Chemical Analog Computing with Negative Numbers

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Advantages of chemical computing

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Production rate generating C:

$$V_{\text{prod}}([C]) = \hat{k} \cdot [A] \cdot [B]$$

Consumption rate of C

$$V_{\text{cons}}([C]) = 0$$
$$\frac{\mathrm{d}\, C}{\mathrm{d}\, t} = V_{\text{prod}}([C]) - V_{\text{cons}}([C]) = \hat{k} \cdot [A] \cdot [B]$$

Mass-action Kinetics: General ODE Model

Considering scheme of r reaction and p involved species

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\begin{aligned}
a_{1,1}S_1 + a_{2,1}S_2 \quad + \ldots + a_{p,1}S_p \quad &\xrightarrow{k_1} b_{1,1}S_1 \quad + b_{2,1}S_2 \ldots \quad + b_{p,1}S_p \\
a_{1,2}S_1 + a_{2,2}S_2 \quad + \ldots + a_{p,2}S_p \quad &\xrightarrow{k_2} b_{1,2}S_1 \quad + b_{2,2}S_2 \ldots \quad + b_{p,2}S_p \\
&\vdots \\
a_{1,r}S_1 + a_{2,r}S_2 \quad + \ldots + a_{p,r}S_p \quad &\xrightarrow{k_r} b_{1,r}S_1 \quad + b_{2,r}S_2 \ldots \quad + b_{p,r}S_p
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Results in system of ordinary differential equations (ODEs):

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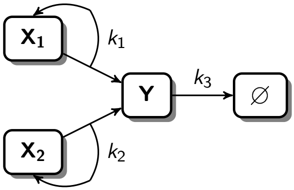
\end{aligned}
$$

Results in system of ordinary differential equations (ODEs):

$$
[\dot{S_i}] = \frac{\mathrm{d}[S_i]}{\mathrm{d}\,t} = \sum_{h=1}^{r} \left(k_h \cdot (b_{i,h} - a_{i,h}) \cdot \prod_{j=1}^{p} [S_j]^{a_{j,h}} \right) \quad \text{with } i = 1, \ldots, p
$$

Chemical Calculations: Addition



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\begin{aligned}
[\dot{X_1}] &= 0 \\
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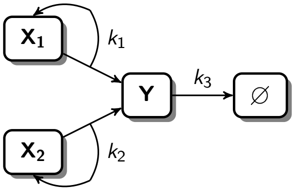

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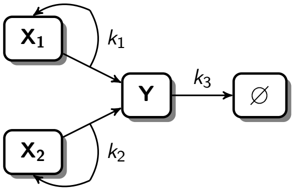

asymptotic solution in a stationary state with $k_1 = k_2 = k_3$

$$[Y](\infty) = \lim_{t\to\infty}(1 - e^{-k_1 t}) \cdot ([X_1](t) + [X_2](t)) = [X_1](0) + [X_2](0)$$

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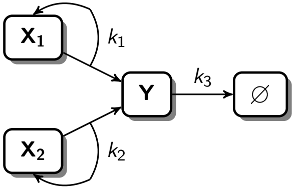

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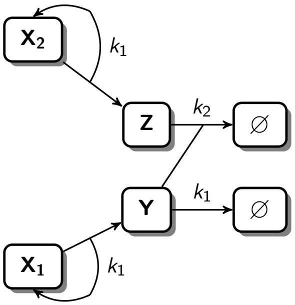
Chemical Calculations: Non-negative Subtraction



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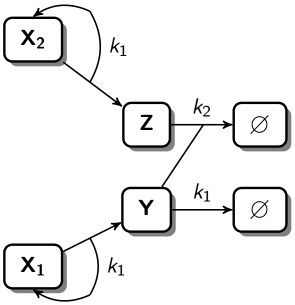

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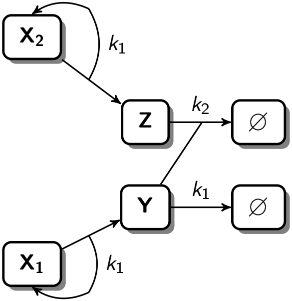

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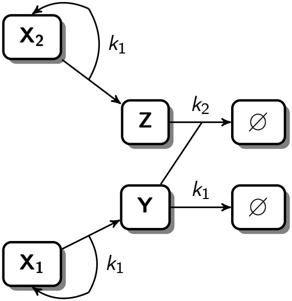

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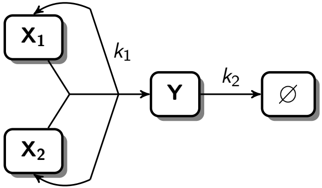

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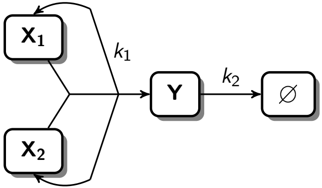

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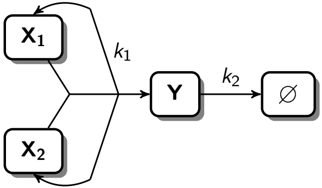

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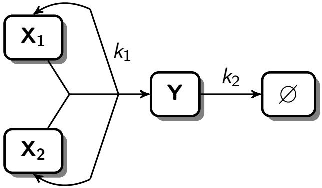

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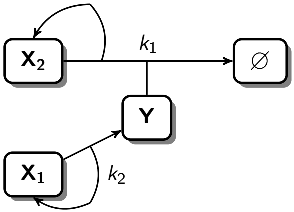

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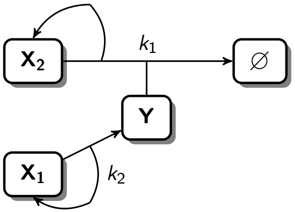

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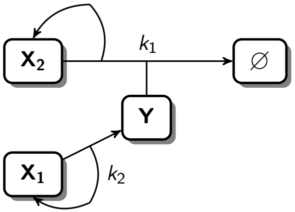

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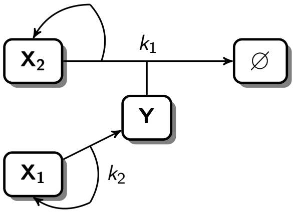

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$$[Y] = [X_1]/[X_2] \text{ if } [X_2] > 0$$

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if $[T]$ **then**
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if $[T]$ **then**
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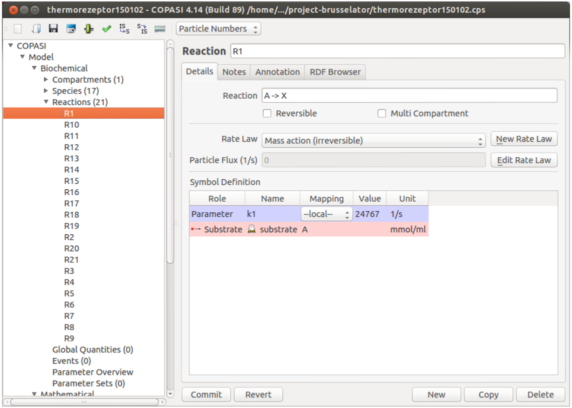
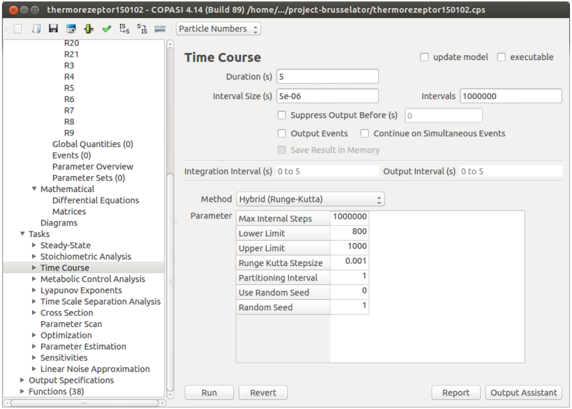
$$[C] = [A] \cdot [B] \cdot [T] + [F] \cdot [A]$$

Copasi: Software for Chemical Reaction's Simulation



- Copasi: Complex Pathway Simulator
- Freely available at www.copasi.org
- Very stable and reliable tool, convenient user interface
- Particle numbers (multiset of molecular counts) as output

Estimation of Time Course using Copasi



- Numerical ODE solver based on adaptive Runge-Kutta method
- Variable time discretisation stepsize according to volatility
- High internal numerical precision
- Output rounded to obtain integer numbers for molecular counts

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  - Bi-Concentration Representation

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  - $[P] = \begin{cases} 1 & \text{if } [X_1] > [X_2] \\ 0 & \text{else} \end{cases}$

Signed Number Representation

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- Use another substance (Y) for the number
  - $[Y] = \begin{cases} [X_1] - [X_2] & \text{if } [X_1] > [X_2] \\ [X_2] - [X_1] & \text{if } [X_2] > [X_1] \\ 0 & \text{else} \end{cases}$

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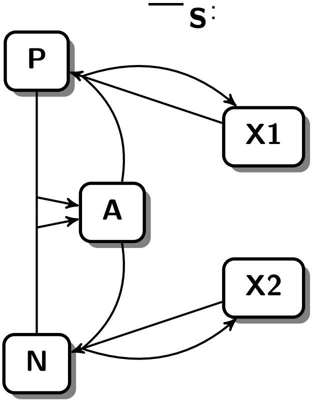
$\Rightarrow -_s : (\mathbb{R}^+)^2 \rightarrow \mathbb{R}^+ \times \{(1,0),(0,1)\}$

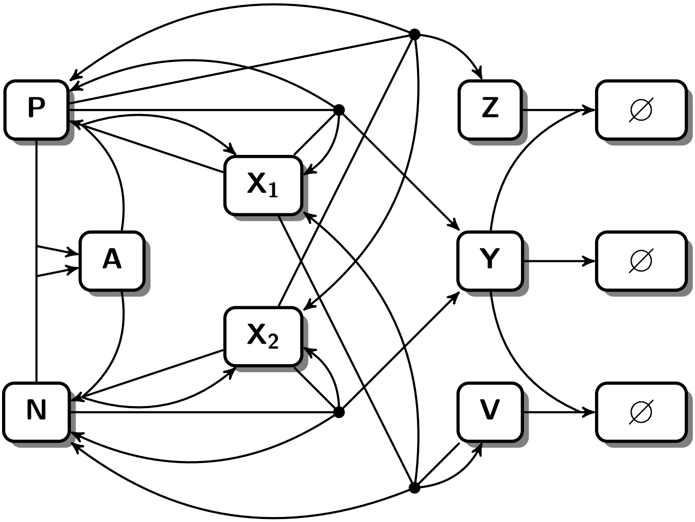
Signed Number Representation: Reactive Network



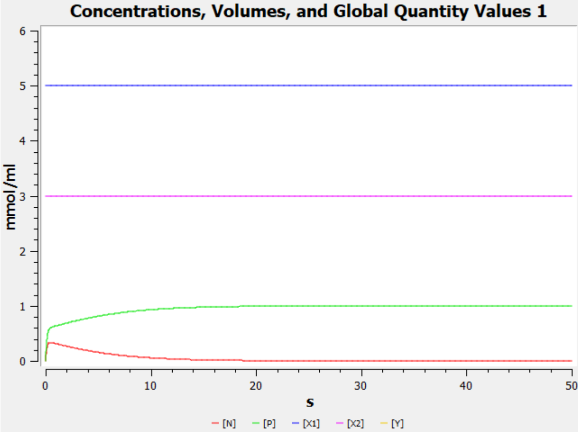
$$[A](0) = 1$$

Signed Number Representation: Reactive Network

— S :



Signed Number Representation: Example



$$[X1] = 5 \quad [X2] = 3$$

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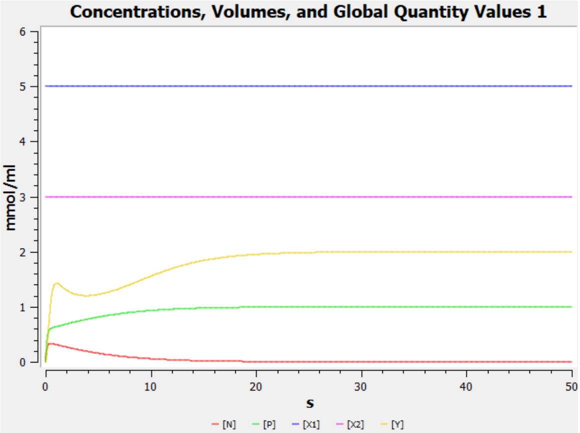

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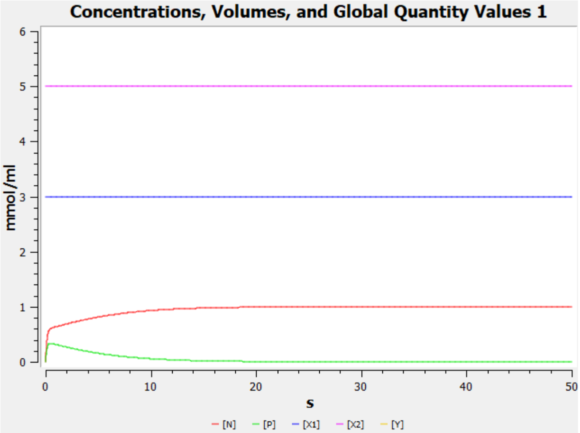

$$[X1] = 3 \quad [X2] = 5$$

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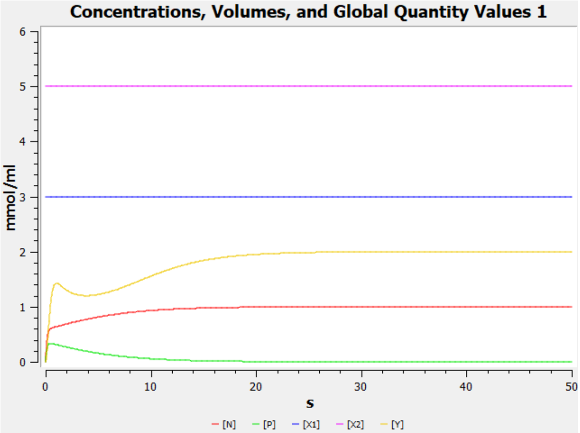

$$[X1] = 3 \quad [X2] = 5$$

Signed Number Representation: Addition

Input : $X_1 = ([X1],[X1P],[X1N]),$
$X_2 = ([X2],[X2P],[X2N])$
Output: $Y = ([Y],[YP],[YN]) = X_1 + X_2$

if $[X1P]$ *AND* $[X2P]$ **then**
  $[Y] = [X1] + [X2], [YP] = 1, [YN] = 0$
end
if $[X1N]$ *AND* $[X2N]$ **then**
  $[Y] = [X1] + [X2], [YP] = 0, [YN] = 1$
end
if $[X1P]$ *AND* $[X2N]$ **then**
  $[Y],[YP],[YN] = [X1] -_s [X2]$
end
if $[X1N]$ *AND* $[X2P]$ **then**
  $[Y],[YN],[YP] = [X2] -_s [X1]$
end
return $[Y],[YP],[YN]$

Signed Number Representation: Subtraction

Input : $X_1 = ([X1], [X1P], [X1N])$,
$X_2 = ([X2], [X2P], [X2N])$
Output: $Y = ([Y], [YP], [YN]) = X_1 - X_2$

if $[X1P]$ *AND* $[X2P]$ **then**
| $[Y], [YP], [YN] = [X1] -_s [X2]$
end
if $[X1N]$ *AND* $[X2N]$ **then**
| $[Y], [YN], [YP] = [X2] -_s [X1]$
end
if $[X1P]$ *AND* $[X2N]$ **then**
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if $[X1N]$ *AND* $[X2P]$ **then**
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Signed Number Representation: Multiplication

Input : $X_1 = ([X1], [X1P], [X1N])$,
$X_2 = ([X2], [X2P], [X2N])$
Output: $Y = ([Y], [YP], [YN]) = X_1 \cdot X_2$

$[Y] = [X1] \cdot [X2]$
$[YP] = [X1P] \cdot [X2P] + [X1N] \cdot [X2N]$
$[YN] = [X1P] \cdot [X2N] + [X1N] \cdot [X2P]$
return $[Y], [YP], [YN]$

Signed Number Representation: Division

Input : $X_1 = ([X1], [X1P], [X1N]),$
$X_2 = ([X2], [X2P], [X2N])$
Output: $Y = ([Y], [YP], [YN]) = X_1/X_2$

$[Y] = [X1]/[X2]$
$[YP] = [X1P] \cdot [X2P] + [X1N] \cdot [X2N]$
$[YN] = [X1P] \cdot [X2N] + [X1N] \cdot [X2P]$
return $[Y], [YP], [YN]$

Bi-Concentration Representation

Idea

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- One substance (YP) for the positive part

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- One substance (YN) for the negative part
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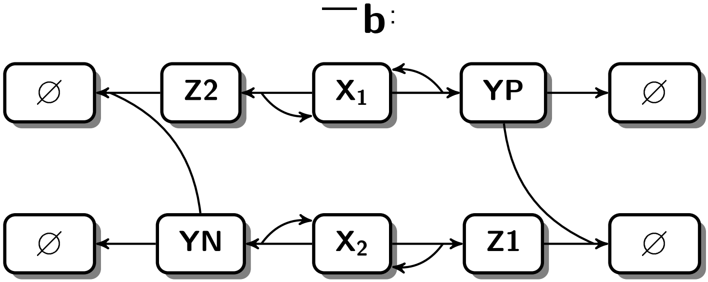
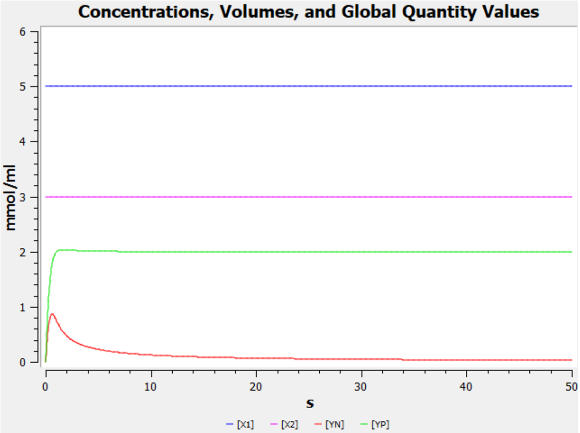
$\Rightarrow -_b : (\mathbb{R}^+)^2 \rightarrow (\mathbb{R}^+)^2$

Bi-Concentration Representation: Reaction Network

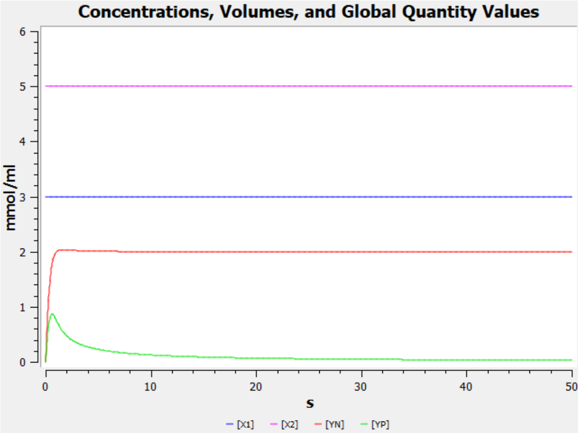


Bi-Concentration Representation: Example



$$[X1] = 5 \quad [X2] = 3$$

Bi-Concentration Representation: Example



$$[X1] = 3 \quad [X2] = 5$$

Bi-Concentration Representation: Addition

Input : $X_1 = ([X1P], [X1N])$,
$X_2 = ([X2P], [X2N])$
Output: $Y = ([YP], [YN]) = X_1 + X_2$

$[YP], [YN] = ([X1P] + [X2P]) -_b ([X1N] + [X2N])$
return $[YP], [YN]$

Bi-Concentration Representation: Subtraction

Input : $X_1 = ([X1P], [X1N])$,
$X_2 = ([X2P], [X2N])$
Output: $Y = ([YP], [YN]) = X_1 - X_2$

$[YP], [YN] = ([X1P] + [X2N]) -_b ([X1N] + [X2P])$
return $[YP], [YN]$

Bi-Concentration Representation: Multiplication

Input : $X_1 = ([X1P], [X1N]),$
$X_2 = ([X2P], [X2N])$
Output: $Y = ([YP], [YN]) = X_1 \cdot X_2$

$[YP] = [X1P] \cdot [X2P] + [X1N] \cdot [X2N]$
$[YN] = [X1P] \cdot [X2N] + [X1N] \cdot [X2P]$
return $[YP], [YN]$

Bi-Concentration Representation: Division

Input : $X_1 = ([X1P], [X1N]),$
$X_2 = ([X2P], [X2N])$
Output: $Y = ([YP], [YN]) = X_1/X_2$

$[Z] = ([X1P] + [X1N])/([X2P] + [X2N])$
if $([X1P] \cdot [X2P] + [X1N] \cdot [X2N]) > 0$ **then**
  $[YP] = [Z]$
else
  $[YN] = [Z]$
end

return $[YP], [YN]$

Comparison

	Signed Number	Bi-Concentration

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Speed	Depends on concentration	2-3 times faster

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Speed	Depends on concentration	2-3 times faster
Result near zero	Very slow	Very slow
Result exact zero	Very bad, sign is indicator	Very bad ($[VP] == [VN]$ is indicator)
Elementary arithmetic	Addition and subtraction, complex, multiplication and division simple	Addition, subtraction and multiplication simple, division complex

Conclusion

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Thank you for your attention

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