## Stoichiometric vector and matrix

- The stoichiometric coefficients of a reaction are collected to a vector $s_r$
- In $s_r$ there is a one position for each metabolite in the metabolic system, and the stoichiometric co-efficient of the reaction are inserted to appropriate positions, e.g. for the reaction

$$r : A + B \mapsto 2C,$$

$$s_r = \begin{array}{c} \cdot \\ \cdot \\ A \\ \cdot \\ \cdot \\ B \\ \cdot \\ \cdot \\ C \end{array} \begin{bmatrix} 0 \\ 0 \\ -1 \\ 0 \\ 0 \\ -1 \\ 0 \\ 0 \\ 2 \end{bmatrix}$$

## Example: stoichiometric matrix

- Consider the set of reactions from the penthose-phospate pathway:
- The stoichiometric matrix is a 10-by-7 matrix:

$R_1$: $\beta$G6P + NADP$^+$ $\overset{zwf}{\Rightarrow}$ 6PGL + NADPH

$R_2$: 6PGL + $H_2O$ $\overset{pgl}{\Rightarrow}$ 6PG

$R_3$: 6PG + NADP$^+$ $\overset{gnd}{\Rightarrow}$ R5P + NADPH

$R_4$: R5P $\overset{rpe}{\Rightarrow}$ X5P

$R_5$: $\alpha$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$G6P

$R_6$: $\alpha$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$F6P

$R_7$: $\beta$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$F6P

$$S = \begin{array}{c} \\ \beta G6P \\ \alpha G6P \\ \beta F6P \\ 6PGL \\ 6PG \\ R5P \\ X5P \\ NADP^+ \\ NADPH \\ H_2O \end{array} \begin{bmatrix} -1 & 0 & 0 & 0 & 1 & 0 & -1 \\ 0 & 0 & 0 & 0 & -1 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 \\ 1 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ -1 & 0 & -1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

## Systems equations

In a network of $n$ metabolites and $r$ reactions, the dynamics of the system are characterized by the systems equations

$$\frac{dX_i}{dt} = \sum_{j=1}^{r} s_{ij} v_j, \text{ for } i = 1, \ldots, n$$

- $X_i$ is the concentration of the $i$th metabolite
- $v_j$ is the rate of the $j$th reaction and
- $s_{ij}$ is the stoichiometric coefficient of $i$th metabolite in the $j$th reaction.

Intuitively, each system equation states that the rate of change of concentration of a metabolite is the sum of metabolite flows to and from the metabolite.

## Systems equation example

- Assume our example metabolic network has the following rate vector $\mathbf{v} = (1, 1, 0, 0, 1, 0, 0)$
- Let us compute the rate of change for metabolites

$R_1$: $\beta$G6P + NADP$^+$ $\stackrel{zwf}{\Rightarrow}$ 6PGL + NADPH
$R_2$: 6PGL + $H_2O$ $\stackrel{pgl}{\Rightarrow}$ 6PG
$R_3$: 6PG + NADP$^+$ $\stackrel{gnd}{\Rightarrow}$ R5P + NADPH
$R_4$: R5P $\stackrel{rpe}{\Rightarrow}$ X5P
$R_5$: $\alpha$G6P $\stackrel{gpi}{\Leftrightarrow}$ $\beta$G6P
$R_6$: $\alpha$G6P $\stackrel{gpi}{\Leftrightarrow}$ $\beta$F6P
$R_7$: $\beta$G6P $\stackrel{gpi}{\Leftrightarrow}$ $\beta$F6P

$$\frac{d\beta G6P}{dt} = -1v_{R_1} + 1v_{R_5} - 1v_{R_7} = 0$$
$$\frac{d\alpha G6P}{dt} = -1v_{R_5} - 1v_{R_6} = -1 \Rightarrow \text{net consumption!}$$
$$\frac{d\beta F6P}{dt} = 1v_{R_6} + 1v_{R_7} = 0$$
$$\frac{d6GPL}{dt} = 1v_{R_1} - 1v_{R_2} = 0$$
$$\frac{d6PG}{dt} = 1v_{R_2} - 1v_{R_3} = 1 \Rightarrow \text{net production!}$$
$$\frac{dR5P}{dt} = 1v_{R_3} - 1v_{R_4} = 0$$
$$\frac{dX5P}{dt} = 1v_{R_4} = 0$$
$$\frac{dNADPH}{dt} = 1v_{R_1} + 1v_{R_3} = 1 \Rightarrow \text{net production!}$$
$$\frac{dNADP^+}{dt} = -1v_{R_1} - 1v_{R_3} = -1 \Rightarrow \text{net consumption!}$$
$$\frac{dH_20}{dt} = -1v_{R_2} = -1 \Rightarrow \text{net consumption!}$$

## Steady state analysis

- The requirements a steady state, i.e. non-changing concentrations

$$\frac{dX_i}{dt} = \sum_{j=1}^{r} s_{ij} v_j = 0, \text{ for } i = 1, \ldots, n$$

  constitute a set of linear equations constraining to the reaction rates $v_j$.

- We can write this set of linear constraints in matrix form with the help of the stoichiometric matrix $S$ and the reaction rate vector $\mathbf{v}$

$$\frac{d\mathbf{X}}{dt} = S\mathbf{v} = \mathbf{0},$$

- A reaction rate vector $\mathbf{v}$ satisfying the above is called a *flux* vector.

## Null space of the stoichiometrix matrix (1/2)

- Any flux vector $\mathbf{v}$ that the cell can maintain in a steady-state is a solution to the system of equations

$$S\mathbf{v} = \mathbf{0}$$

- The null space of the stoichiometric matrix

$$\mathcal{N}(S) = \{\mathbf{u}|S\mathbf{u} = 0\}$$

  contains all valid flux vectors

- Therefore, studying the null space of the stoichiometric matrix can give us important information about the cell's capabilities

## Null space of the stoichiometric matrix (2/2)

The null space $\mathcal{N}(S)$ is a linear vector space, so all properties of linear vector spaces follow, e.g:

- $\mathcal{N}(S)$ contains the zero vector, and closed under linear combination:
  $\mathbf{v}_1, \mathbf{v}_2 \in \mathcal{N}(S) \implies \alpha_1 \mathbf{v}_1 + \alpha \mathbf{v}_2 \in \mathcal{N}(S)$
- The null space has a basis $\{\mathbf{k_1}, \ldots, \mathbf{k}_q\}$, a set of $q \leq \min(n, r)$ linearly independent vectors, where $r$ is the number of reactions and $n$ is the number of metabolites.
- The choice of basis is not unique, but the number $q$ of vector it contains is determined by the rank of $S$.

## Null space and feasible steady state rate vectors

- The kernel $K = (\mathbf{k}_1, \ldots, \mathbf{k}_q)$ of the stoichiometric matrix formed by the above basis vectors has a row corresponding to each reaction.
- $K$ characterizes the feasible steady state reaction rate vectors: for each feasible flux vector $\mathbf{v}$, there is a vector $\mathbf{b} \in \mathbb{R}^q$ such that $K\mathbf{b} = \mathbf{v}$
- In other words, any steady state flux vector is a linear combination

$$b_1\mathbf{k}_1 + \cdots + b_q\mathbf{k}_q$$

of the basis vectors of $\mathcal{N}(N)$.

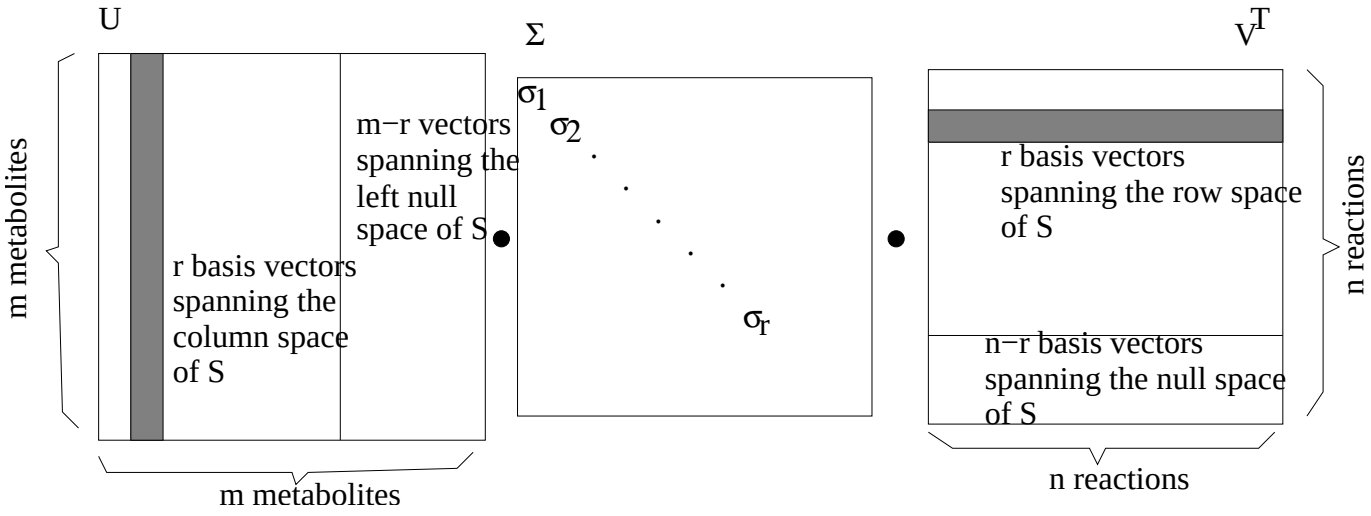
## Singular value decomposition of $S$ (1/3)

- A basis for the null space can be obtained via the singular value decomposition (SVD)
- The SVD of $S$ is the product $S = U\Sigma V^T$, where
  - $U$ is a $m \times m$ orthonormal matrix, where $r$ first columns are the eigenvectors of the column space of $S$, and $m - r$ last columns span the left null space of $S$.
  - $\Sigma = diag(\sigma_1, \sigma_2, \ldots, \sigma_r)$ is $m \times n$ matrix containing the singular values $\sigma_i$ on its diagonal
  - $V$ is a $n \times n$ orthonormal matrix, where $r$ first columns span the row space of $S$, and $n - r$ last columns span the null space of $S$

## Singular value decomposition of $S$ (2/3)

The subspaces spanned by the columns of $U$ are interpreted as follows:

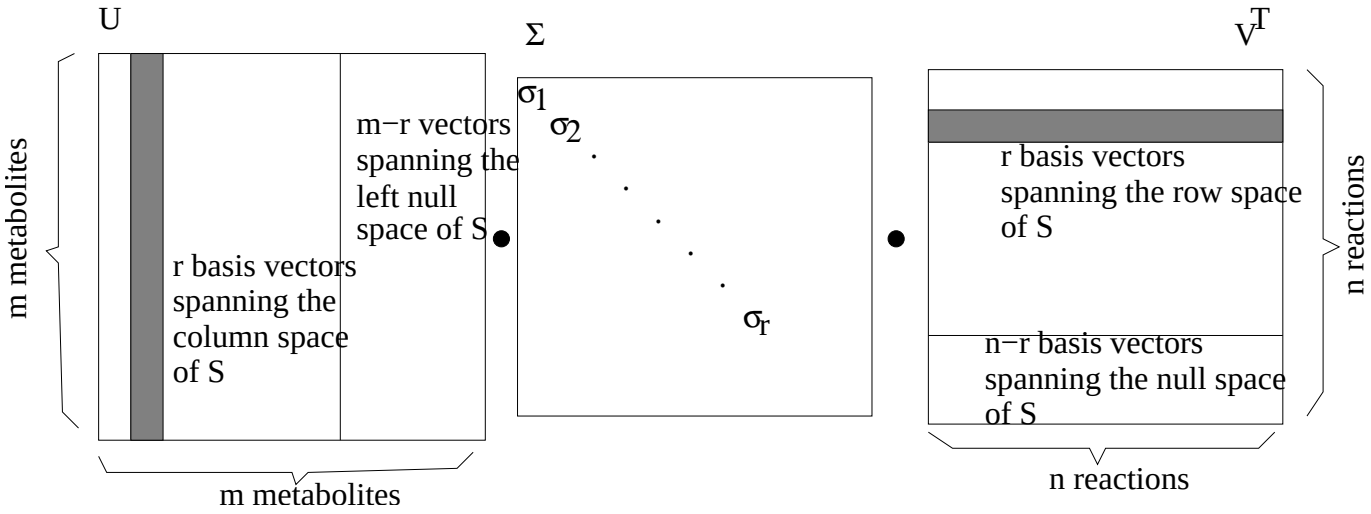
- The set of $r$ $m$-dimensional eigenvectors of the column space of $S$ can be seen as prototypical or 'eigen-' reactions: all reaction stoichiometries in the metabolic system can be expressed as linear combinations of the eigen-reactions.
- The $m - r$ vectors $u_{r+l}$ spanning the left null space of $S$ represent conservation relations between metabolites or *pools* of metabolites whose concentration stays invariant.



## Singular value decomposition of $S$ (3/3)

The subspaces spanned by the columns of $V$ are interpreted as follows:

- The set of $r$ $n$-dimensional eigenvectors of the row space of $S$ can be seen as systems equations of prototypical 'eigen-' metabolites: all systems equations of the metabolism can be expressed as their linear combinations
- The set of $n - r$ $n$-dimensional vectors spanning the null space are flux vectors that can operate in steady state, i.e. statifying $S\mathbf{v}_l = 0, l = r + 1, \ldots, n$: these can be taken as the kernel $K$ used to analyze steady state fluxes.

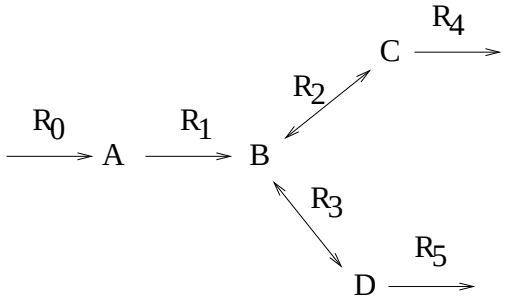


## Basis steady state flux modes from SVD

- A basis for the null space is thus obtained by picking the $n - r$ last columns of $V$ from the SVD of $S$:

$$K = [v_{r+1}, \ldots, v_n]$$

- In MATLAB, the same operation is performed directly by the command $null(S)$.
- Let us examine the following simple system

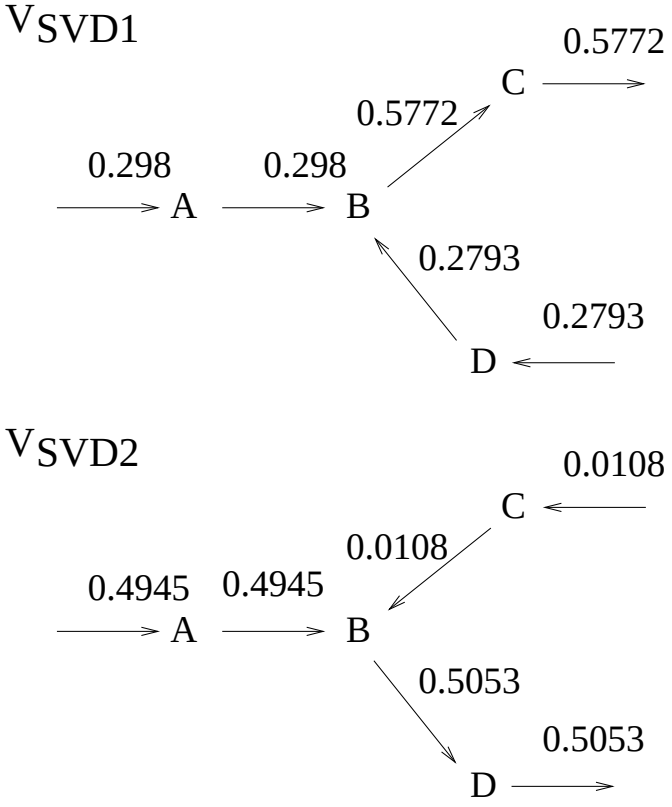



$$S = \begin{bmatrix} 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 & 0 & -1 \end{bmatrix}$$

## Basis steady state flux modes from SVD

- The two flux modes given by SVD for our example system
- All steady state flux vectors can be expressed as linear combinations of these two flux modes

$$K = \begin{bmatrix} 0.2980 & 0.4945 \\ 0.2980 & 0.4945 \\ 0.5772 & -0.0108 \\ -0.2793 & 0.5053 \\ 0.5772 & -0.0108 \\ -0.2793 & 0.5053 \end{bmatrix}$$



## Null space of PPP

- Consider again the set of reactions from the penthose-phospate pathway
- The stoichiometric matrix is a 10-by-9 matrix

$R_1$: $\beta$G6P + NADP$^+$ $\overset{zwf}{\Rightarrow}$ 6PGL + NADPH
$R_2$: 6PGL + $H_2O$ $\overset{pgl}{\Rightarrow}$ 6PG
$R_3$: 6PG + NADP$^+$ $\overset{gnd}{\Rightarrow}$ R5P + NADPH
$R_4$: R5P $\overset{rpe}{\Rightarrow}$ X5P
$R_5$: $\alpha$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$G6P
$R_6$: $\alpha$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$F6P
$R_7$: $\beta$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$F6P
$R_8$ :$\Rightarrow \alpha G6P$
$R_9 : X5P \Rightarrow$

$$S = \begin{array}{c} \\ \beta G6P \\ \alpha G6P \\ \beta F6P \\ 6PGL \\ 6PG \\ R5P \\ X5P \\ NADP^+ \\ NADPH \\ H_2O \end{array} \begin{bmatrix} -1 & 0 & 0 & 0 & 1 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 & -1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & -1 \\ -1 & 0 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

## Null space of PPP

- Null space of this system has only one vector $K = (0, 0, 0, 0, 0.5774, -0.5774, 0.5774, 0, 0, 0)^T$
- Thus, in a steady state only reactions $R_5$, $R_6$ and $R_7$ can have non-zero fluxes.
- The reason for this is that there are no producers of $NADP^+$ or $H_2O$ and no consumers of NADPH.
- Thus our PPP is effectively now a dead end!

$R_1$: $\beta$G6P + $NADP^+ \overset{zwf}{\Rightarrow}$ 6PGL + NADPH

$R_2$: 6PGL + $H_2O \overset{pgl}{\Rightarrow}$ 6PG

$R_3$: 6PG + $NADP^+ \overset{gnd}{\Rightarrow}$ R5P + NADPH

$R_4$: R5P $\overset{rpe}{\Rightarrow}$ X5P

$R_5$: $\alpha$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$G6P

$R_6$: $\alpha$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$F6P

$R_7$: $\beta$G6P $\overset{gpi}{\Leftrightarrow}$ $\beta$F6P

$R_8 :\Rightarrow \alpha G6P$

$R_9 : X5P \Rightarrow$

## Null space of PPP

- To give our PPP non-trivial (fluxes different from zero) steady states, we need to modify our system
- We add reaction $R_{10} :\Rightarrow \mathrm{H_2O}$ as a water source
- We add reaction $R_{11}$: NADPH $\Rightarrow$ $\mathrm{NADP^+}$ to regenerate $\mathrm{NADP^+}$ from NADPH.
- We could also have removed the metabolites in question to get the same effect

$R_1$: $\beta$G6P + $\mathrm{NADP^+} \stackrel{zwf}{\Rightarrow}$ 6PGL + NADPH
$R_2$: 6PGL + $\mathrm{H_2O} \stackrel{pgl}{\Rightarrow}$ 6PG
$R_3$: 6PG + $\mathrm{NADP^+} \stackrel{gnd}{\Rightarrow}$ R5P + NADPH
$R_4$: R5P $\stackrel{rpe}{\Rightarrow}$ X5P
$R_5$: $\alpha$G6P $\stackrel{gpi}{\Leftrightarrow}$ $\beta$G6P
$R_6$: $\alpha$G6P $\stackrel{gpi}{\nLeftrightarrow}$ $\beta$F6P
$R_7$: $\beta$G6P $\stackrel{gpi}{\nLeftrightarrow}$ $\beta$F6P
$R_8 :\Rightarrow \alpha G6P$
$R_9 : X5P \Rightarrow$
$R_{10}$: $\Rightarrow \mathrm{H_2O}$
$R_{11}$: NADPH $\Rightarrow$ $\mathrm{NADP^+}$

## Enzyme subsets of PPP

From the kernel, we can immediately identify enzyme subsets that operate with fixed flux ratios in any steady state:

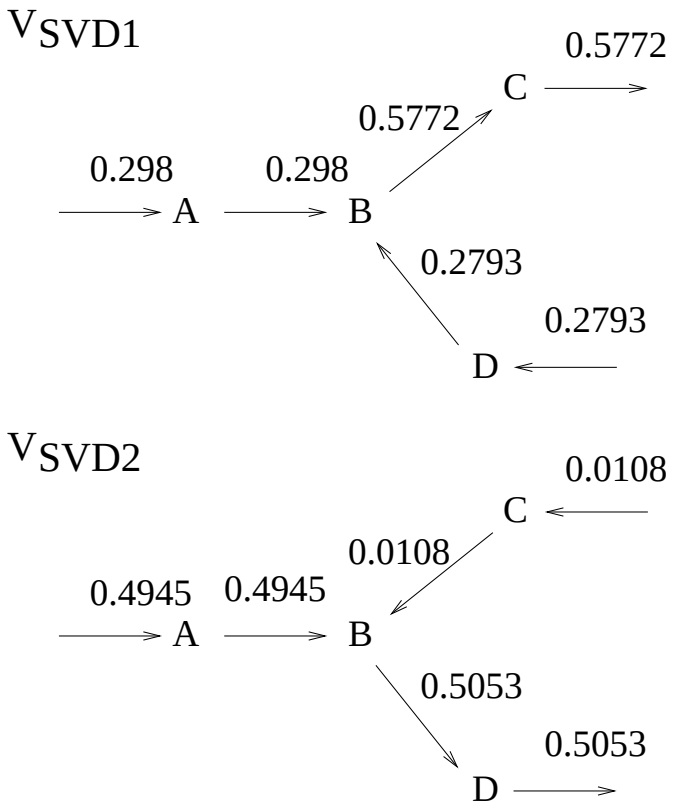
- reactions $\{R_1 - R_4, R_8 - R_{11}\}$ are one subset: $R_{11}$ has double rate to all the others
- $\{R_6, R_7\}$ are another: $R_6$ has the opposite sign of $R_7$
- $R_5$ does not belong to non-trivial enzyme subsets, so it is not forced to operate in lock-step with other reactions

$$K = \begin{bmatrix} 0.2727 & 0.1066 \\ 0.2727 & 0.1066 \\ 0.2727 & 0.1066 \\ 0.2727 & 0.1066 \\ 0.3920 & -0.4667 \\ -0.1193 & 0.5733 \\ 0.1193 & -0.5733 \\ 0.2727 & 0.1066 \\ 0.2727 & 0.1066 \\ 0.2727 & 0.1066 \\ 0.5454 & 0.2132 \end{bmatrix}$$

## Basis steady state flux modes from SVD

The kernel matrix obtained from SVD suffers from two shortcomings, illustrated by our small example system

- Reaction reversibility constraints are violated: in $v_{svd1}$, $R5$ operates in wrong direction, in $v_{svd2}$, $R_4$ operates in wrong direction
- All reactions are active in both flux modes, which makes visual interpretation impossible for all but very small systems
- The flux values are all non-integral



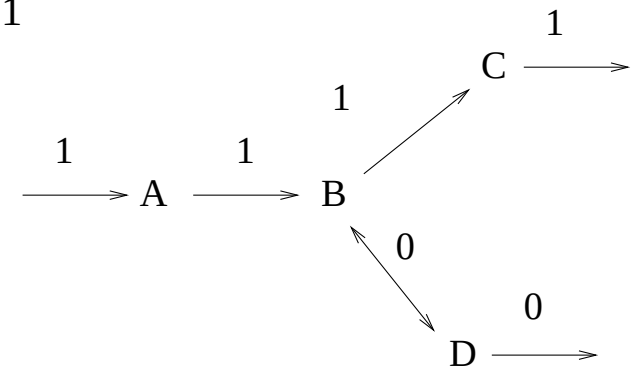
## Choice of basis

- SVD is only one of the many ways that a basis for the null space can be defined.
- The root cause for hardness of interpretation is the orthonormality of matrix $V$ in SVD $S = U\Sigma V^T$
  - The basis vectors are orthogonal: $v_{svd1}^T v_{svd2} = 0$
  - The basis vectors have unit length $||v_{svd1}|| = ||v_{svd1}|| = 1$
- Neither criteria has direct biological relevance!

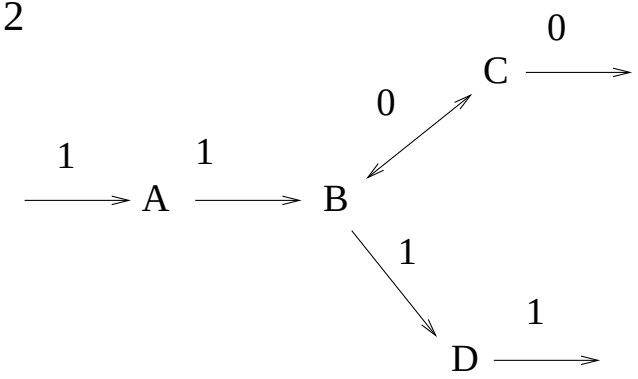
## Biologically meaningful pathways

- From our example system, it is easy to find flux vectors that are more meaningful than those given by SVD
- Both pathways on the right statisfy the steady state requirement
- Both pathways obey the sign restrictions of the system
- One can easily verify (by solving $b$ form the equation $Kb = v$) that they are linear combinations of the flux modes given by SVD, e.g. $v_1 = 0.0373 v_{svd1} + 1.997 v_{svd2}$

$V_1$




$V_2$

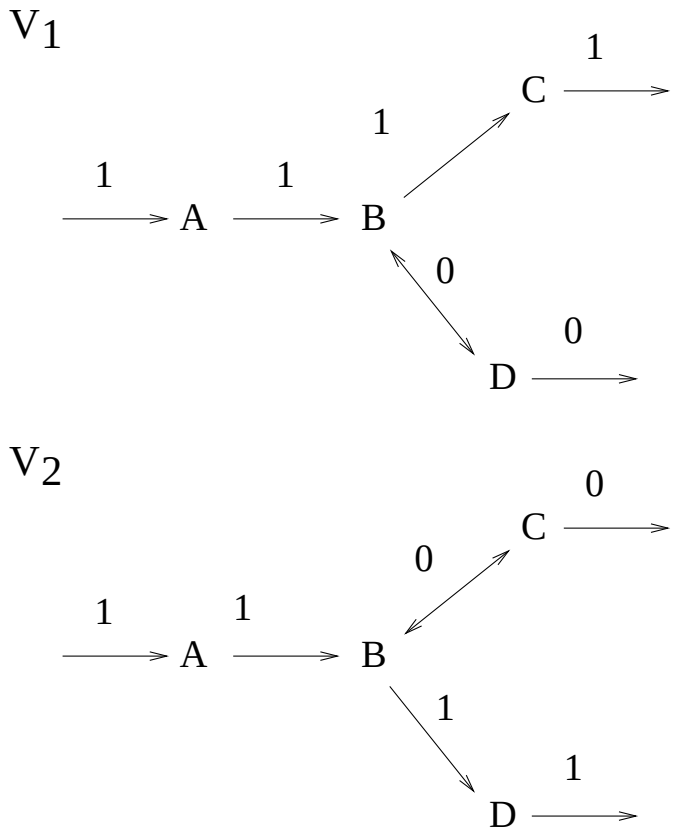


## Elementary flux modes

The two pathways are examples of elementary flux modes

The study of elementary flux modes (EFM) and concerns decomposing the metabolic network into components that

- can operate independently from the rest of the metabolism, in a steady state,
- any steady state can be described as a combination of such components.



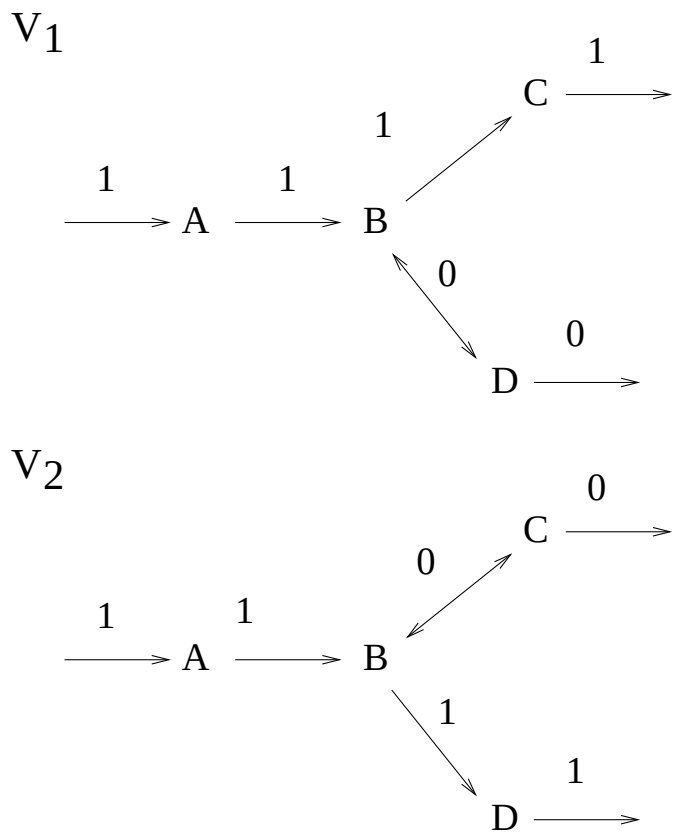
## Representing EFMs

- Elementary flux modes are given as reaction rate vectors

$$\mathbf{e} = (e_1, \ldots, e_n),$$

- EFMs typically consists of many zeroes, so they represent pathways in the network given by the non-zero components

$$P(\mathbf{e}) = \{j | e_j \neq 0\}$$



## Properties of elementary flux modes

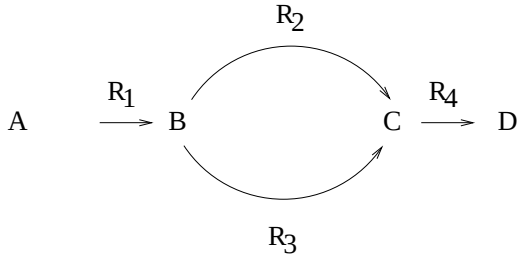
The following properties are statisfied by EFMs:

- (Quasi-) Steady state
- Thermodynamical feasibility. Irreversible reactions need to proceed in the correct direction. Formally, one requires $e_j \geq 0$ and that the stoichiometric coefficients $s_{ij}$ are written with the sign that is consistent with the direction
- Non-decomposability. One cannot remove a reaction from an EFM and still obtain a reaction rate vector that is feasible in steady state. That is, if $\mathbf{e}$ is an EFM there is no vector $\mathbf{v}$ that satisfies the above and $P(\mathbf{v}) \subset P(\mathbf{e})$

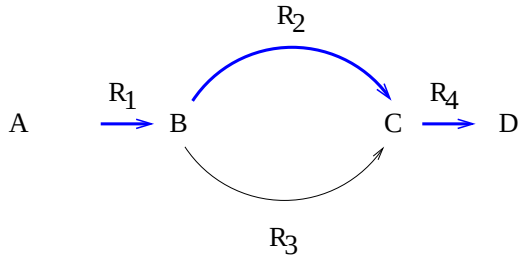
These properties define EFMs upto a scaling factor: if $\mathbf{e}$ is an EFM $\alpha\mathbf{e}, \alpha > 0$ is also an EFM.

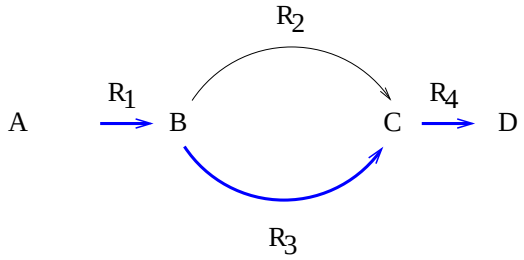
# Example

Metabolic system:

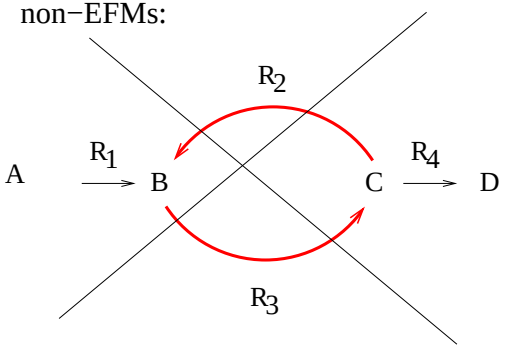


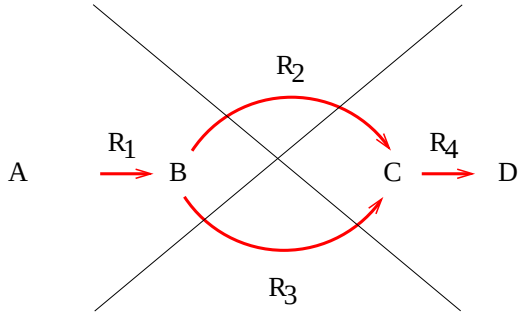

EFMs:




non−EFMs:



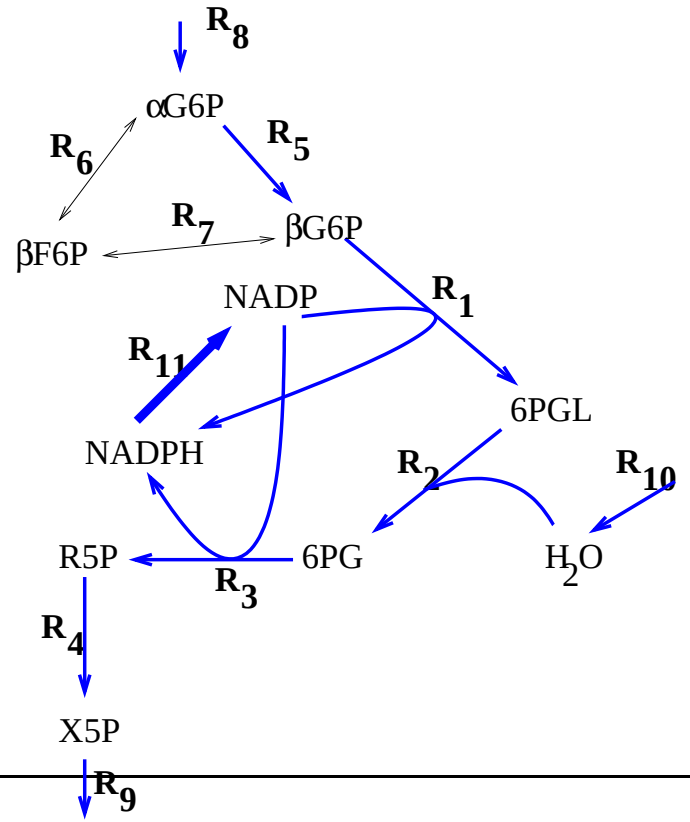
## EFMs and steady state fluxes

- Any steady state flux vector $\mathbf{v}$ can be represented as a non-negative combination of the elementary flux modes: $\mathbf{v} = \sum_j \alpha_j \mathbf{e}_j$, where $\alpha_j \geq 0$.
- However, the representation is not unique: one can often find several coefficient sets $\alpha$ that satisfy the above.
- Thus, a direct composition of a flux vector into the underlying EFPs is typically not possible. However, the *spectrum* of potential contributions can be analysed

## EFMs of PPP

- One of the elementary flux modes of our PPP system is given below
- It consist of a linear pathway through the system, exluding reactions $R_6$ and $R_7$
- Reaction $R_{11}$ needs to operate with twice the rate of the others

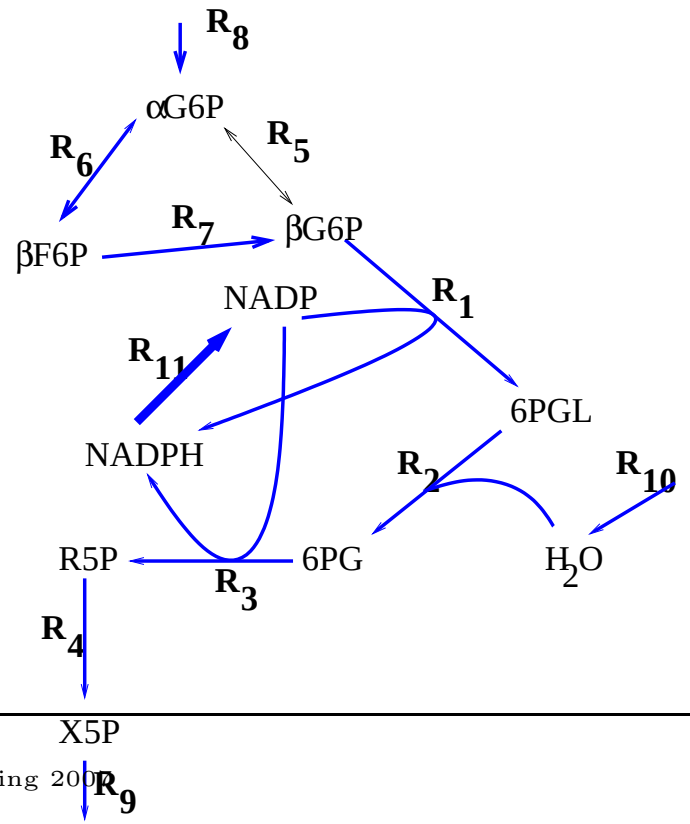
$$efm_1 = \begin{matrix} R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \\ R_6 \\ R_7 \\ R_8 \\ R_9 \\ R_{10} \\ R_{11} \end{matrix} \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 0 \\ 0 \\ 1 \\ 1 \\ 1 \\ 2 \end{bmatrix}$$



## EFMs of PPP

- Another elementary flux modes of our PPP system
- Similar linear pathway through the system, but exluding reactions $R_5$ and using $R_7$ in reverse direction
- Again, reaction $R_{11}$ needs to operate with twice the rate of the others

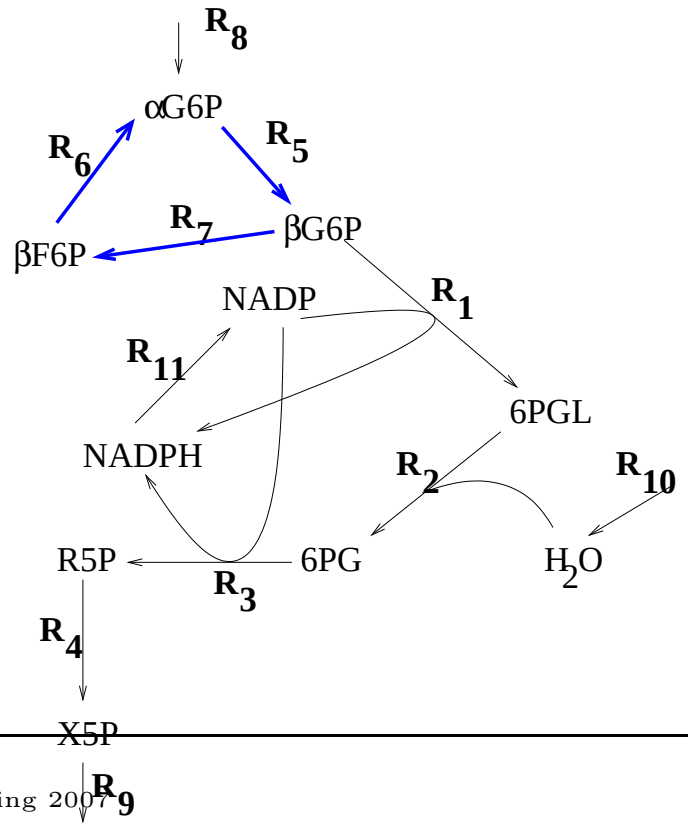
$$efm_2 = \begin{array}{c|c} R_1 & 1 \\ R_2 & 1 \\ R_3 & 1 \\ R_4 & 1 \\ R_5 & 0 \\ R_6 & 1 \\ R_7 & -1 \\ R_8 & 1 \\ R_9 & 1 \\ R_{10} & 1 \\ \hline R_{11} & 2 \end{array}$$



## EFMs of PPP

- Third elementary flux mode contains only the small cycle composed of $R_5$, $R_7$ and $R_6$. $R_6$ is used in reverse direction
- A yet another EFM would be obtained by reversing all the reactions in this cycle

$$efm_3 = \begin{array}{c} \\ R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \\ R_6 \\ R_7 \\ R_8 \\ R_9 \\ R_{10} \\ R_{11} \end{array} \begin{bmatrix} \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ -1 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$



## Building the kernel from EFMs

- In general there are more elementary flux modes than the dimension of the null space
- Thus a linearly independent subset of elementary flux modes suffices to span the null space
- In our PPP system, any two of the three EFMs together is linearly independent, and can thus be taken as the representative vectors

$$EFM = \begin{array}{c} \\ R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \\ R_6 \\ R_7 \\ R_8 \\ R_9 \\ R_{10} \\ R_{11} \end{array} \begin{bmatrix} & & \\ 0 & 1 & 1 \\ 0 & 1 & 1 \\ 0 & 1 & 1 \\ 0 & 1 & 1 \\ 1 & 1 & 0 \\ -1 & 0 & 1 \\ 1 & 0 & -1 \\ 0 & 1 & 1 \\ 0 & 1 & 1 \\ 0 & 1 & 1 \\ 0 & 2 & 2 \end{bmatrix}$$

## Software for finding EFMs

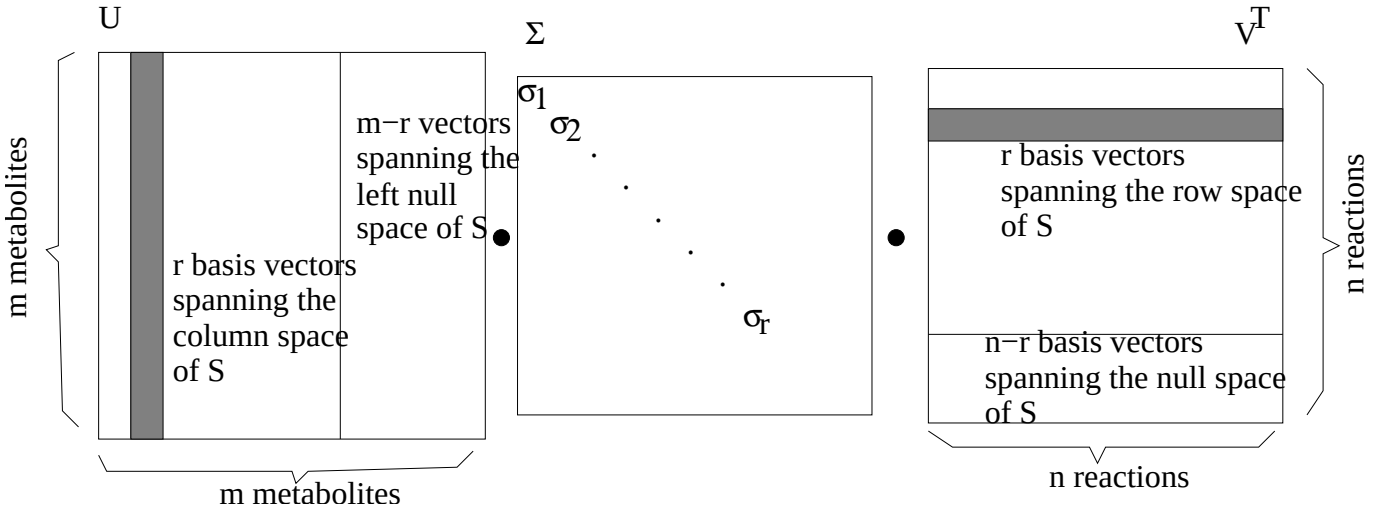
- From small systems it is relatively easy to find the EFMs by manual inspection
- For larger systems this becomes impossible, as the number of EFMs grows easily very large
- Computational methods have been devised for finding the EFMs by Heinrich & Schuster, 1994 and Urbanczik and Wagner, 2005
- Implemented in MetaTool package

## Conservation relations

- As chemical reactions do not create or destroy matter, they obey conservation relations
- The counts of substrate and product molecules are balanced
- In the example reaction $r : A + B \mapsto 2C$, the sum $A + B + 2C = const$ is constant.
- Other conserved quantitites:
  - Elemental balance: for each element species (C,N,O,P,...) the number of elements is conserved
  - Charge balance: total electrical charge, the total number of electrons in a reaction does not change.
  - Moiety balancing: it is possible to write balances for larger chemical moieties such as the co-factors (NAD,NADH, ATP, ADP,...)

## Conservation relations from the stoichiometric matrix

- From the stoichiometric matrix conservation relations of metabolites can be found by examining the left null space of $S$, i.e. the set $\{\mathbf{l}|\mathbf{l}S = 0\}$
- A basis spanning the left null space can be obtained from SVD $S = U\Sigma V^T$: the last $m - r$ columns of the matrix $U$ span the left null space, where $r$ is the rank of $S$
- In MATLAB the basis can be computed by the command $null(S')$.



## Conservation in PPP

The left null space of our PPP system only contains a single vector, stating that the sum of $\mathrm{NADP}^+$ and $NADPH$ is constant in all reactions.

$$\mathbf{l}^T = \begin{array}{c} \\ \beta G6P \\ \alpha G6P \\ \beta F6P \\ 6PGL \\ 6PG \\ R5P \\ X5P \\ NADP^+ \\ NADPH \\ H_2O \end{array} \begin{bmatrix} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0.7071 \\ 0.7071 \\ 0 \end{bmatrix}$$