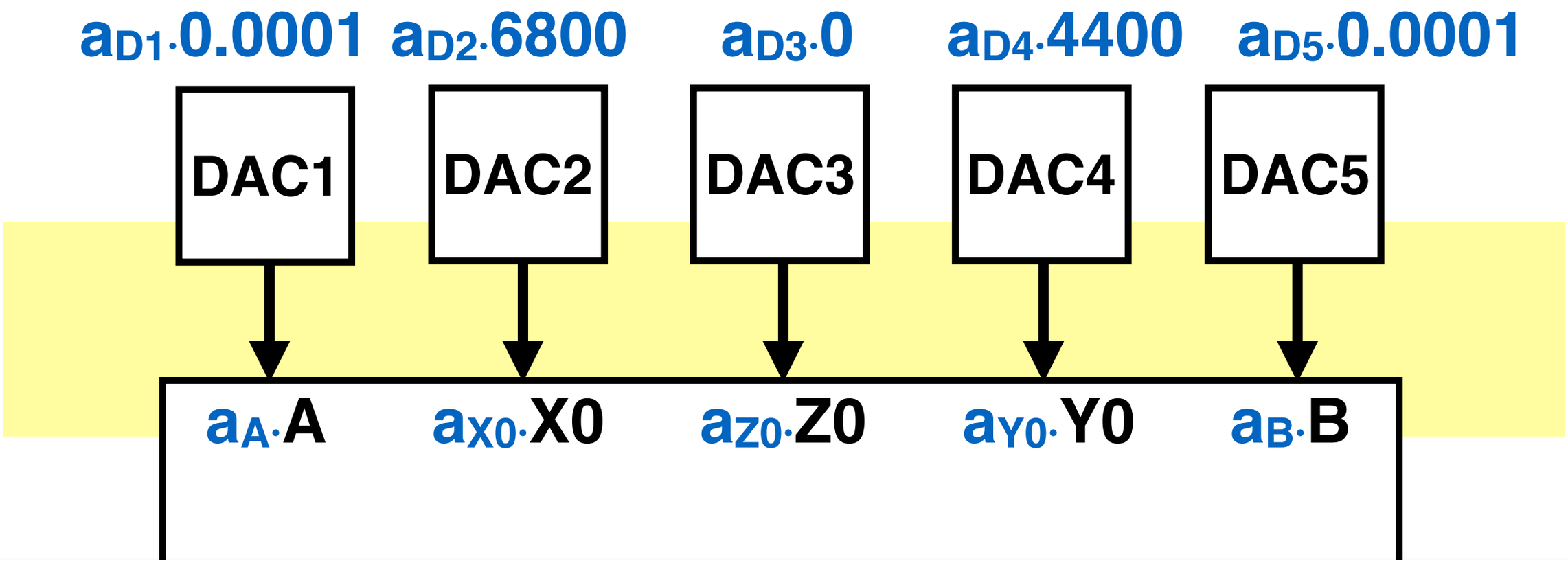
Connection Constraints

Factor Constraints

} **physically realizable**

} **recoverable**

Connection Constraints



$a_{D1} = a_A$

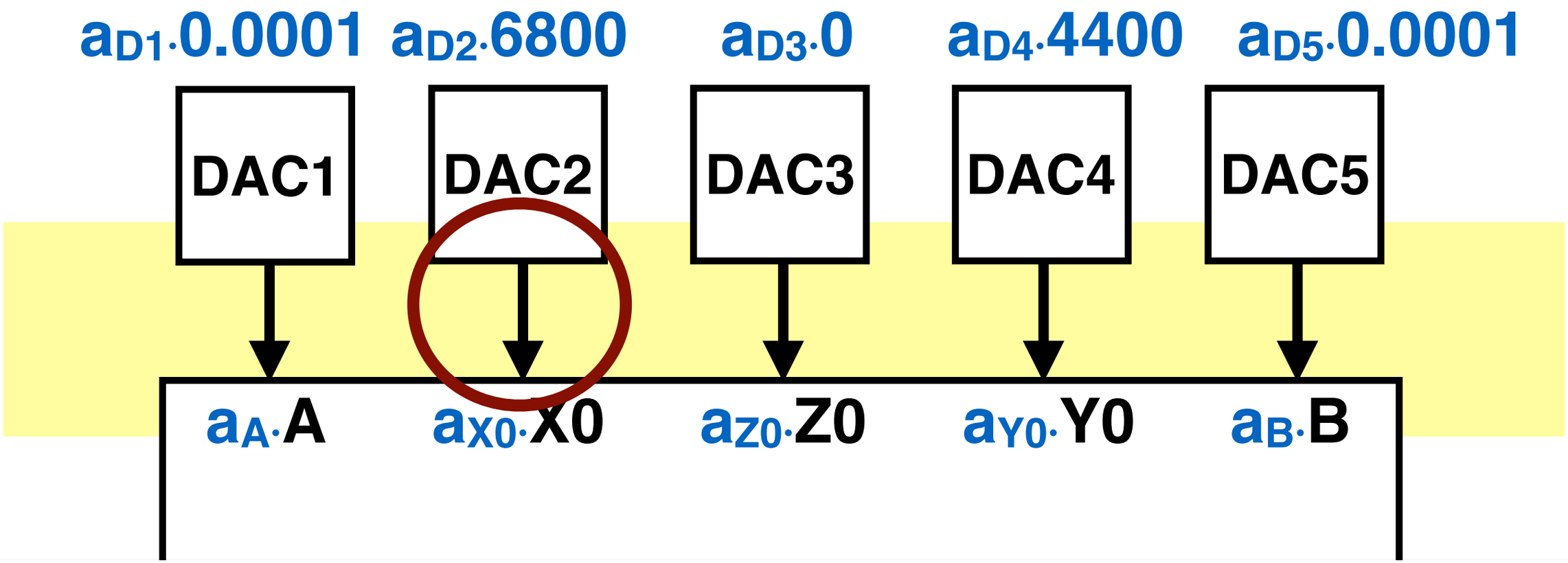
$a_{D2} = a_{X0}$

$a_{D3} = a_{Z0}$

$a_{D4} = a_{Y0}$

$a_{D5} = a_B$

Connection Constraints



$a_{D1} = a_A$

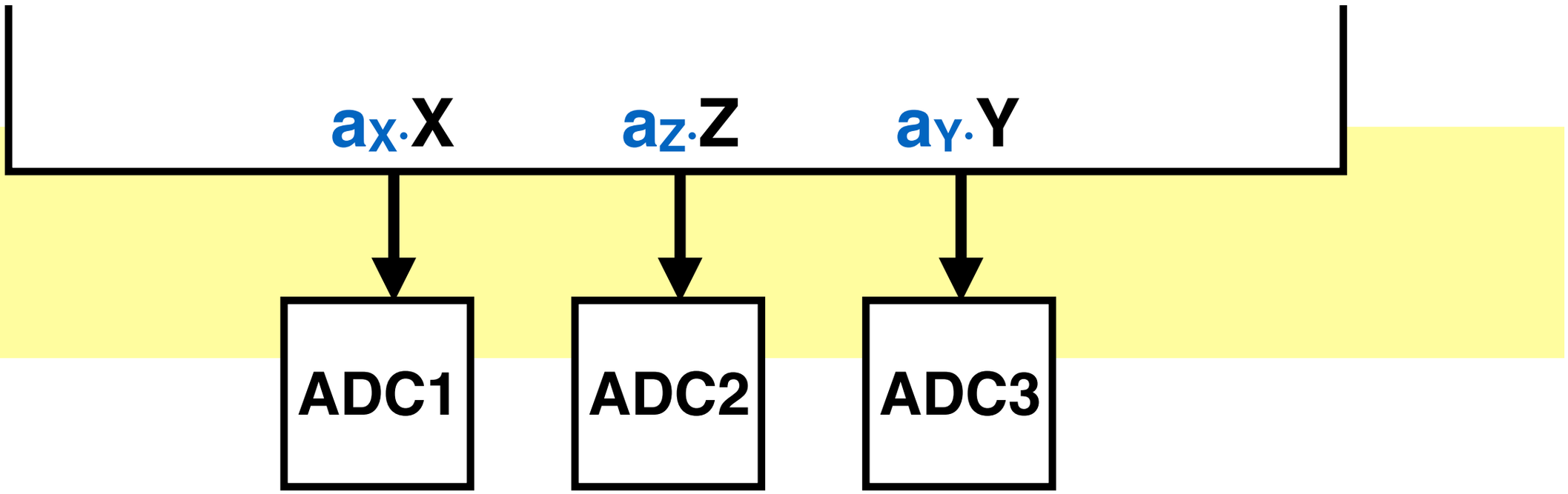
$a_{D2} = a_{X0}$

$a_{D3} = a_{Z0}$

$a_{D4} = a_{Y0}$

$a_{D5} = a_B$

Connection Constraints



$a_{A1} \cdot E$ $a_{A2} \cdot ES$ $a_{A3} \cdot S$

$a_X = a_{A1}$ $a_Z = a_{A2}$ $a_Y = a_{A3}$

Geometric Program Generation

maximize T

subject to:

Operating Range Constraints

Sampling Constraints

} **physically realizable**

Connection Constraints

Factor Constraints

} **recoverable**

Geometric Program Generation

maximize T

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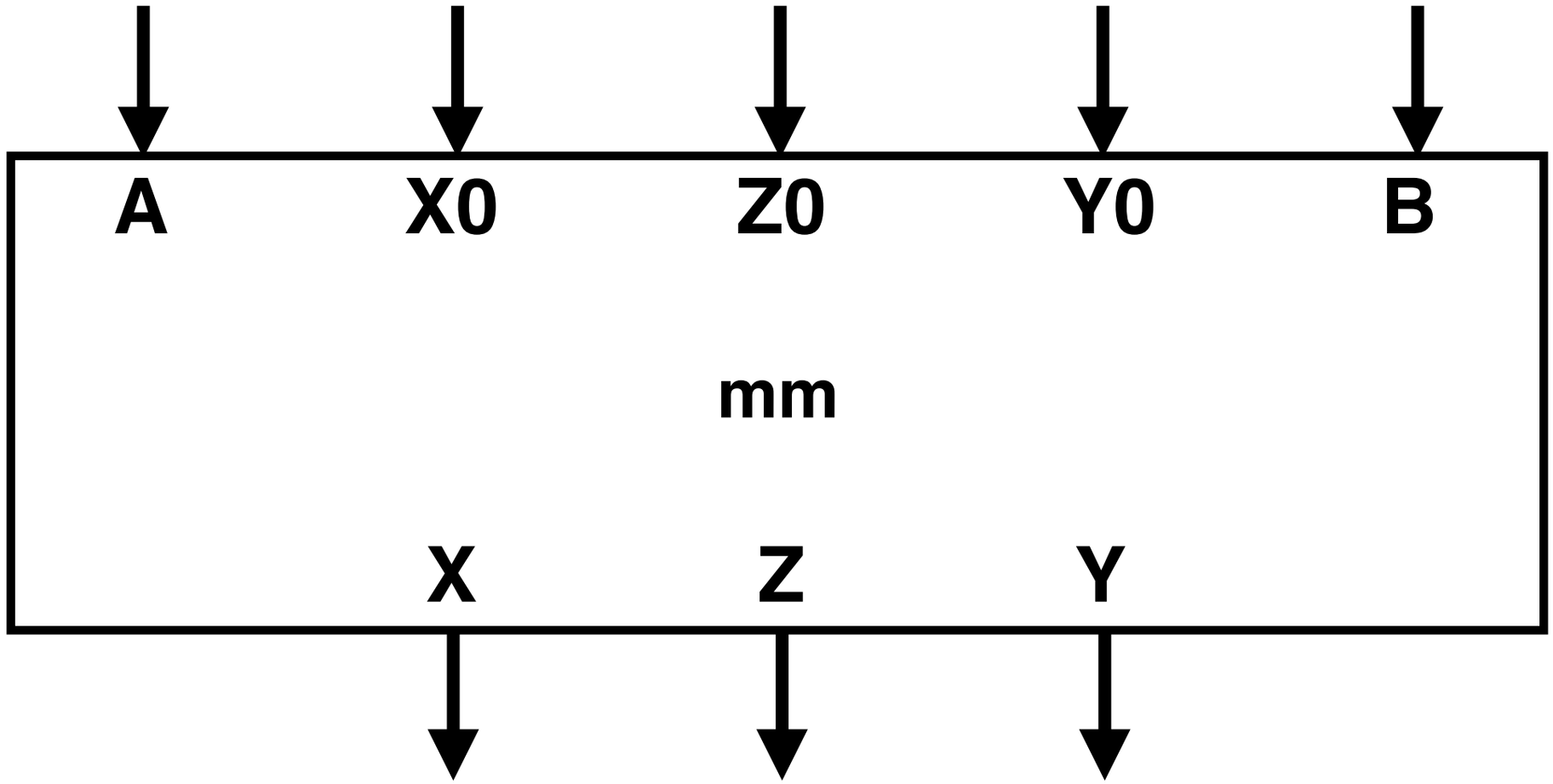
Factor Constraints

} **recoverable**

Factor Constraints



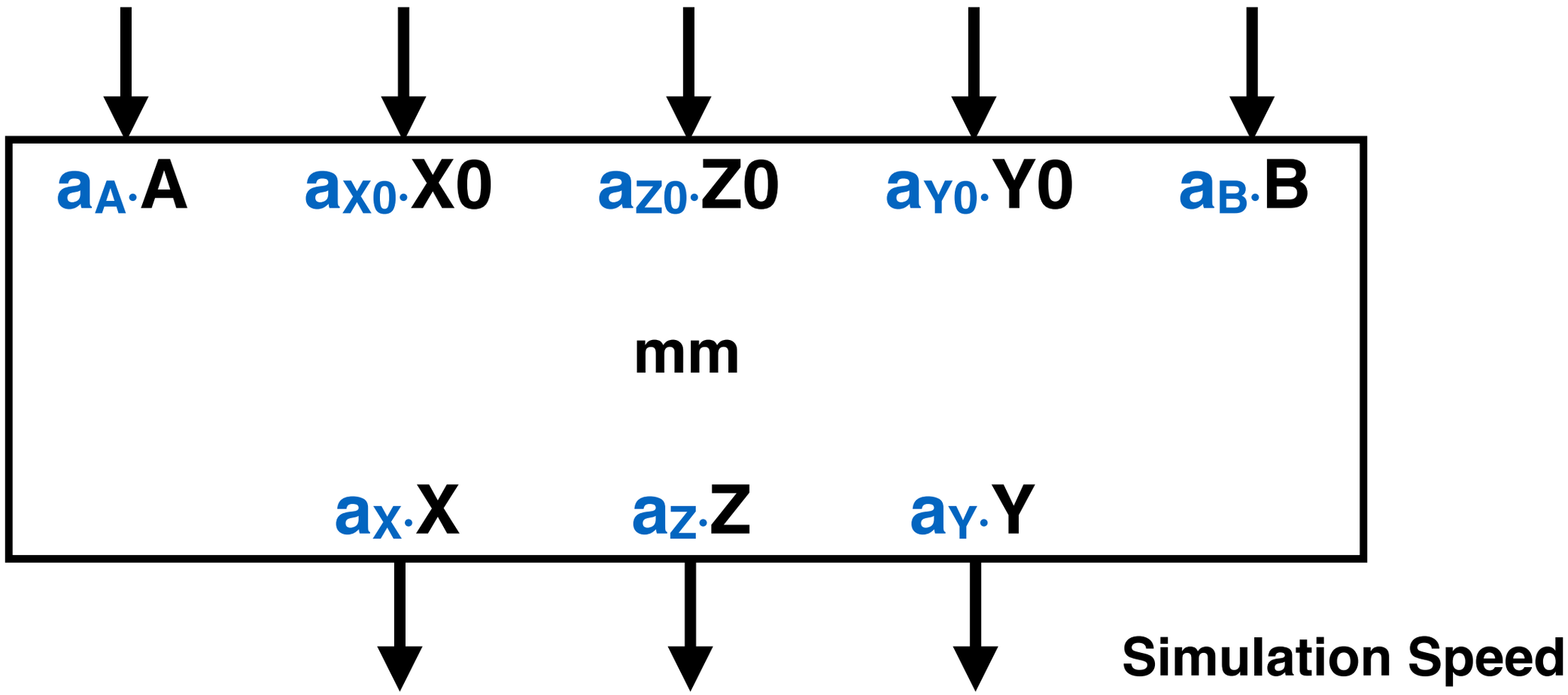
$$X = X0 - Z$$

$$Y = Y0 - Z$$

$$Z = \int A \cdot X \cdot Y - B \cdot Z \, dt$$

$$Z = Z0 \ @ \ t=0$$

Factor Constraints



$$a_X X = a_{X0} X0 - a_Z Z$$

$$a_Y Y = a_{Y0} Y0 - a_Z Z$$

$$a_Z Z = \int [a_A A \cdot a_X X \cdot a_Y Y - a_B B \cdot a_Z Z \,] \, \tau^{-1} \, dt$$

$$a_Z Z = a_{Z0} Z0 \;@\; t=0$$

Factor Constraints

$$a_X X = a_{X0} X0 - a_Z Z$$

Factor Constraints

$$a_X X = a_{X0}[X0 - Z]$$

$$\mathbf{a_{X0} = a_Z}$$

Factor Constraints

$$a_X[X = X0–Z]$$

$a_{X0} = a_Z$ $a_X = a_{X0}$

Factor Constraints

$$a_X[X = X0 - Z]$$

$$\mathbf{a_{X0} = a_Z} \qquad\qquad \mathbf{a_X = a_{X0}}$$

$$a_Y Y = a_{Y0} Y0 - a_Z Z$$

Factor Constraints

$$a_X[X = X0 - Z]$$

$a_{X0} = a_Z$ $\qquad$ $a_X = a_{X0}$

$$a_Y[Y = Y0 - Z]$$

$a_{Y0} = a_Y$ $\qquad$ $a_{Y0} = a_Z$

Factor Constraints

$$a_X[X = X0 - Z]$$

$$a_{X0} = a_Z \qquad a_X = a_{X0}$$

$$a_Y[Y = Y0 - Z]$$

$$a_{Y0} = a_Y \qquad a_{Y0} = a_Z$$

$$a_Z Z = \int [a_A A \cdot a_X X \cdot a_Y Y - a_B B \cdot a_Z Z\ ]\ \tau^{-1}\ dt$$

Factor Constraints

$$a_X[X = X0 - Z]$$

$$\mathbf{a_{X0} = a_Z} \qquad \mathbf{a_X = a_{X0}}$$

$$a_Y[Y = Y0 - Z]$$

$$\mathbf{a_{Y0} = a_Y} \qquad \mathbf{a_{Y0} = a_Z}$$

$$a_Z Z = \int a_B \cdot a_Z [A \cdot X \cdot Y - B \cdot Z] \tau^{-1} dt$$

$$\mathbf{a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z}$$

Factor Constraints

$$a_X[X = X0 - Z]$$

$$\mathbf{a_{X0} = a_Z} \qquad \mathbf{a_X = a_{X0}}$$

$$a_Y[Y = Y0 - Z]$$

$$\mathbf{a_{Y0} = a_Y} \qquad \mathbf{a_{Y0} = a_Z}$$

$$a_Z Z = a_B \cdot a_Z \cdot \tau^{-1} \int [A \cdot X \cdot Y - B \cdot Z] \, dt$$

$$\mathbf{a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z}$$

Factor Constraints

$$a_X[X = X0 - Z]$$

$$\mathbf{a_{X0} = a_Z} \qquad \mathbf{a_X = a_{X0}}$$

$$a_Y[Y = Y0 - Z]$$

$$\mathbf{a_{Y0} = a_Y} \qquad \mathbf{a_{Y0} = a_Z}$$

$$a_Z\,[\,Z = \int [A \cdot X \cdot Y - B \cdot Z\ dt]$$

$$\mathbf{a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z} \qquad \mathbf{a_Z = a_B \cdot a_Z \cdot \tau^{-1}}$$

Factor Constraints

$$a_X[X = X0 - Z]$$

$$a_{X0} = a_Z \qquad a_X = a_{X0}$$

$$a_Y[Y = Y0 - Z]$$

$$a_{Y0} = a_Y \qquad a_{Y0} = a_Z$$

$$a_Z\,[\,Z = \int [A \cdot X \cdot Y - B \cdot Z\ dt]$$

$$a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z \qquad a_Z = a_B \cdot a_Z \cdot \tau^{-1}$$

$$a_Z\,Z = a_{Z0}\,Z0\ @\ t{=}0$$

$$a_{Z0} = a_Z$$

Geometric Program

maximize τ

subject to:

$a_Z = a_B \cdot a_Z \cdot \tau^{-1}$

$a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z$

$a_{Y0} = a_Y$

$a_{Y0} = a_Z$

...

Geometric Programming Library (GPKit)

Convert to Convex Program

Convex Solver (cvxopt)

Numerical Assignments

$\tau = 0.50$

$a_{D1} = 8.28$

$a_A = 8.28$

$a_{D5} = 0.50$

$a_B = 0.50$

$a_{D2\text{-}D4} = 0.06$

$a_{X0} = 0.06$

$a_{Y0} = 0.06$

$a_{Z0} = 0.06$

$a_X = 0.06$

$a_Y = 0.06$

$a_Z = 0.06$

$a_{A1\text{-}A3} = 0.06$

Geometric Program

maximize τ

subject to:

$a_Z = a_B \cdot a_Z \cdot \tau^{-1}$

$a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z$

$a_{Y0} = a_Y$

$a_{Y0} = a_Z$

...

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$a_{Z0} = 0.06$

$a_X = 0.06$

$a_Y = 0.06$

$a_Z = 0.06$

$a_{A1\text{-}A3} = 0.06$

Geometric Program

maximize τ

subject to:

$a_Z = a_B \cdot a_Z \cdot \tau^{-1}$

$a_A \cdot a_X \cdot a_Y = a_B \cdot a_Z$

$a_{Y0} = a_Y$

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...

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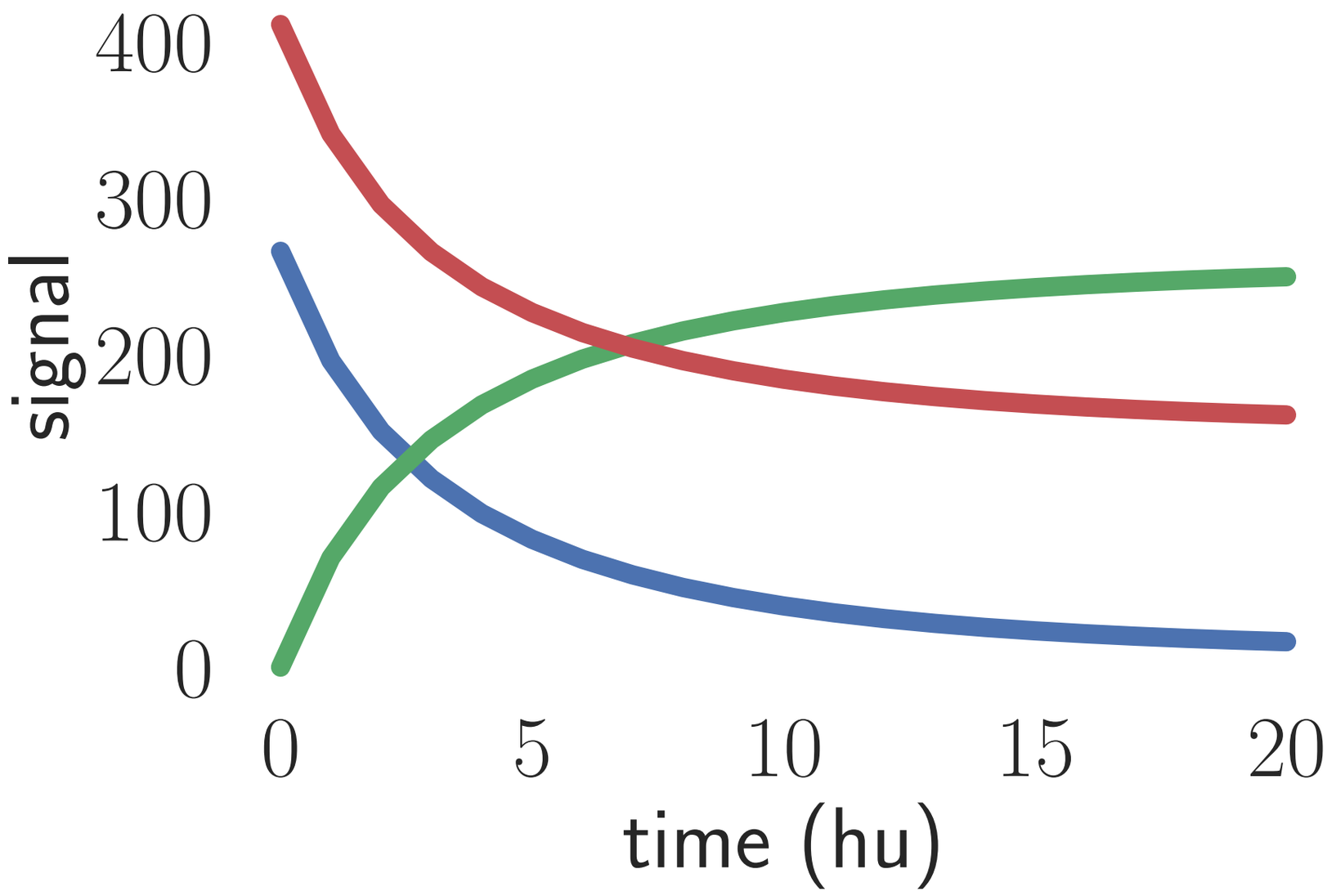
$a_{Z0} = 0.06$

$a_X = 0.06$

$a_Y = 0.06$

$a_Z = 0.06$

$a_{A1\text{-}A3} = 0.06$



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$a_{Y0} = 0.06$

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$a_Y = 0.06$

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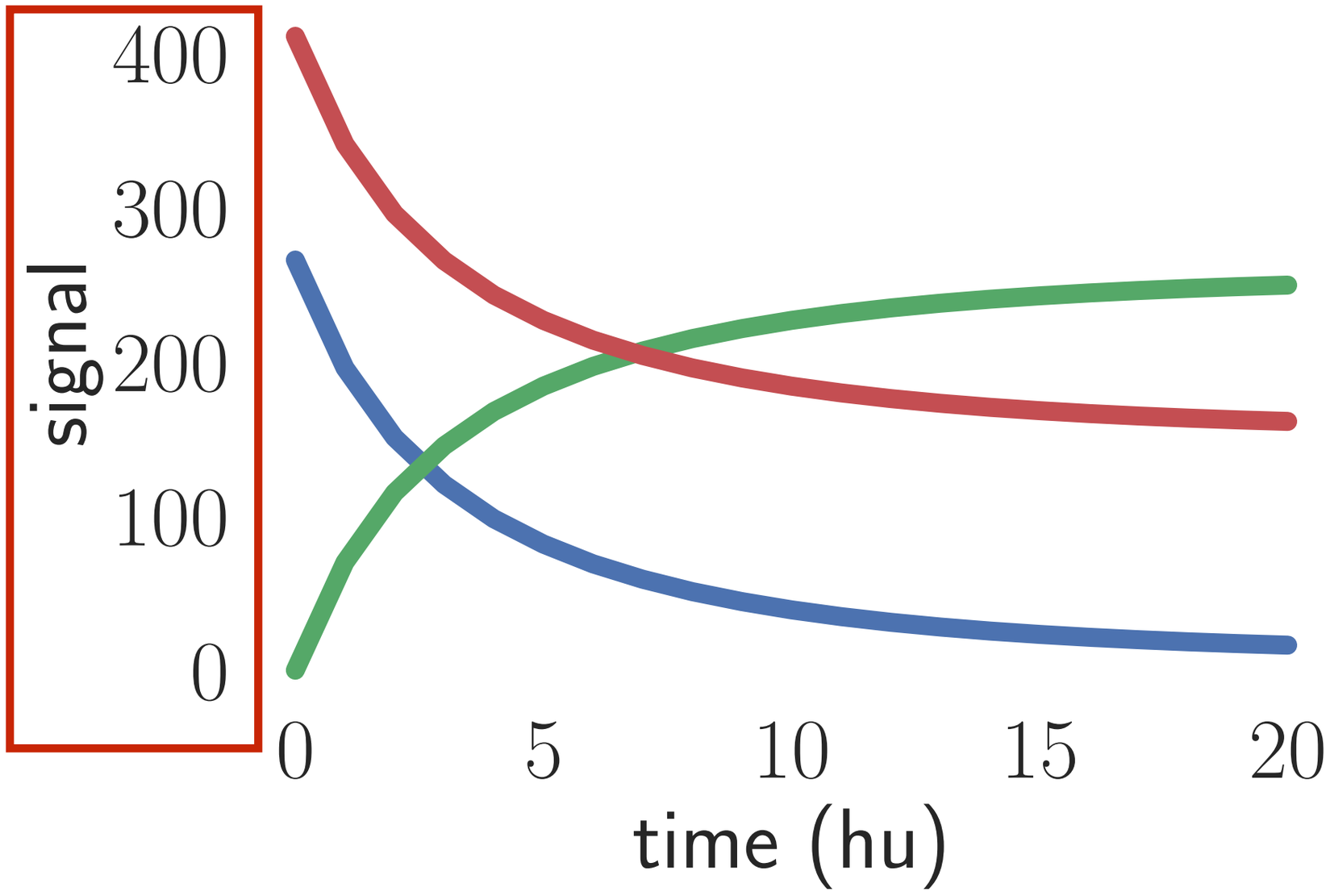

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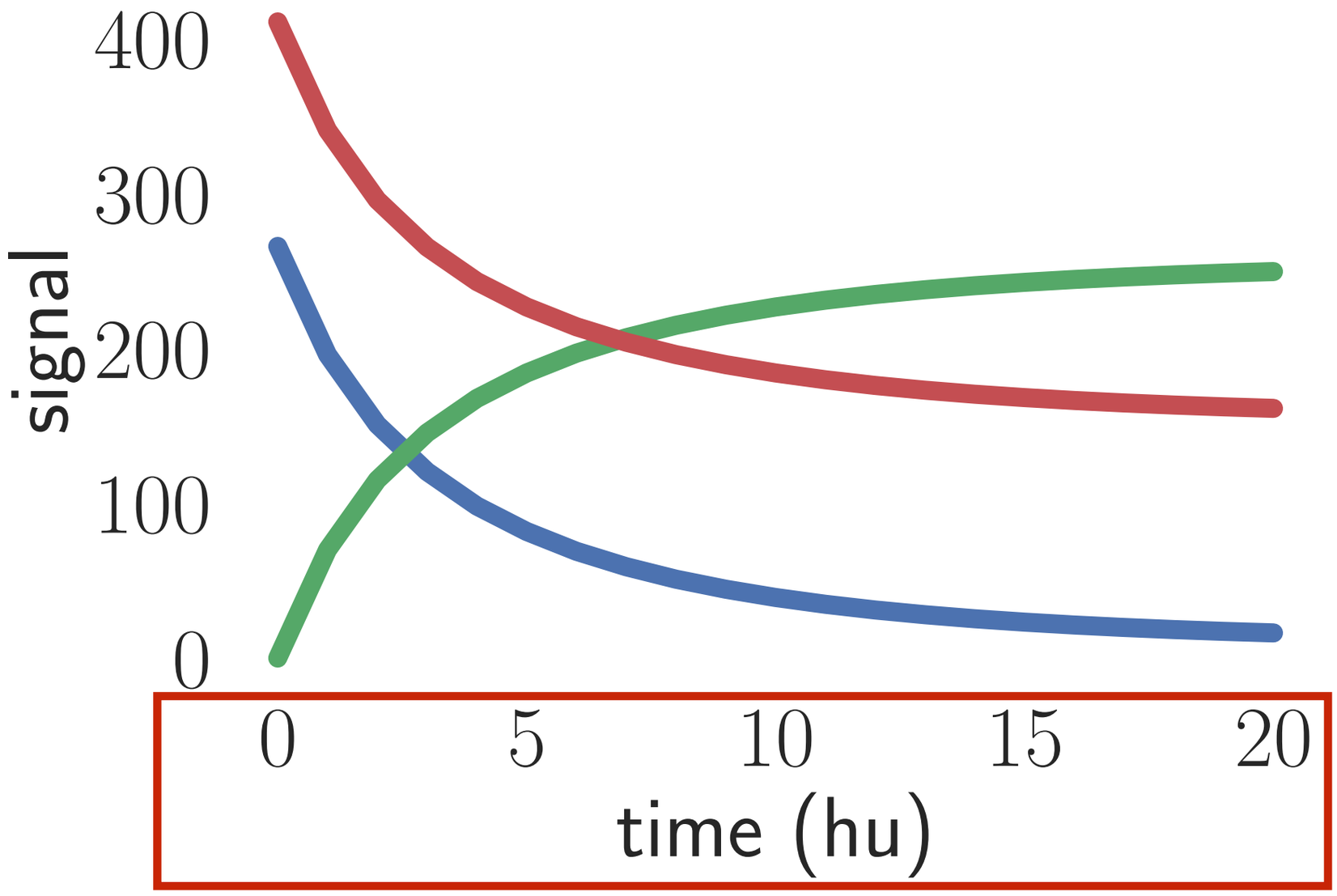

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$a_{Y0} = 0.06$

$a_{Z0} = 0.06$

$a_X = 0.06$

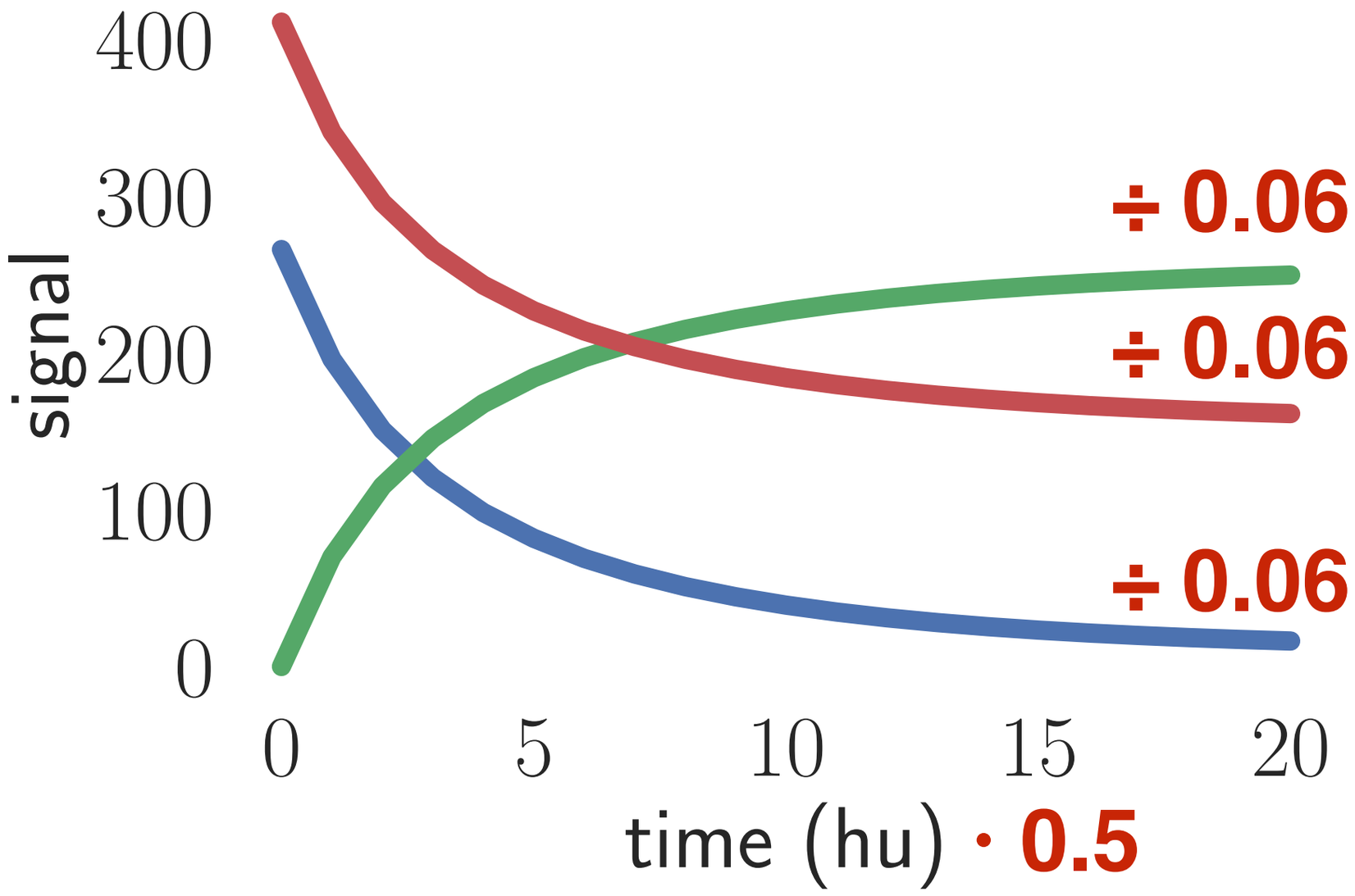
$a_Y = 0.06$

$a_Z = 0.06$

$a_{A1\text{-}A3} = 0.06$

2x slower than real-time

Recover Original Simulation



$\tau = 0.50$

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$a_B = 0.50$

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$a_{X0} = 0.06$

$a_{Y0} = 0.06$

$a_{Z0} = 0.06$

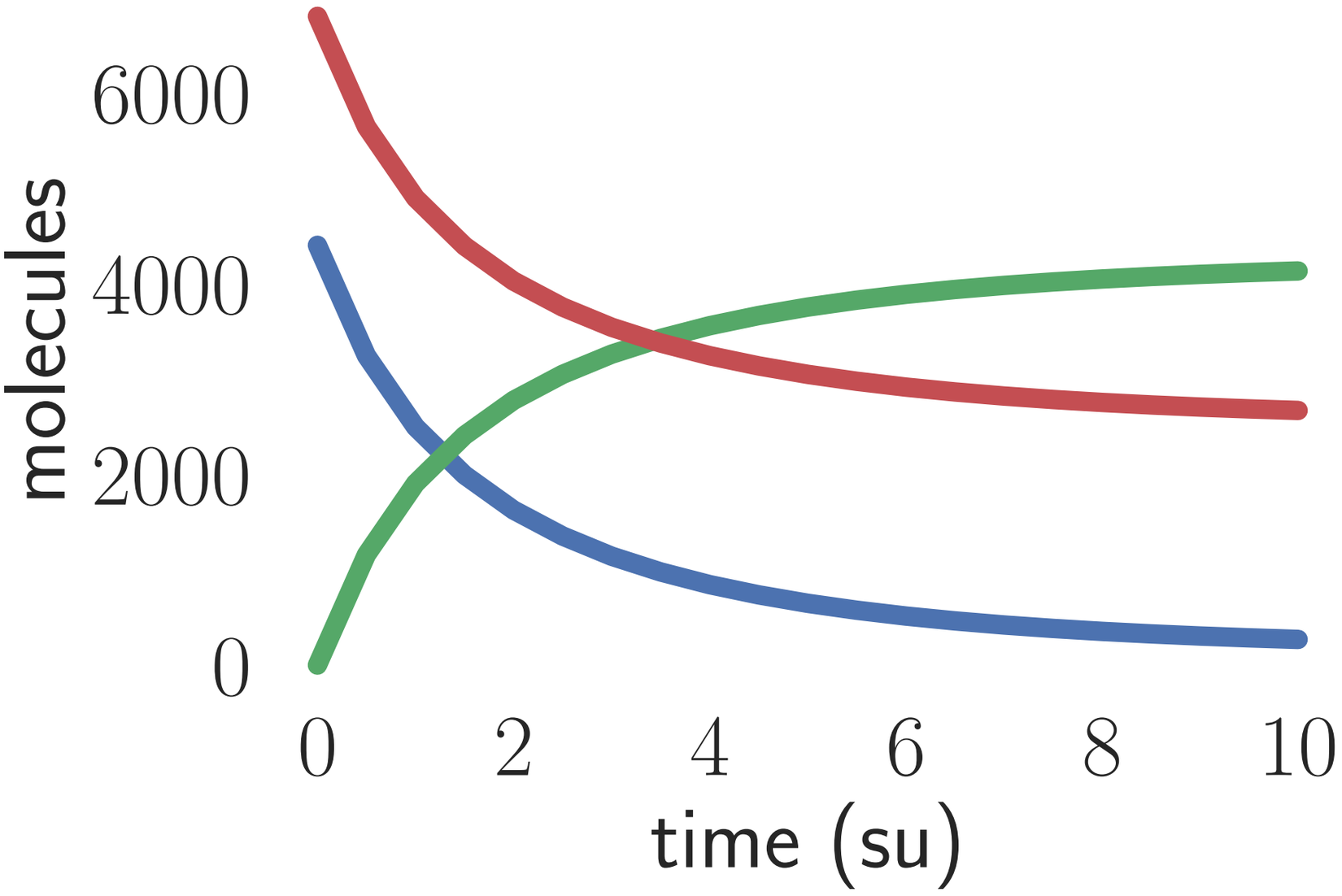
$a_X = 0.06$

$a_Y = 0.06$

$a_Z = 0.06$

$a_{A1\text{-}A3} = 0.06$

Recovered Simulation



$\tau = 0.50$

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$a_{D5} = 0.50$

$a_B = 0.50$

$a_{D2\text{-}D4} = 0.06$

$a_{X0} = 0.06$

$a_{Y0} = 0.06$

$a_{Z0} = 0.06$

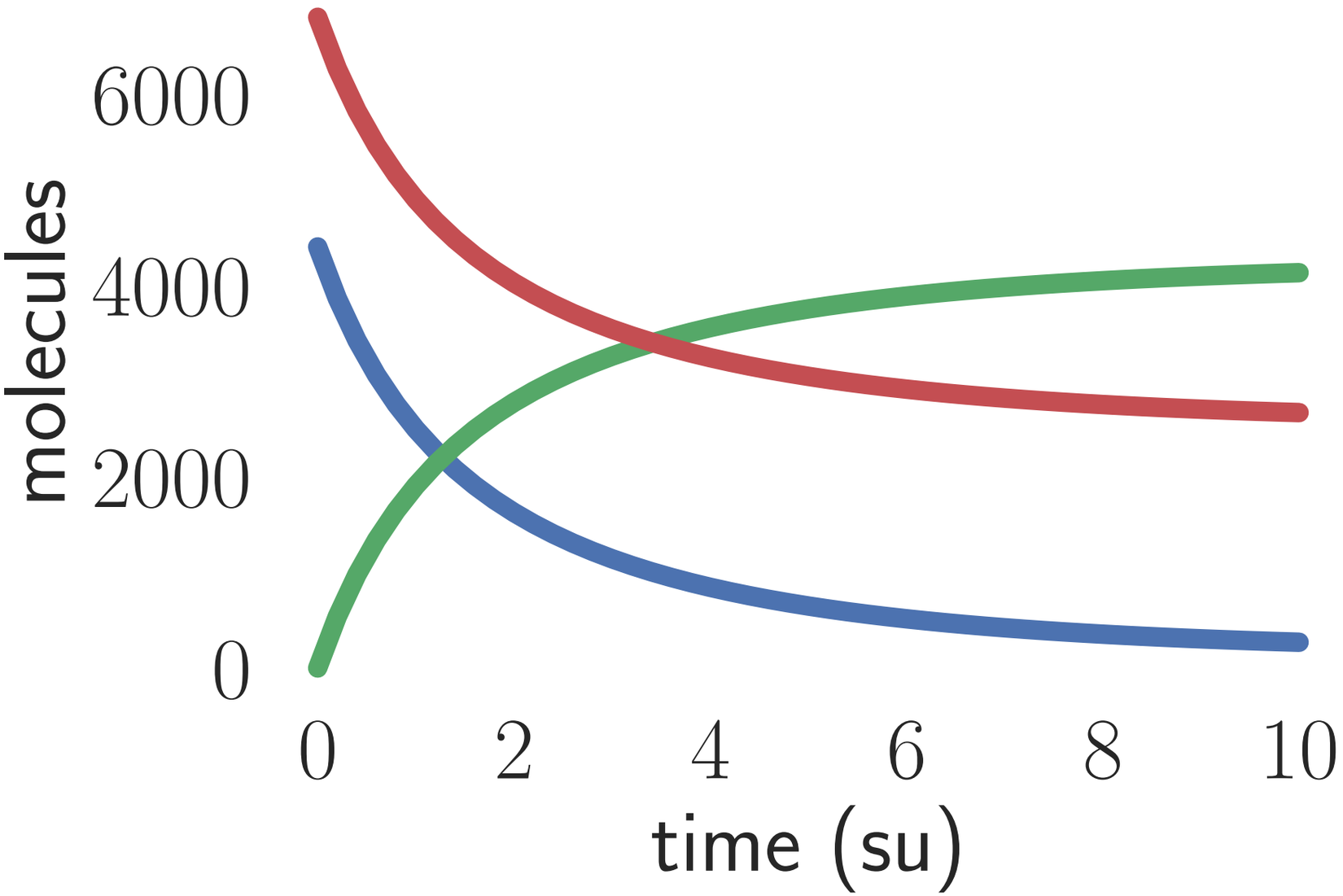
$a_X = 0.06$

$a_Y = 0.06$

$a_Z = 0.06$

$a_{A1\text{-}A3} = 0.06$

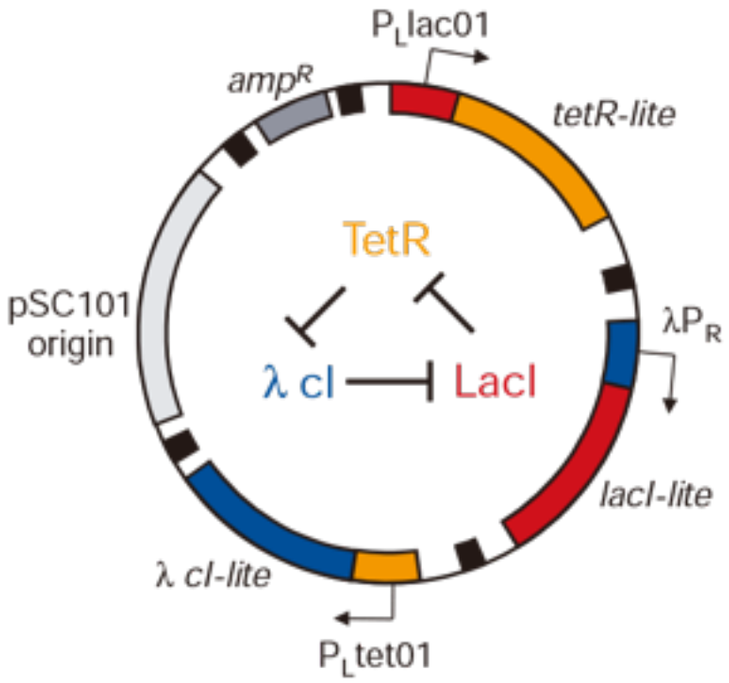
Expected Simulation

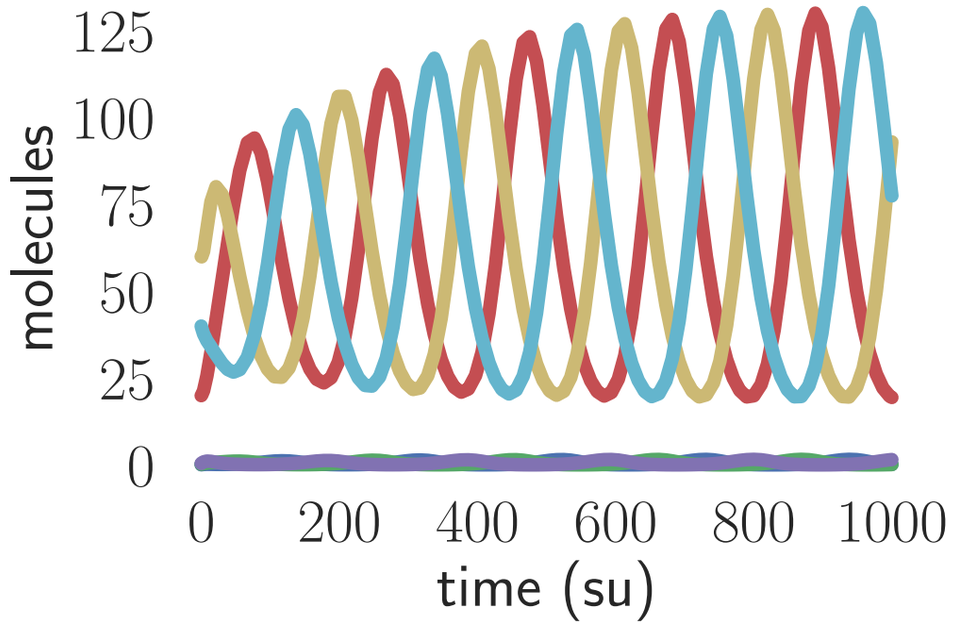


Results

reprissilator

- Gene regulatory network that generates oscillations
  - synthetic genetic clock
- Model:
  - 9 diffeqs
  - 7 parameters
- Simulation
  - time: 1000 su
  - sample: 20 su

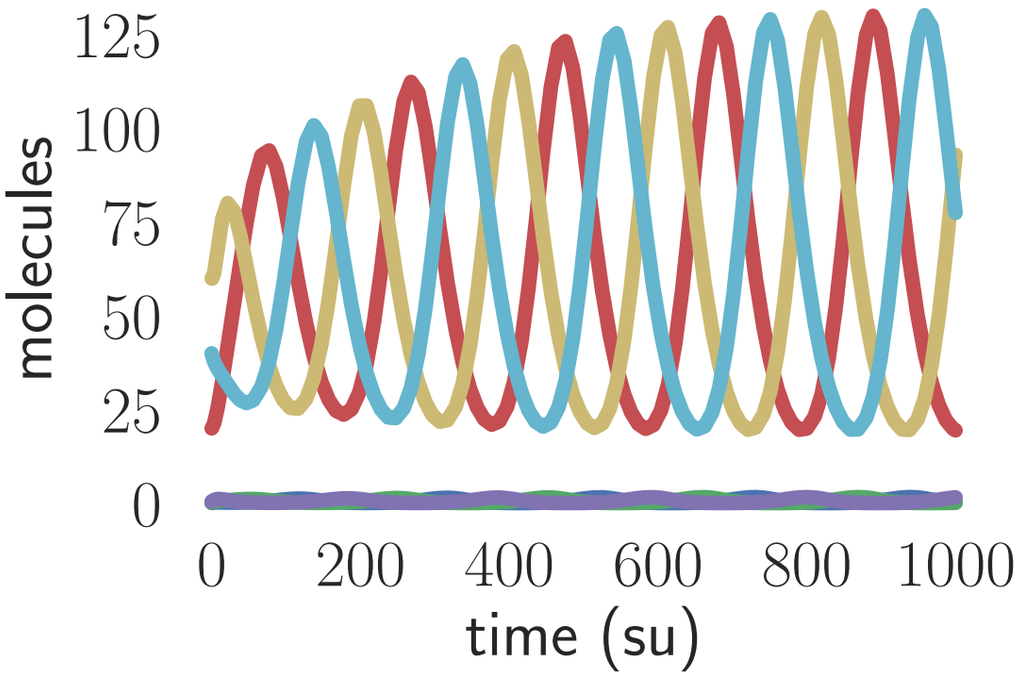




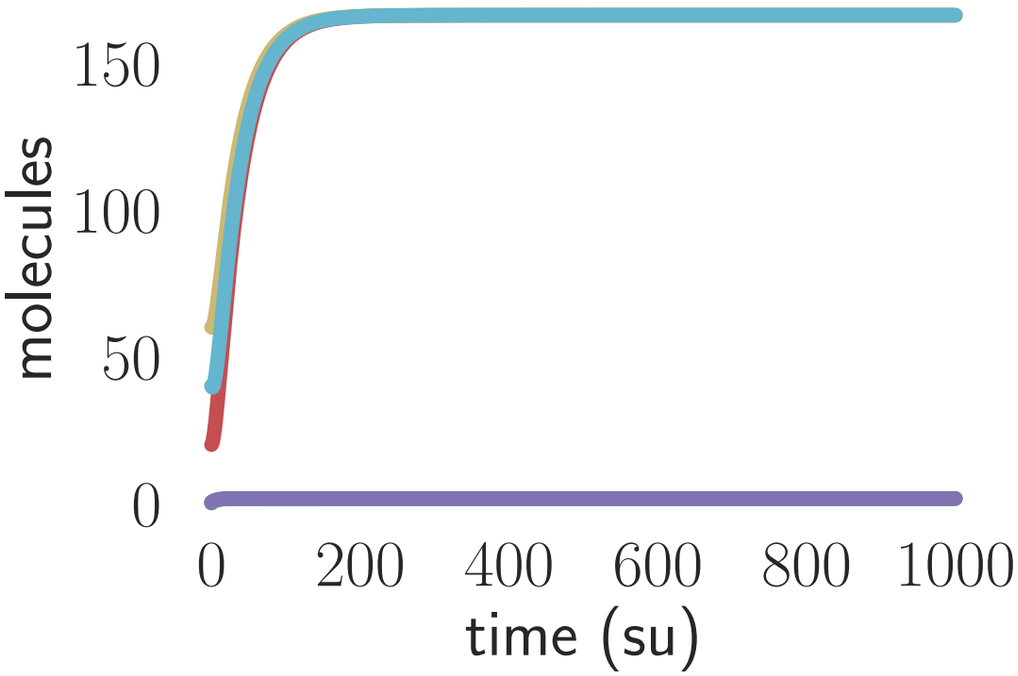
[1] Michael B Elowitz and Stanislas Leibler. A synthetic oscillatory network of transcriptional regulators. Nature, 403(6767):335–338, 2000.

reprissilator

Reference

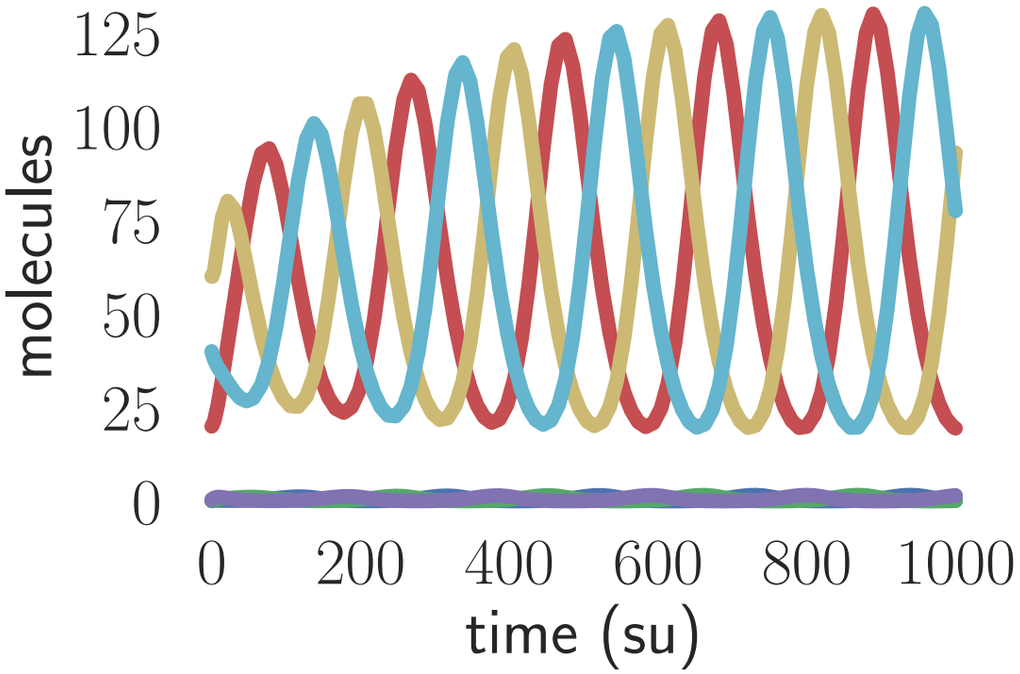


No Jaunt

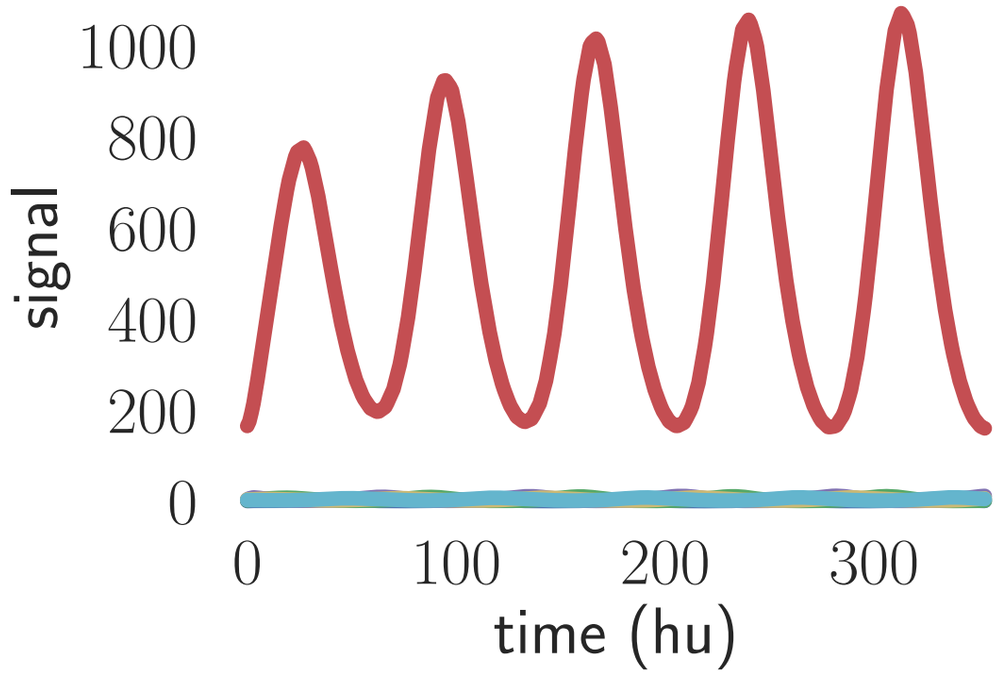


reprissilator

Reference



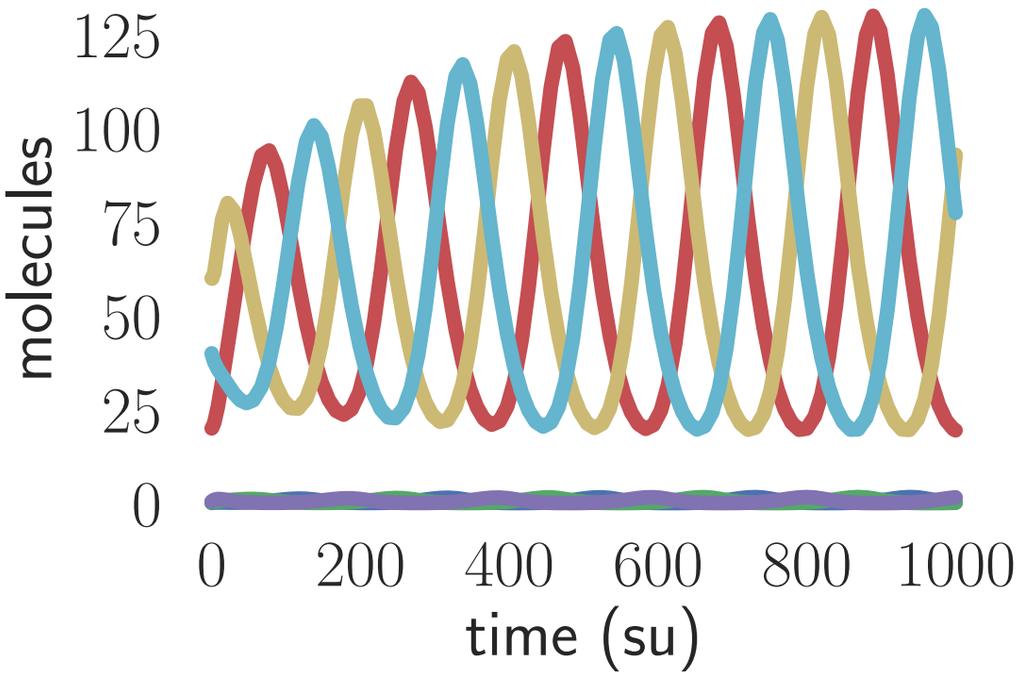
Jaunt + No Recover



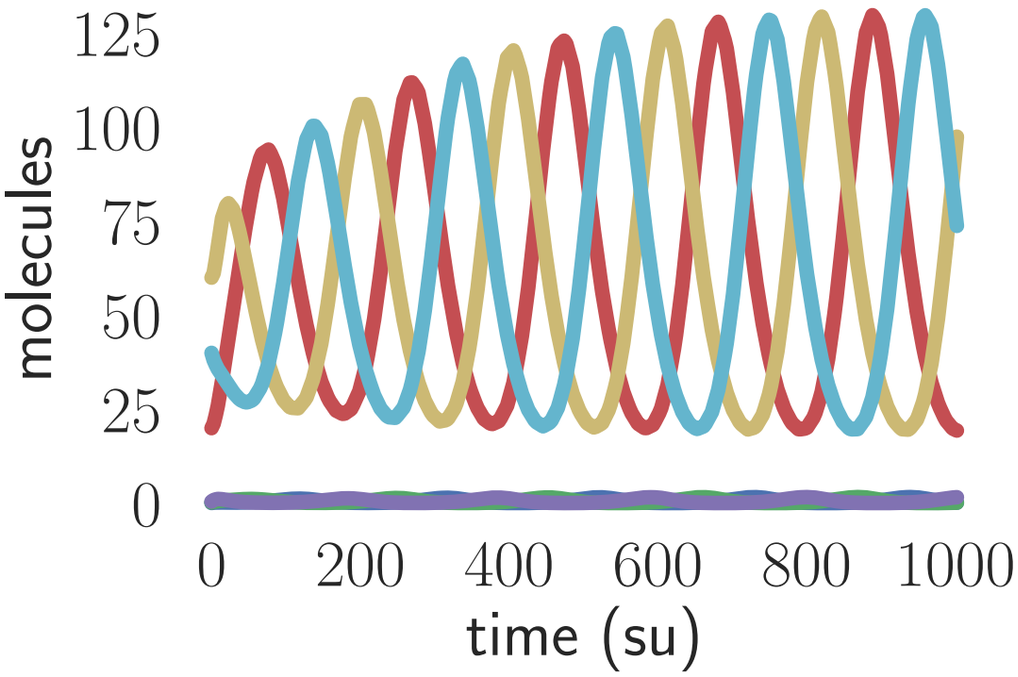
2.839x faster

reprissilator

Reference

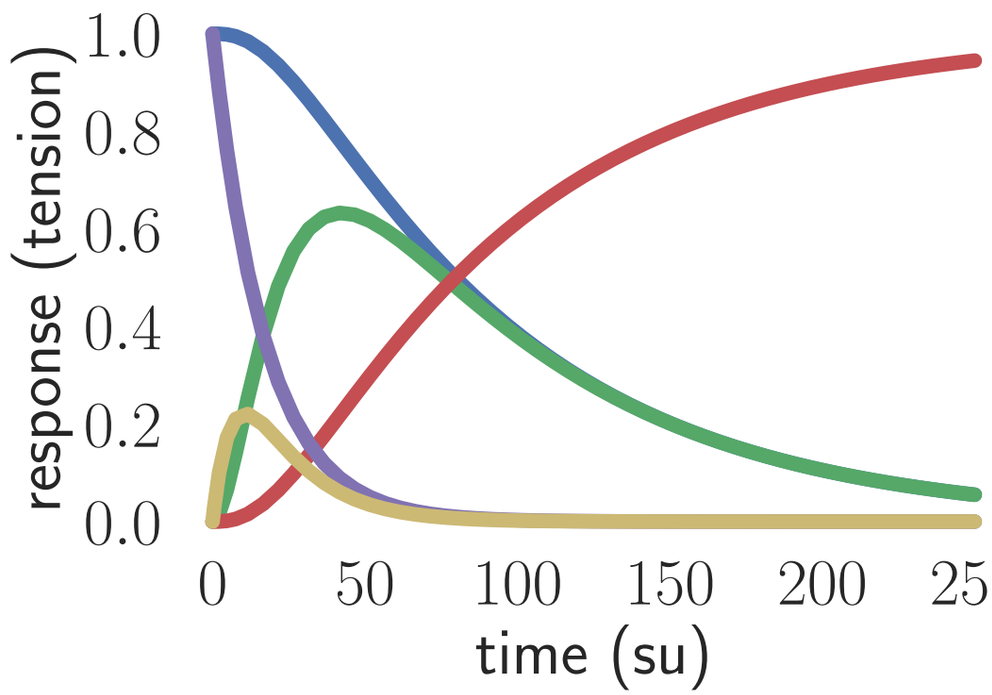


Jaunt + Recover



Botulinum Neurotoxin A Response

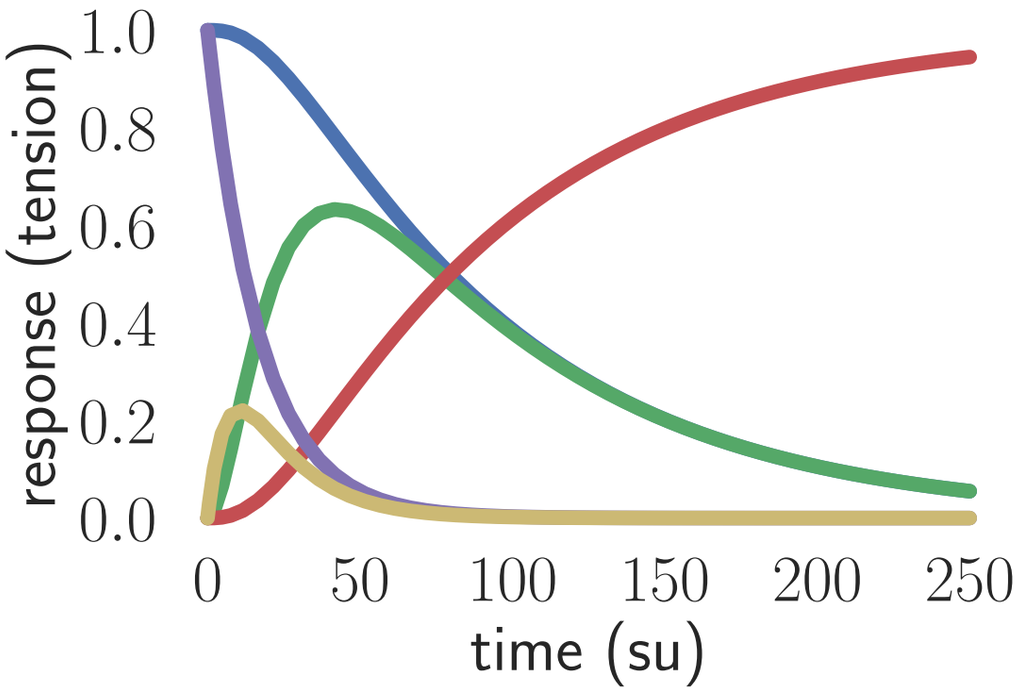
- Models the Paralysis of skeletal muscles after the introduction on Botulinum Neurotoxin A
- Model:
  - 5 diffeqs
  - 1 function
  - 8 parameters
- Simulation
  - time: 250 su
  - sample: 5 su



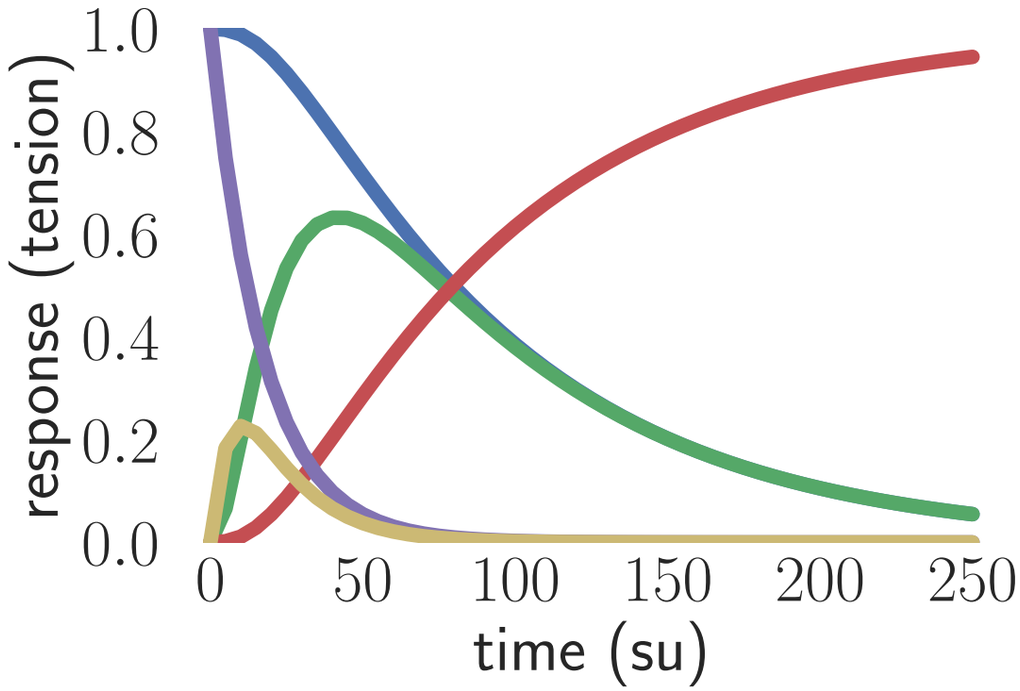
[1] Frank J Lebeda, Michael Adler, Keith Erickson, and Yaroslav Chushak. Onset dynamics of type a botulinum neurotoxin-induced paralysis. Journal of pharmacokinetics and pharmacodynamics, 35(3):251, 2008.

Botulinum Neurotoxin A Response

Reference



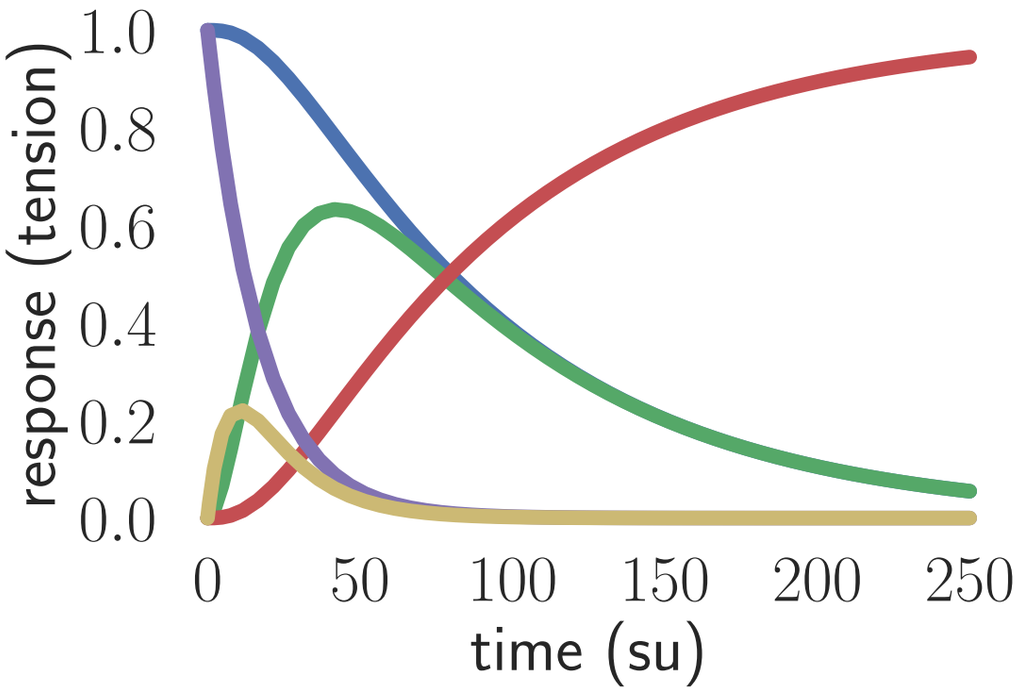
No Jaunt



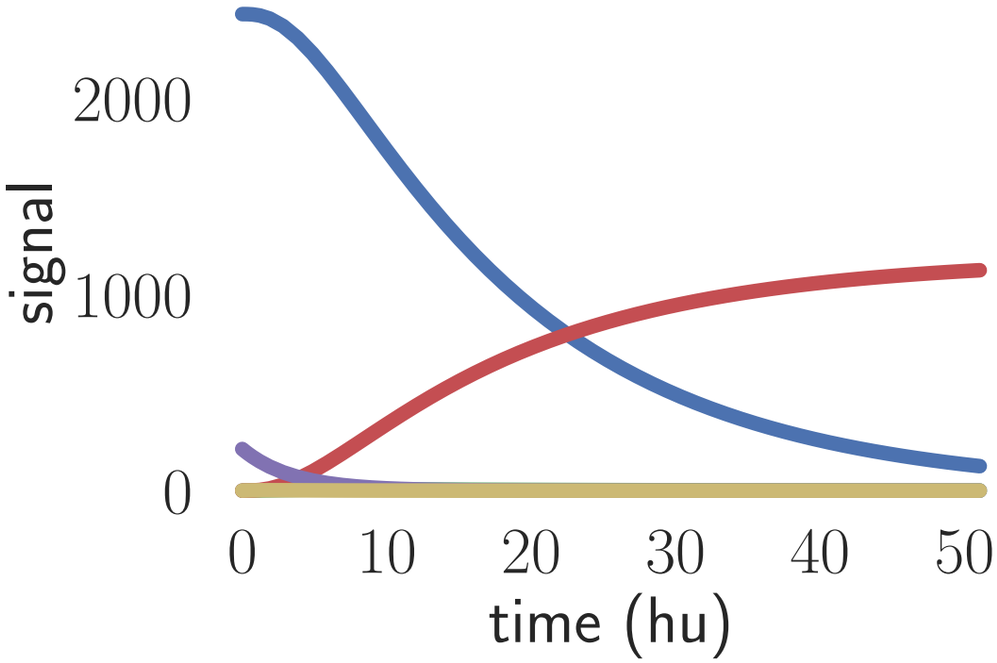
*Jaunt still used for pruning search space

Botulinum Neurotoxin A Response

Reference



Jaunt + No Recover



5x faster

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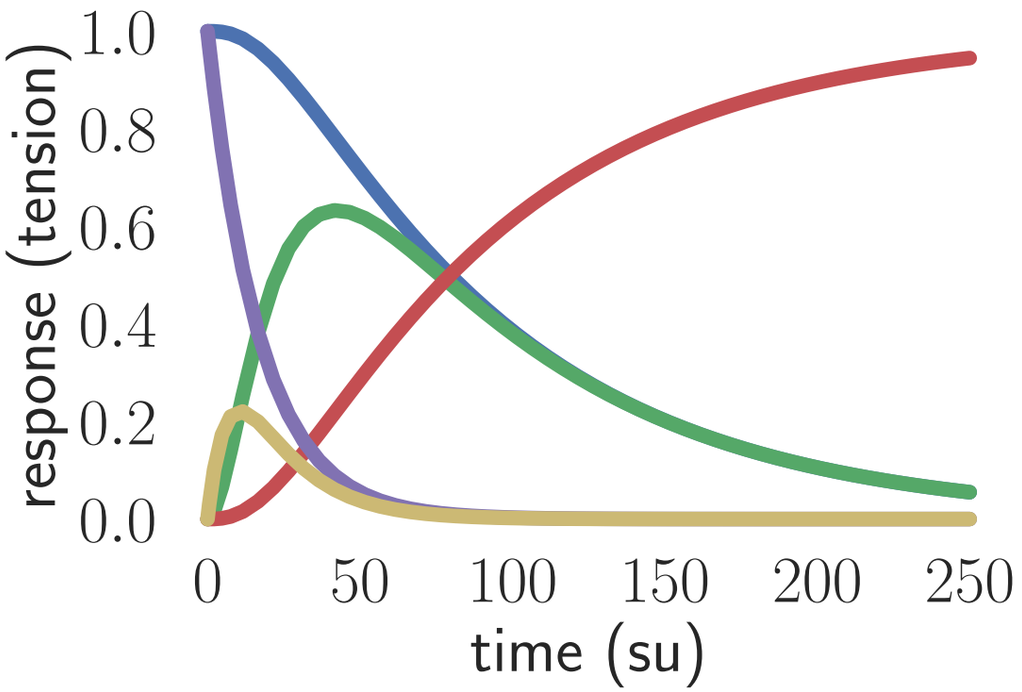
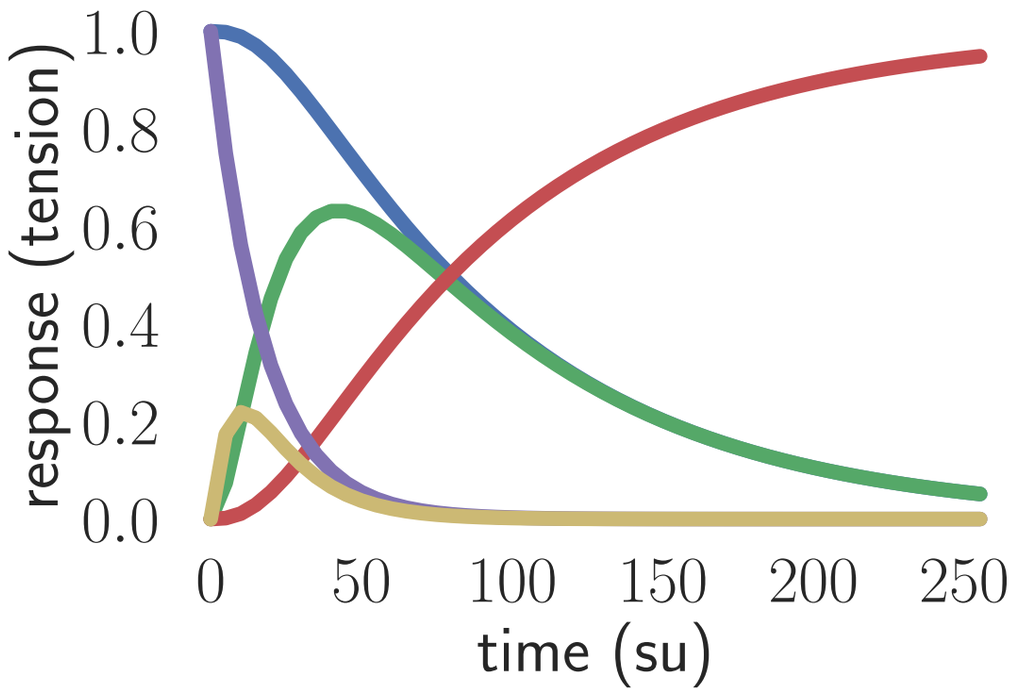
Reference



Jaunt + Recover



Correctness+Speedup Results

benchmark	speedup	No Jaunt	Jaunt
smol	**0.50x**		✓
sconc	**1.00x**		✓
mmrxnp	77.48x		✓
repri	2.839x		✓
bont	**5.00x**	✓*	✓
epor	0.142x		✓
gtoggle	**0.1x**		✓

Conclusion

- Powerful new computing substrate for biochemical models
- Jaunt transforms mapped simulations to:
  - respect physical limitations of hardware
  - accelerate simulation