TECHNICAL REPORT

Stability analysis of networks

Concepts of topological equivalence, bifurcations and structural stability of dynamical systems are relatively well established, thus we will not introduce these extensive theories (Guckenheimer and Holmes, 1983; Kubíček and Marek, 1983; Kuznetsov, 1995). In this report we will describe the stability analysis of chemical networks and sort them according to their stability.

1 Introduction

The time evolution of many physical, chemical and biological systems can be described by a set of nonlinear ordinary differential equations (ODEs) of the first order

$$\begin{aligned} \dot{x}_1 &= f_1(x_1, \ldots, x_n)\,, \\ \dot{x}_2 &= f_2(x_1, \ldots, x_n)\,, \\ &\vdots \\ \dot{x}_n &= f_n(x_1, \ldots, x_n)\,. \end{aligned} \tag{1}$$

where f_i, $i = 1, \ldots, n$ are real functions of n real variables. Using vector notation we may rewrite Eq. (1) into short form

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})\,, \tag{2}$$

where $\mathbf{x} = (x_1, \ldots, x_n)^{\mathrm{T}} \in \mathbb{R}^n$ and $\mathbf{f} : \mathbb{R}^n \to \mathbb{R}^n$ is a mapping of class C^r, $r \geqslant 1$. We may interpret Eq. (1) or Eq. (2) as a mathematical model of a real dynamical system, whose state in time t is $\mathbf{x}(t)$. Geometrically, Eq. (2) assigns to each $\mathbf{x} \in \mathbb{R}^n$ the vector $\mathbf{f}(\mathbf{x})$ which is based at $\mathbf{x}$ and corresponds to the vector $\dot{\mathbf{x}}$, the rate of change of the state $\mathbf{x}$.

A set of all states of the system $\mathbb{R}^n$ will be called a *state space*. The term *phase space* is also used for the state space in the physics literature. A mapping $\mathbf{F}(\mathbf{x}) = (\mathbf{x}, \mathbf{f}(\mathbf{x}))$, $\mathbf{x} \in \mathbb{R}^n$ will be called a *vector field*. The mapping $\mathbf{f}$ is the main part of the vector field.
REMARK: For convenience, below the term vector field will usually stand for the main part of the vector field.

The solution of ODEs Eq. (1) is a differentiable mapping $\boldsymbol{\varphi} : I \to \mathbb{R}^n$ from $I = \{t \in \mathbb{R} \mid a < t < b\}$ into the state space $\mathbb{R}^n$, which satisfies the initial condition $\boldsymbol{\varphi}(0) = \mathbf{x}$ and

$$\frac{\mathrm{d}\boldsymbol{\varphi}(t)}{\mathrm{d}t} = \dot{\boldsymbol{\varphi}}(t) = \mathbf{f}(\boldsymbol{\varphi}(t)), \qquad \forall\, t,\, t \in I\,. \tag{3}$$

2 The linearized dynamics

The dynamical behaviour of the system is described by the evolution equation

$$\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}t} = \dot{\mathbf{x}} = \underline{\boldsymbol{\nu}}\, \mathbf{v}(\mathbf{x}, \mathbf{k})\,. \tag{4}$$

Since we are interested in the dynamics close to the steady state $\mathbf{x}^0$, we will analyse linearized form of Eq. (4)

$$\frac{\mathrm{d}\delta x_i}{\mathrm{d}t} = \sum_{j=1}^{r} \nu_{ij}\, [v_j(\mathbf{x}^0,\, \mathbf{k}) + \sum_{m=1}^{n} \frac{\partial v_j(\mathbf{x}^0,\, \mathbf{k})}{\partial x_m}\, \delta x_m + \ldots], \qquad i = 1, \ldots, n\,, \tag{5}$$

where $\delta x_i \equiv x_i - x_i^0$ is the deviation from the steady state concentration of species $\mathcal{S}_i$. According to $\underline{\boldsymbol{\nu}}\, \mathbf{v}^0(\mathbf{x}^0, \mathbf{k}) = \mathbf{0}$, the leading term vanishes at steady state. Let $\boldsymbol{\zeta} = \boldsymbol{\delta}\mathbf{x}$, such that $\zeta_i = \delta x_i$. We can write Eq. (5) in matrix form

$$\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}t} = \mathbf{M}_\zeta\, \boldsymbol{\zeta}\,, \tag{6}$$

where $\mathbf{M}_\zeta \in \mathbb{R}^{n\times n}$ is the Jacobi matrix of the right hand side of Eq. (4). The element of the Jacobi matrix M_{ij} is defined as

$$M_{ij} = \sum_{m=1}^{r} \nu_{im} \frac{\partial v_m(\mathbf{x}^0,\, \mathbf{k})}{\partial x_j}\,. \tag{7}$$

Now we express the partial derivative in M_{ij}. Assume that

$$\frac{\partial v_j(\mathbf{x}^0,\, \mathbf{k})}{\partial x_i} = \frac{\partial v_j(\mathbf{x}^0,\, \mathbf{k})}{\partial \ln x_i}\, \frac{\mathrm{d} \ln x_i}{\mathrm{d}x_i}\,. \tag{8}$$

Multiplying the right hand side of Eq. (8) by $\partial \ln v_j / \partial \ln v_j$ gives

$$\frac{\partial v_j(\mathbf{x}^0,\, \mathbf{k})}{\partial x_i} = \frac{\partial \ln v_j}{\partial \ln v_j}\, \frac{\partial v_j}{\partial \ln x_i}\, \frac{\mathrm{d} \ln x_i}{\mathrm{d}x_i}\,. \tag{9}$$

Upon rearranging the right hand side of Eq. (9)

$$\frac{\partial v_j(\mathbf{x}^0,\, \mathbf{k})}{\partial x_i} = \frac{\mathrm{d}v_j}{\mathrm{d} \ln v_j}\, \frac{\partial \ln v_j}{\partial \ln x_i}\, \frac{\mathrm{d} \ln x_i}{\mathrm{d}x_i}\,, \tag{10}$$

we can substitute the known derivatives into Eq. (10) to obtain

$$\frac{\partial v_j(\mathbf{x}^0,\,\mathbf{k})}{\partial x_i} = v_j\,\frac{\partial \ln v_j}{\partial \ln x_i}\,\frac{1}{x_i^0}\,. \tag{11}$$

Recall that the effective power function defined

$$\kappa_{ij} \equiv \frac{\partial \ln v_j(\mathbf{x}, \mathbf{k})}{\partial \ln x_i} \tag{12}$$

can be a function of the redundant parameters

$$\kappa_{ij}(\mathbf{p}_R) \equiv \frac{\partial \ln v_j(\mathbf{x}^0(\mathbf{p}_R),\,\mathbf{k}(\mathbf{p}_R))}{\partial \ln x_i}\,. \tag{13}$$

By combining Eq. (5), Eq. (11), and Eq. (13) we obtain

$$\frac{\mathrm{d}\delta x_i}{\mathrm{d}t} = \sum_{j=1}^{r} \nu_{ij} \sum_{m=1}^{n} \frac{v_j(\mathbf{x}^0,\,\mathbf{k})}{x_m^0}\,\kappa_{mj}(\mathbf{p}_R)\,\delta x_m\,. \tag{14}$$

With the use of $\mathbf{v}^0 = \mathbf{E}\,\mathbf{j}$ and $h_i = \frac{1}{x_i^0}$ the Eq. (14) reads

$$\frac{\mathrm{d}\delta x_i}{\mathrm{d}t} = \sum_{j=1}^{r} \nu_{ij} \sum_{q=1}^{f} E_{jq}\,j_q \sum_{m=1}^{n} \kappa_{mj}\,(\mathbf{p}_R)\,h_m\,\delta x_m\,. \tag{15}$$

By comparing Eq. (6) and Eq. (15), we can write Eq. (7) in matrix notation,

$$\mathbf{M}_\zeta(\mathbf{h},\mathbf{j}) = \underline{\boldsymbol{\nu}}\,\mathrm{diag}(\mathbf{E}\,\mathbf{j})\,\underline{\boldsymbol{\kappa}}^{\mathrm{T}}(\mathbf{h},\,\mathbf{j})\,\mathrm{diag}(\mathbf{h})\,. \tag{16}$$

Sometimes it is useful to define new variables $\zeta' = \mathrm{diag}(\mathbf{h}^{\frac{1}{2}})\zeta$ and $\zeta'' = \mathrm{diag}(\mathbf{h})\zeta$. Then

$$\mathbf{M}_{\zeta'}(\mathbf{h},\mathbf{j}) = \mathrm{diag}(\mathbf{h}^{\frac{1}{2}})\,\underline{\boldsymbol{\nu}}\,\mathrm{diag}(\mathbf{E}\,\mathbf{j})\,\underline{\boldsymbol{\kappa}}^{\mathrm{T}}(\mathbf{h},\mathbf{j})\,(\mathrm{diag}\,\mathbf{h}^{\frac{1}{2}})\,, \tag{17}$$

$$\mathbf{M}_{\zeta''}(\mathbf{h},\mathbf{j}) = \mathrm{diag}(\mathbf{h})\,\underline{\boldsymbol{\nu}}\,\mathrm{diag}(\mathbf{E}\,\mathbf{j})\,\underline{\boldsymbol{\kappa}}^{\mathrm{T}}(\mathbf{h},\mathbf{j})\,. \tag{18}$$

Here the parameter h_i multiplies the ith column of $\mathbf{M}_\zeta$ and the ith row of $\mathbf{M}_{\zeta''}$. The matrix $\mathbf{M}_{\zeta'}$ is symmetric in the parameters $\mathbf{h}$.

There is a one-to-one correspondence between the accessible concentration states $\mathbf{x} \in \Pi_x(\mathbf{C})$ and the accessible extents of reaction $\boldsymbol{\xi} \in \Pi_\xi(\mathbf{C})$, we can transform variables $\mathbf{x}$ by $\boldsymbol{\xi}$ in Eq. (5). Let $\boldsymbol{\eta} \equiv \boldsymbol{\xi} - \boldsymbol{\xi}^0$. Then

$$\boldsymbol{\zeta} = \underline{\boldsymbol{\nu}}\,\boldsymbol{\eta}\,. \tag{19}$$

gives the transformation equation. Combining Eq. (6) and Eq. (16) and substituting for $\boldsymbol{\zeta}$ from Eq. (19) yields

$$\underline{\boldsymbol{\nu}}\,\dot{\boldsymbol{\eta}} = \underline{\boldsymbol{\nu}}\,\mathrm{diag}(\mathbf{E}\,\mathbf{j})\,\underline{\boldsymbol{\kappa}}^{\mathrm{T}}(\mathbf{h},\mathbf{j})\,\mathrm{diag}(\mathbf{h})\,\underline{\boldsymbol{\nu}}\,\boldsymbol{\eta}\,. \tag{20}$$

These d independent equations are sufficient to determine $\boldsymbol{\eta}$ if $\boldsymbol{\xi} \in \mathcal{R}(\underline{\boldsymbol{\nu}}^{\mathrm{T}})$, which implies $\boldsymbol{\eta} \in \mathcal{R}(\underline{\boldsymbol{\nu}}^{\mathrm{T}})$. We may remove $\underline{\boldsymbol{\nu}}$ from both sides, provided we will use the projection operator $\mathbf{P}_\xi$ to ensure that the right side of Eq. (20) lies in $\mathcal{R}(\underline{\boldsymbol{\nu}}^{\mathrm{T}})$. The final linearized equation for $\boldsymbol{\eta}$ has the same form as Eq. (6),

$$\frac{\mathrm{d}\boldsymbol{\eta}}{\mathrm{d}t} = \mathbf{M}_\eta \, \boldsymbol{\eta} \,, \tag{21}$$

and the Jacobi matrix $\mathbf{M}_\eta$ is

$$\mathbf{M}_\eta(\mathbf{h}, \mathbf{j}) = \mathbf{P}_\xi \, \mathrm{diag}(\mathbf{E}\,\mathbf{j}) \, \underline{\boldsymbol{\kappa}}^{\mathrm{T}}(\mathbf{h}, \mathbf{j}) \, \mathrm{diag}(\mathbf{h}) \, \underline{\boldsymbol{\nu}} \,. \tag{22}$$

We may convert Eq. (16) and Eq. (22) from redundant parameters to convex parameters by replacing $\mathbf{E}\,\mathbf{j}$ with $\mathbf{E}^*_i \, \mathbf{j}^*$. The effective power function may also contain additional parameters beyond $\mathbf{p}_R \in D_R$. Consider two special cases when $\underline{\boldsymbol{\kappa}}(\mathbf{p})$ is constant and when $\underline{\boldsymbol{\kappa}}(\mathbf{p})$ can vary over a wide range via the additional parameters.

Let $\underline{\boldsymbol{\kappa}}(\mathbf{p}) = \underline{\boldsymbol{\kappa}}$ be a constant matrix. Define a matrix $\mathbf{S}^{(i)}$ which contains all essential information for the ith extreme current

$$\mathbf{S}^{(i)} \equiv -\underline{\boldsymbol{\nu}} \, \mathrm{diag}(\mathbf{E}_i) \, \underline{\boldsymbol{\kappa}}^{\mathrm{T}} \,, \tag{23}$$

where $\mathbf{E}_i$ is the corresponding column of $\mathbf{E}$. We can also define

$$\mathbf{V}(\mathbf{j}) \equiv -\underline{\boldsymbol{\nu}} \, \mathrm{diag}(\mathbf{E}\mathbf{j}) \, \underline{\boldsymbol{\kappa}}^{\mathrm{T}} \,. \tag{24}$$

Eq. (23) and Eq. (24) relate to the Jacobi matrix $\mathbf{M}_\zeta$ as follows

$$\mathbf{M}_\zeta(\mathbf{h}, \mathbf{j}) = -\sum_{i=1}^{f} j_i \, \mathbf{S}^{(i)} \mathrm{diag}(\mathbf{h}) = -\mathbf{V}(\mathbf{j}) \, \mathrm{diag}(\mathbf{h}) \,, \tag{25}$$

$$\mathbf{M}_{\zeta'}(\mathbf{h}, \mathbf{j}) = -\sum_{i=1}^{f} j_i \, \mathrm{diag}(\mathbf{h}^{\frac{1}{2}}) \, \mathbf{S}^{(i)} \, \mathrm{diag}(\mathbf{h}^{\frac{1}{2}}) = -\mathrm{diag}(\mathbf{h}^{\frac{1}{2}}) \, \mathbf{V}(\mathbf{j}) \, \mathrm{diag}(\mathbf{h}^{\frac{1}{2}}) \,, \tag{26}$$

$$\mathbf{M}_{\zeta''}(\mathbf{h}, \mathbf{j}) = -\sum_{i=1}^{f} j_i \, \mathrm{diag}(\mathbf{h}) \, \mathbf{S}^{(i)} = -\mathrm{diag}(\mathbf{h}) \, \mathbf{V}(\mathbf{j}) \,. \tag{27}$$

Clarke (1980) derived a special form of the Jacobi matrix $\mathbf{M}^*_{\zeta\,R}$ for the case, when the effective power function $\underline{\boldsymbol{\kappa}}(\mathbf{p})$ is not constant.

This complicated formula for $\mathbf{M}^*_\zeta$, see page 47 in (Clarke, 1980), is rarely used.

For further purposes, $\mathbf{M}_\zeta(\mathbf{h}, \mathbf{j})$ and $\mathbf{M}_{\zeta''}(\mathbf{h}, \mathbf{j})$ are the most useful matrices.

3 Stability of systems and networks

Let $\mathbf{u}$ represent the perturbed variables $\boldsymbol{\zeta}$, $\boldsymbol{\zeta}'$, $\boldsymbol{\zeta}''$, or $\boldsymbol{\eta}$. Let the nonlinear equation of motion be

$$\dot{\mathbf{u}} = \mathbf{f}(\mathbf{u}, \mathbf{p})\,. \tag{28}$$

Let the linearized system be

$$\dot{\mathbf{u}} = \mathbf{M}(\mathbf{p})\mathbf{u}\,, \tag{29}$$

where $\mathbf{M}(\mathbf{p})$ is the Jacobi matrix discussed above and the parameter vector $\mathbf{p}$ lies in a domain D. The set of linear ODEs (29) has always a formal solution

$$\mathbf{u}(t) = e^{t\,\mathbf{M}(\mathbf{p})}\,\mathbf{u}(0)\,, \tag{30}$$

where $e^{\mathbf{M}(\mathbf{p})\,t}$ is the matrix exponential given by the power series

$$e^{t\,\mathbf{M}(\mathbf{p})} = \sum_{k=0}^{\infty} \frac{1}{k!}\,t^k\,\mathbf{M}(\mathbf{p})^k\,. \tag{31}$$

The series may be expressed as the product of two matrices. Hence the general form of the ith component of $\mathbf{u}(t)$ is a sum over eigenvalues λ_j

$$u_i(t) = \sum_j u_j(0)\,\theta_{ij}(t)\,e^{\lambda_j\,t}\,, \tag{32}$$

where $\theta_{ij}(t)$ is a polynomial in t and $\theta_{ij}(0) = 1$. The imaginary part of λ_j, $\Im(\lambda_j)$, makes the corresponding term in Eq. (32) periodic and does not affect the stability. If the real parts of all the eigenvalues are negative ($\Re(\lambda_j) < 0$), then $u_i(t) \to 0$ and the origin $\mathbf{u} = 0$ is said to be *asymptotically stable*. If $\Re(\lambda_j) > 0$ for any j such that $\theta_{ij}(t) \neq 0$, then $u_i(t)$ increases without limit and the origin is said to be *unstable*. The remaining possibility is when $\Re(\lambda_j) = 0$ for some j and $\Re(\lambda_j) \leqslant 0$ for all j. This case can lead to stability or instability depending on the circumstances. We now examine this situation in detail by first considering how zero eigenvalues arise.

The motion of $\mathbf{u}$ is confined to a polyhedron $\Pi(\mathbf{C})$ of dimension d, such as $\Pi_x(\mathbf{C})$ or $\Pi_\xi(\mathbf{C})$. Hence $\dot{\mathbf{u}}$ is a linear combination of the columns of $\mathbf{M}(\mathbf{p})$ by Eq. (29) and must lie in this d-dimensional subspace. Then it is clear that

$$\operatorname{rank}\mathbf{M}(\mathbf{p}) \leqslant d\,. \tag{33}$$

Assume that the matrix $\mathbf{M}(\mathbf{p})$ is either an $n \times n$ or an $r \times r$ matrix. Let $\rho = n - d$ in the first case, and let $\rho = r - d$ in the second one. Then Eq. (33) implies that $\mathbf{M}(\mathbf{p})$ has at least ρ zero eigenvalues. These eigenvalues contribute a constant term to Eq. (32) and a perturbation in the corresponding eigenspace, i.e. space spanned by the corresponding eigenvectors, takes the system into a new steady state. Thus there is a ρ-dimensional set of steady states near any particular steady state. Let the original steady state lies in $\Pi(\mathbf{C}^0)$. Then there must be a nearby steady state lying in $\Pi(\mathbf{C})$, for $\mathbf{C}$ close to $\mathbf{C}^0$. Since $\mathbf{C} \in \mathbb{R}_+^{n-d}$, the nearby steady states form an $(n-d)$-dimensional set. If $\mathbf{M}(\mathbf{p}) \in \mathbb{R}^{n\times n}$, these steady states are the steady states associated with the generalized eigenspace of the $n - d$ vanishing eigenvalues. If $\mathbf{M}(\mathbf{p}) \in \mathbb{R}^{r\times r}$, the generalized eigenspace of the $r - d$ vanishing eigenvalues has $r - n$ more dimensions than the set of adjacent steady states in the set of nearby polyhedra $\Pi(\mathbf{C})$. These $r - n$ extra dimensions correspond to the $r - n$ physically meaningless reaction extents in $\boldsymbol{\xi}$ which are removed by the projection operator $\mathbf{P}_\xi$.

Perturbations outside of $\Pi(\mathbf{C}^0)$ are not physically possible because they violate the conservation condition $\underline{\boldsymbol{\gamma}}\ \mathbf{x} = \mathbf{C}$. Since $\mathbf{M}(\mathbf{p})$ has a ρ-dimensional set of steady states located close to $\mathbf{x}^0$ outside of $\Pi(\mathbf{C}^0)$, the perturbations from $\mathbf{x}^0$ to these steady states are irrelevant for stability and the ρ associated eigenvalues of $\mathbf{M}(\mathbf{p})$ are also irrelevant. Therefore we may remove a factor λ^ρ from the characteristic polynomial

$$\det|\lambda\mathbf{I} - \mathbf{M}(\mathbf{p})| = \lambda^\rho\, \chi(\lambda,\, \mathbf{p})\,, \tag{34}$$

and the *relevant eigenvalues* are solutions of

$$\chi(\lambda,\, \mathbf{p}) = 0\,. \tag{35}$$

The following precise definitions of stability are valid for the general (nonlinear) case.

A system is *asymptotically stable* if there exists $\delta > 0$, such that half-trajectory $\mathbf{u}(t)$ initially in the appropriate polyhedron with $\|\mathbf{u}(0)\| < \delta$, approaches the origin $\mathbf{0}$ in the limit

$$\lim_{t\to\infty} \|\mathbf{u}(t)\| = 0. \tag{36}$$

A system is *marginally stable* if for every $\varepsilon > 0$, there exists $\delta > 0$ such that all semi-trajectories $\mathbf{u}(t)$ initially in the appropriate polyhedron with $\|\mathbf{u}(0)\| < \delta$ satisfy $\|\mathbf{u}(t)\| < \varepsilon$ for all $t > 0$.

A system is *stable* if it is asymptotically stable or marginally stable, otherwise it is *unstable*. Hence a system is unstable if and only if there exists $\varepsilon > 0$ such that for every $\delta > 0$, the set of semi-trajectories $\mathbf{u}(t)$ initially in the appropriate polyhedron with $\|\mathbf{u}(0)\| < \delta$, contains a trajectory $\|\mathbf{u}(t)\| \geq \varepsilon$ with for some t.

3.1 Linear systems

For linear system, the following conclusions follow easily from Eq. (32). The system is asymptotically stable if and only if $\Re(\lambda_j) < 0$ for all relevant eigenvalues λ_j. A necessary (but not sufficient) condition for marginal stability is that $\Re(\lambda_j) \leqslant 0$ for all relevant eigenvalues λ_j. A sufficient (but not necessary) condition for instability is that $\Re(\lambda_j) > 0$ for some eigenvalue λ_j. These rules determine the stability in all cases, except the case when $\Re(\lambda_j) \leqslant 0$ for all j and $\Re(\lambda_j) = 0$ for some relevant eigenvalue λ_j. The system is marginally stable if $\theta_{ij}(t)$ in Eq. (32) contains no terms in t^k, $k \geqslant 1$, whenever $\Re(\lambda_j) = 0$. Otherwise the system is unstable. This property of the functions $\theta_{ij}(t)$ may be ascertained by examining the *minimal polynomial* $\mu(\lambda, \mathbf{p})$. $\mu(\lambda, \mathbf{p})$ is defined to be the polynomial of least degree that divides $\chi(\lambda, \mathbf{p})$ and has the property that $\mu(\mathbf{M}(\mathbf{p})) = 0$. If $\Re(\lambda_j) = 0$, the origin is marginally stable if λ_j is a simple root of $\mu(\lambda, \mathbf{p})$ and unstable if λ_j is a multiple root. When this instability occurs, the deviation from steady state is proportional to t^k. Hence we call this case a *weak instability* to distinguish it from the *exponential instability*, if $\Re(\lambda_j) > 0$.

Let $\Lambda(\mathbf{p})$ be the set of relevant eigenvalues of the matrix $\mathbf{M}(\mathbf{p})$. For each $\mathbf{p} \in D$, we may define the domains where the linearized system is asymptotically stable and exponentially unstable, respectively,

$$\begin{aligned} D_a^L &\equiv \{\mathbf{p} \in D \,|\, \Re(\lambda) < 0,\ \forall \lambda \in \Lambda(\mathbf{p})\}\,, \\ D_e^L &\equiv \{\mathbf{p} \in D \,|\, \Re(\lambda) > 0,\ \exists \lambda \in \Lambda(\mathbf{p})\}\,. \end{aligned} \tag{37}$$

The domain

$$\begin{aligned} D_{mw}^L \equiv \{\mathbf{p} \in D \,|\, \Re(\lambda) \leq 0,\ \forall \lambda \in \Lambda(\mathbf{p})\,, \\ \Re(\lambda) = 0,\ \exists \lambda \in \Lambda(\mathbf{p})\} \end{aligned} \tag{38}$$

can be divided into two domains D_m^L and D_w^L, where the system is respectively marginally stable or weakly unstable. Then

$$\chi(\lambda, \mathbf{p}) = D_a^L \cup D_m^L \cup D_w^L \cup D_e^L\,,$$

and none of the four sets D_a^L, D_m^L, D_w^L, or D_e^L intersect. The linear system is stable on the set $D_s^L \equiv D_a^L \cup D_m^L$ and unstable on the set $D_u^L \equiv D_w^L \cup D_e^L$. It is *semistable* on the set $D_{\text{semi}}^L \equiv D_a^L \cup D_m^L \cup D_w^L$.

3.2 Nonlinear systems

Further complications arise in nonlinear systems. We may write the nonlinear equation of motion (28) as

$$\dot{\mathbf{u}} = \mathbf{M}(\mathbf{p})\mathbf{u} + \mathbf{g}(\mathbf{u},\, \mathbf{p})\,, \tag{39}$$

where $\mathbf{g}(\mathbf{u},\, \mathbf{p})$ contains nonlinear corrections to the linearized system which come from Taylor series expansion in Eq. (5). Hence $\mathbf{g}(\mathbf{u},\, \mathbf{p})$ are polynomials that involve terms of at least the degree 2. If every eigenvalue of $\mathbf{M}(\mathbf{p})$ satisfies $\Re(\lambda) \neq 0$, corrections $\mathbf{g}(\mathbf{u},\, \mathbf{p})$ become negligible close to a steady state and the motion is similar to the linearized system. Hence a sufficient (but not necessary) condition for the nonlinear system to be asymptotically stable is that $\mathbf{p} \in D_a^L$. Also a sufficient (but not necessary) condition for the nonlinear system to be unstable is that $\mathbf{p} \in D_e^L$. We discussed all situations except the one where $\mathbf{p} \in D_{mw}^L = D_m^L \cup D_w^L$. Then the first term in Eq. (39) does not give a radial component to the motion (marginally stable case) or gives a weakly divergent (t^k) radial dependence (unstable case). In these cases, the nonlinear term is not always negligible with respect to the linear terms. Then the nonlinear system may be asymptotically stable, marginally stable, or unstable, independently of the linearized system.

For each $\mathbf{p} \in D$, the nonlinear system is either asymptotically stable, marginally stable, or unstable. Thus we may divide D into three mutually exclusive subsets D_a, D_m, and D_u respectively. The stable set is $D_s = D_a \cap D_m$. Hence we may write

$$D_a \supset D_a^L\,, \tag{40}$$

$$D_u \supset D_e^L\,, \tag{41}$$

and then

$$D_m \subset D_{mw}^L\,. \tag{42}$$

3.3 Stability of networks

Let $\mathcal{N}$ be the set of all chemical networks. The set of *asymptotically stable networks* is

$$\mathcal{N}_a \equiv \{N \in \mathcal{N} \mid D_m = \emptyset,\, D_u = \emptyset\}\,, \tag{43}$$

the set of *marginally stable networks* is

$$\mathcal{N}_m \equiv \{N \in \mathcal{N} \mid D_m \neq \emptyset,\, D_u = \emptyset\}\,, \tag{44}$$

and the set of *unstable networks* is

$$\mathcal{N}_u \equiv \{N \in \mathcal{N} \mid D_u \neq \emptyset\} \,. \tag{45}$$

Our task is to find sets $\mathcal{N}_a$, $\mathcal{N}_m$, and $\mathcal{N}_u$. This task is difficult because some networks in each set are networks whose linearized dynamics are marginally stable or weakly unstable, with nonlinear terms deciding the true stability. Hence it is useful to define sets of networks according to the stability of their linearization. The set of *linearly asymptotically stable networks* is

$$\mathcal{N}_a^L \equiv \{N \in \mathcal{N} \mid D_a^L = D\} \,, \tag{46}$$

the set of *linearly marginally stable networks* is

$$\mathcal{N}_m^L \equiv \{N \in \mathcal{N} \mid D_m^L \neq \emptyset,\, D_w^L = D_e^L = \emptyset\} \,, \tag{47}$$

the set of *linearly weakly unstable networks* is

$$\mathcal{N}_w^L \equiv \{N \in \mathcal{N} \mid D_w^L \neq \emptyset,\, D_e^L = \emptyset\} \,, \tag{48}$$

and the set of *linearly exponentially unstable networks* is

$$\mathcal{N}_e^L \equiv \{N \in \mathcal{N} \mid D_e^L \neq \emptyset\} \,. \tag{49}$$

Using these sets we may define the set of *linearly semistable networks* to be

$$\mathcal{N}_{\text{semi}}^L \equiv \mathcal{N}_a^L \cup \mathcal{N}_m^L \cup \mathcal{N}_w^L \,, \tag{50}$$

and the set of *linearly stable networks* to be

$$\mathcal{N}_s^L \equiv \mathcal{N}_a^L \cup \mathcal{N}_m^L \,. \tag{51}$$

Equations (40–41) give relationships

$$\mathcal{N}_a \supset \mathcal{N}_a^L \,, \qquad \mathcal{N}_u \supset \mathcal{N}_e^L \,. \tag{52}$$

Finally, we may obtain following relationships

$$\mathcal{N}_{\text{semi}}^L = \{N \in \mathcal{N} \mid D_e^L \neq \emptyset\} = \mathcal{N} \backslash \mathcal{N}_e^L, \tag{53}$$

$$\mathcal{N} = \mathcal{N}_a^L \cup \mathcal{N}_m^L \cup \mathcal{N}_w^L \cup \mathcal{N}_e^L \,. \tag{54}$$

However, $\mathcal{N}_{\text{semi}}^L$ and $\mathcal{N}_e^L$ are particularly useful since it is probably easiest to find necessary and sufficient conditions for a network to be in $\mathcal{N}_{\text{semi}}^L$, or $\mathcal{N}_e^L$.

3.4 Extreme networks

A network is an *extreme network* if it contains only one extreme current. The set of extreme networks is

$$\mathcal{E} \equiv \{N \in \mathcal{N} \mid \dim \Pi_v(N) = 0\}\,. \tag{55}$$

The extreme currents of the general network $N \in \mathcal{N}$ are the columns of the matrix $\mathbf{E}$ that form the set $\{\mathbf{E}_i \mid i \in [1, f]\}$. Each vector $\mathbf{E}_i \in \mathbf{E}$ corresponds to the extreme network $E \in \mathcal{E}$ which consists of the reactions of the network N whose corresponding components of $\mathbf{E}_i$ do not vanish. Only the species in these reactions are species of the extreme network E. We call E an *extreme subnetwork* of the network N. The correspondence between $\mathbf{E}_i$ and E can be represented by a mapping $E = \Xi(N, \mathbf{E}_i)$. Then the set of extreme subnetworks of N is $\Xi(N, \mathbf{E})$. We can relate many of the stability properties of networks can to the stability of their extreme subnetworks. Hence we define

$$\mathcal{E}_i \equiv \mathcal{N}_i \cap \mathcal{E}\,, \qquad \mathcal{E}_i^L \equiv \mathcal{N}_i^L \cap \mathcal{E} \tag{56}$$

where i is any of the subscripts appearing in definitions in Eq. (43–49).

4 Stability proofs using Hurwitz determinants

The signs of the Hurwitz determinants determine the number of eigenvalues with positive, zero, and negative real parts. Here we will mention the important theorems only. The details can be found in (Gantmacher, 1959).

The relevant part of the characteristic polynomial of $\mathbf{M}(\mathbf{p})$ is a polynomial in λ. Let $\alpha_i(\mathbf{p})$ denote the coefficient of λ^{d-i}. Then we may rewrite Eq. (34) as

$$\det|\lambda \mathbf{I} - \mathbf{M}(\mathbf{p})| = \lambda^{\rho} \sum_{i=0}^{d} \lambda^{d-i}\, \alpha_i(\mathbf{p})\,, \tag{57}$$

where $\alpha_i(\mathbf{p})$ is a polynomial in $\mathbf{p}$. We write $\lambda \mathbf{I} - \mathbf{M}(\mathbf{p})$ rather than $\mathbf{M}(\mathbf{p}) - \lambda \mathbf{I}$ to avoid factors $(-1)^i$ in the characteristic polynomial. The leading term of Eq. (57) is $\lambda^{\rho+d}$, so $\alpha_0(\mathbf{p}) = 1$. It is convenient to extend the sum to infinity and define $\alpha_i(\mathbf{p}) = 0$ for $i > d$.

Let an infinite array $\mathbf{A}$ be

$$\begin{array}{ccccc}
\alpha_1(\mathbf{p}) & \alpha_3(\mathbf{p}) & \alpha_5(\mathbf{p}) & \alpha_7(\mathbf{p}) & \ldots \\
\alpha_0(\mathbf{p}) & \alpha_2(\mathbf{p}) & \alpha_4(\mathbf{p}) & \alpha_6(\mathbf{p}) & \ldots \\
0 & \alpha_1(\mathbf{p}) & \alpha_3(\mathbf{p}) & \alpha_5(\mathbf{p}) & \ldots \\
0 & \alpha_0(\mathbf{p}) & \alpha_2(\mathbf{p}) & \alpha_4(\mathbf{p}) & \ldots \\
0 & 0 & \alpha_1(\mathbf{p}) & \alpha_3(\mathbf{p}) & \ldots \\
0 & 0 & \alpha_0(\mathbf{p}) & \alpha_2(\mathbf{p}) & \ldots
\end{array} \tag{58}$$

The diagonal of $\mathbf{A}$ is $(\alpha_1, \alpha_2, \alpha_3, \ldots)$ and the columns of $\mathbf{A}$ contain the coefficients in descending order. The *Hurwitz determinant* $\Delta_i(\mathbf{p})$ is defined to be the determinant of the square matrix formed from the elements found in the first i rows and columns of $\mathbf{A}$. Thus

$$\begin{aligned}
\Delta_1(\mathbf{p}) &= \alpha_1(\mathbf{p})\,, \\
\Delta_2(\mathbf{p}) &= \alpha_1(\mathbf{p})\alpha_2(\mathbf{p}) - \alpha_0(\mathbf{p})\alpha_3(\mathbf{p})\,, \\
\Delta_3(\mathbf{p}) &= \begin{vmatrix} \alpha_1(\mathbf{p}) & \alpha_3(\mathbf{p}) & \alpha_5(\mathbf{p}) \\ \alpha_0(\mathbf{p}) & \alpha_2(\mathbf{p}) & \alpha_5(\mathbf{p}) \\ 0 & \alpha_1(\mathbf{p}) & \alpha_3(\mathbf{p}) \end{vmatrix}\,, \\
&\ldots .
\end{aligned}$$

These determinants belong to the set of the *principal minors* of the matrix $\mathbf{A}$.

The Routh-Hurwitz Theorem (Gantmacher (1959), Theorem 4, p. 230). The number of eigenvalues λ_i with $\Re(\lambda_i) > 0$ equals the sum of the number of changes in the sequences

$$\begin{aligned}
&1,\ \Delta_1(\mathbf{p}),\ \Delta_3(\mathbf{p}),\ \Delta_5(\mathbf{p}),\ \ldots \\
&1,\ \Delta_2(\mathbf{p}),\ \Delta_4(\mathbf{p}),\ \Delta_6(\mathbf{p}),\ \ldots
\end{aligned}$$

If $\Delta_i(\mathbf{p}) > 0$ for $i = 1, \ldots, d$, the sequences have no sign changes, so $\Re(\lambda_i) < 0$ for all i, hence $\mathbf{p} \in D_a^L$. Conversely, if $\mathbf{p} \in D_a^L$, it follows that $\Re(\lambda_i) < 0$ for all i, so $\Delta_i(\mathbf{p}) > 0$ for $i = 1, \ldots, d$. Hence a necessary and sufficient condition for $\mathbf{p} \in D_a^L$ is that $\Delta_i(\mathbf{p}) > 0$ for $i = 1, \ldots, d$. Thus we may write

$$D_a^L = \{\mathbf{p} \in D \mid \Delta_i(\mathbf{p}) > 0\,, \forall\, i,\ i \in [1,\, d]\}\,. \tag{59}$$

where $[1,\, d] \equiv \{1, \ldots, d\}$. A similar line of argument yields

$$D_e^L = \{\mathbf{p} \in D \mid \Delta_i(\mathbf{p}) < 0\,, \exists\, i,\ i \in [1,\, d]\}\,, \tag{60}$$

$$\begin{aligned}
D_{mw}^L = \{\mathbf{p} \in D \mid \Delta_i(\mathbf{p}) \geqslant 0\,, \forall\, i,\ i \in [1,\, d]\,, \\
\Delta_i(\mathbf{p}) = 0 \qquad \exists i,\ i \in [1,\, d]\}\,.
\end{aligned} \tag{61}$$

We may rearrange the polynomial $\chi(\lambda, \mathbf{p})$ from Eq. (34) into linear factors and quadratic factors. The linear factors have the form $(\lambda - \lambda_i)$ and correspond to each real root λ_i. Whereas the quadratic factors have the form $\lambda^2 - (\lambda_i + \overline{\lambda}_i)\lambda + \lambda_i\overline{\lambda}_i$ and correspond to each pair of complex conjugated roots λ_i and $\overline{\lambda}_i$. If $\Delta_i(\mathbf{p}) > 0$ for $i \in [1, d]$, $\Re(\lambda_i) < 0$ and the coefficients in the linear and quadratic factors are all real and positive. Note that when we multiply out these factors to obtain $\chi(\lambda, \mathbf{p})$, the coefficients we obtain must be positive. Thus the condition

$$\alpha_i(\mathbf{p}) > 0\,, \qquad i \in [1,\, d]\,, \tag{62}$$

must be satisfied for all $\mathbf{p} \in D_a^L$. The condition (62) may also be satisfied for some $\mathbf{p} \in D_{mw}^L \cup D_u^L$, so it is not a sufficient condition for asymptotic stability.

Liénard-Chipart Theorem (Gantmacher (1959), Theorem 11, p. 263). If all functions in one of the four sets of functions

$$F_1 \equiv \{\Delta_i(\mathbf{p}), \alpha_d(\mathbf{p}), \alpha_j(\mathbf{p}) \,|\, i \text{ even},\ j \text{ odd}\}\,,$$
$$F_2 \equiv \{\Delta_i(\mathbf{p}), \alpha_d(\mathbf{p}), \alpha_j(\mathbf{p}) \,|\, i \text{ odd},\ j \text{ even}\}\,,$$
$$F_3 \equiv \{\Delta_i(\mathbf{p}), \alpha_d(\mathbf{p}), \alpha_j(\mathbf{p}) \,|\, i \text{ even},\ j \text{ even}\}\,,$$
$$F_4 \equiv \{\Delta_i(\mathbf{p}), \alpha_d(\mathbf{p}), \alpha_j(\mathbf{p}) \,|\, i \text{ odd},\ j \text{ odd}\}\,,$$

are positive, where $i,\, j \in [1, d]$, then $\mathbf{p} \in D_a^L$.

It follows from Eq. (59) and Eq. (62) that if $\mathbf{p} \in D_a^L$, all functions mentioned in the theorem are positive. Hence this theorem gives four sets of necessary and sufficient conditions for $\mathbf{p} \in D_a^L$. We generalize Eqs. (59–61) to

$$D_a^L = \{\mathbf{p} \in D \,|\, f(\mathbf{p}) > 0\,, \forall f,\ f \in F_i\} \tag{63}$$
$$D_e^L = \{\mathbf{p} \in D \,|\, f(\mathbf{p}) < 0\,, \exists f,\ f \in F_i\} \tag{64}$$
$$D_{mw}^L = \{\mathbf{p} \in D \,|\, f(\mathbf{p}) \geqslant 0\,, \forall f,\ f \in F_i\}$$
$$f(\mathbf{p}) = 0\,, \exists f,\ f \in F_i\} \tag{65}$$

where F_i is any of the four sets of functions given in the Liénard-Chipart theorem or is $F_5 \equiv \{\Delta_i(\mathbf{p}) \,|\, i \in [1, d]\}$.

The sets of asymptotically stable, marginally stable, and unstable networks may now be reexpressed using one of the sets of functions F_i. Since F_i depends on the network

N, we now write $F_i(N)$ and $D = D(N)$. Combining Eq. (46), Eq. (49), Eq. (63), and Eq. (64), we conclude that for any $i = 1, \ldots, 5$,

$$\mathcal{N}_a^{\mathrm{L}} = \{N \in \mathcal{N} \mid f(\mathbf{p}) > 0\,,\, \forall\, \mathbf{p},\ \mathbf{p} \in D(N) \text{ and } \forall\, f,\ f \in F_i(N)\}\,, \tag{66}$$

$$\mathcal{N}_e^{\mathrm{L}} = \{N \in \mathcal{N} \mid f(\mathbf{p}) < 0\,,\, \exists\, \mathbf{p},\ \mathbf{p} \in D(N) \text{ and } \exists\, f,\ f \in F_i(N)\}\,. \tag{67}$$

The networks that remain are

$$\begin{aligned} \mathcal{N}_m^{\mathrm{L}} \cup \mathcal{N}_w^{\mathrm{L}} = \{N \in \mathcal{N} \mid f(\mathbf{p}) \geqslant 0\,,\, \forall\, \mathbf{p},\ \mathbf{p} \in D(N) \text{ and } \forall\, f,\ f \in F_i(N)\,, \\ f(\mathbf{p}) = 0\,,\, \exists\, \mathbf{p},\ \mathbf{p} \in D(N) \text{ and } \exists\, f,\ f \in F_i(N)\}\,. \end{aligned} \tag{68}$$

The stability of these networks cannot be decided from the linear terms alone. Depending on the nonlinear terms, they may be stable, marginally stable, or unstable.

For all of the forms of $\mathbf{M}(\mathbf{p})$ given in Section 2, the elements of $\mathbf{M}$ are first-order homogeneous polynomial in both $\mathbf{h}$ and $\mathbf{j}$. According to Eq. (57), each polynomial $\alpha_i(\mathbf{h},\, \mathbf{j})$ must be ith order homogeneous in both $\mathbf{h}$ and $\mathbf{j}$. Then $\Delta_i(\mathbf{h},\, \mathbf{j})$ must be homogeneous polynomial of order $i(i+1)/2$ in both $\mathbf{h}$ and $\mathbf{j}$.

Let $T(f,\, \mathbf{p})$ be the set of terms of a polynomial $f(\mathbf{p})$. Then the polynomial $f(\mathbf{p})$ is

$$f(\mathbf{p}) = \sum_{t \in T(f,\, \mathbf{p})} t\,. \tag{69}$$

Since every component of $\mathbf{p} \in D$ is positive, the sign of any element $t \in T(f,\, \mathbf{p})$ is independent of $\mathbf{p}$ and is never zero. The set of networks whose polynomials contain only positive terms in any one of the sets F_i of polynomials is

$$\mathcal{N}_i^{+} \equiv \{N \in \mathcal{N} \mid t > 0,\, \forall\, t \in T(f,\, \mathbf{p}),\, T(f,\, \mathbf{p}) \neq \emptyset,\, \forall\, f \in F_i(N)\}\,. \tag{70}$$

If $t > 0$ for all $T(f,\, \mathbf{p})$, then $f(\mathbf{p}) > 0$ for all $\mathbf{p} \in D(N)$. Hence Eq. (52) and Eq. (66) give

$$\mathcal{N}_i^{+} \subset \mathcal{N}_a^{L} \subset \mathcal{N}_a\,. \tag{71}$$

A term $t \in T(f,\, \mathbf{p})$ is a *potentially dominant term* of f if it is possible to choose $\mathbf{p} \in D$ so that t is arbitrarily larger in magnitude than every other term in $T(f,\, \mathbf{p})$. The set of potential dominant terms of f is

$$T^D(f) \equiv \{t \in T(f,\, \mathbf{p}) \mid \forall\, \varepsilon > 1,\, \exists\, \mathbf{p} \in D,\, |t| > \varepsilon |t'|,\, \forall\, t' \in T(f,\, \mathbf{p})\}\,. \tag{72}$$

Let the network N have a polynomial $f \in F_i(N)$ which contains a negative term that can dominate f. Then f is negative for some $\mathbf{p}$ and thus the network N is unstable, see Eq. (67). The set of such networks is

$$\mathcal{N}_i^{D-} \equiv \{N \in \mathcal{N} \mid \exists\, t \in T^D(f),\, t < 0,\, f \in F_i(N)\}\,. \tag{73}$$

This set contains networks having a *negative potentially dominant term*. Hence Eq. (49) and Eq. (67) for $i \in [1, 5]$ give

$$\mathcal{N}_i^{D-} \subset \mathcal{N}_e^L \subset \mathcal{N}_u \,. \tag{74}$$

The networks that remain fall into two principal classes:

$$\mathcal{N}_i^0 \equiv \{N \in \mathcal{N} \mid \exists\, f \in F_i(N),\, T(f,\, \mathbf{p}) = \emptyset,\, t > 0,\, \forall\, t \in T(f,\, \mathbf{p}),\, \forall\, f \in F_i(N)\}\,, \tag{75}$$

$$\mathcal{N}_i^{I-} \equiv \{N \in \mathcal{N} \mid t > 0,\, \forall\, t \in T^D(f),\, \forall\, t \in T^D(f),\, t < 0,\, \exists\, t \in T(f),\, f \in F_i(N)\}\,. \tag{76}$$

The set of networks with only positive terms is $\mathcal{N}_i^+ \cup \mathcal{N}_i^0$. Hence the remaining networks have a negative terms. In one of the remaining networks, if a negative term can be dominant, the network belongs to $\mathcal{N}_i^{D-}$. Otherwise there is a negative term, but all the dominant terms are positive, so the network belongs to $\mathcal{N}_i^{I-}$. For any $i \in [1, 5]$, we may recall that

$$\mathcal{N} = \mathcal{N}_i^+ \cup \mathcal{N}_i^{D-} \cup \mathcal{N}_i^0 \cup \mathcal{N}_i^{I-} \,. \tag{77}$$

For every network in $\mathcal{N}_i^0$, either some Δ_i is identically zero or some α_i is identically zero. From Eq. (65), $D_{mw}^L = D$, so $D_e^L = \emptyset$, and $D_s^L = \emptyset$. Hence we may obtain from Eq. (47) and Eq. (48)

$$\mathcal{N}_i^0 \subset \mathcal{N}_m^L \cup \mathcal{N}_m^L \equiv \mathcal{N}_{mw}^L \,. \tag{78}$$

Recall that the stability of networks in $\mathcal{N}_{mw}^L$ depends on the nonlinear terms, and such networks may be asymptotically stable, marginally stable, or unstable.

Knowledge of the signs and dominance of the terms in Δ_i and α_i allows us to establish the stability classification of networks in $\mathcal{N}_i^+$ and $\mathcal{N}_i^{D-}$. The problem is to determine the stability of an arbitrary network N. The strategy is to compute the signs and dominance of the terms of each $f \in F_i$ for some $i \in [1, 5]$. If we are lucky, the network N will lie in $\mathcal{N}_i^+$ or $\mathcal{N}_i^{D-}$. If N lies in $\mathcal{N}_i^0$, we must consider the nonlinear terms to decide the stability. If N lies in $\mathcal{N}_i^{I-}$, we have to examine the polynomial in great detail. Using calculus, we find where the polynomial $f(\mathbf{p})$ attains its minimum. Then we test the sign of $f(\mathbf{p})$ at the minimum which resolves the stability.

Clarke (1980) asserted that only a very small fraction of the networks lie in $\mathcal{N}_i^{I-}$, and all these networks possess small groups of terms whose sum can be negative and arbitrarily greater in magnitude than every other term in $T(f, \mathbf{p})$. Thus these networks are exponentially unstable. If we can conjecture that $\mathcal{N}_i^{I-} \subset \mathcal{N}_e^L$, then equations (71), (74), (77), (78), and (79) give

$$\mathcal{N}_a^L = \mathcal{N}_i^+ , \qquad \mathcal{N}_{mw}^L = \mathcal{N}_i^0 , \qquad \mathcal{N}_e^L = \mathcal{N}_i^{D-} \cup \mathcal{N}_i^{I-} . \tag{79}$$

Then necessary and sufficient conditions for a network to be in $\mathcal{N}_e^L$ would be identical to necessary and sufficient conditions for the existence of a negative coefficient in some polynomial $f \in F_i$, $i \in [1, 5]$. Also conditions that a polynomial does not vanish correspond to conditions for a network to be in $\mathcal{N}_a^L$.

Let us conclude that the primary disadvantage to this approach is the large number of terms in the polynomials. The polynomials α_i have the largest number of terms when i is near the midpoint of the interval $i \in [1, d]$ and the least number when $i = 1$ or $i = d$. The number in Δ_i increases extremely rapidly with i. Thus we should never evaluate Δ_d, because by choosing F_i optimally, the largest Hurwitz determinant required is Δ_{d-1}. Hence F_5 is a poor choice because we have to construct d Δ_is instead of approximately $d/2$ Δ_is. Of the remaining possibilities, α_d must be constructed in all cases, so we minimize the number of required α_js by avoiding α_{d-1}. If d is odd, the best set to use is then F_1. If d is even, the best set is F_2.

5 Theorems on matrix stability

The chemical network stability problem has been converted into a matrix stability problem for the matrix function $\mathbf{M}(\mathbf{p})$ defined in Section 2. Considerable work on more general stability problems has already been done. In this section we relate the chemical network problem to some widely used definitions in matrix stability theory and summarize some of the main theorems. Summary of matrix stability theory can be found in works (Barnett and Storey, 1970; Quirk and Rupert, 1965; Maybee and Quirk, 1969; Jefferies *et al.*, 1977).

In matrix stability theory, the stability properties of the steady state are often ascribed to the matrix $\mathbf{M}$. Thus we say $\mathbf{M}$ is *asymptotically stable* (*marginally stable, stable, weakly unstable, semistable, exponentially unstable*) if the steady state $u = 0$ of the linearized system, see Eq. (6), is asymptotically stable (marginally stable, stable, weakly unstable, semistable, exponentially unstable). When $\mathbf{M}$ is asymptotically stable it is sometimes called a *stability matrix.* The matrix $\mathbf{M}$ is *diagonal stable* ($\mathbf{D}$-stable) if $\mathbf{DM}$ is asymptotically stable for for every positive diagonal matrix $\mathbf{D}$. $\mathbf{M}$ is *totally stable* if every principal submatrix of $\mathbf{M}$ (i.e., every submatrix whose determinant is a principal minor of $\mathbf{M}$) is $\mathbf{D}$-stable. From these definitions it follows that every totally stable matrix is $\mathbf{D}$-stable and every $\mathbf{D}$-stable matrix is asymptotically stable.

Consider any $\mathbf{j}$ such that $\mathbf{E}\,\mathbf{j} \in \Pi_v$, and suppose the matrix $-\mathbf{V}(\mathbf{j})$ defined in Eq. (24) is $\mathbf{D}$-stable. Then for all $\mathbf{h} \in \mathbb{R}^n_+$, $-\mathrm{diag}(\mathbf{h})\mathbf{V}(\mathbf{j})$ is asymptotically stable, and from Eq. (27), $\mathbf{M}_{\zeta''}$ is stable. Then we say that $\mathbf{Ej}$ is a *linearly asymptotically stable current.* A current $\mathbf{Ej}$ is linearly asymptotically stable if and only if $-\mathbf{V}(\mathbf{j})$ is $\mathbf{D}$-stable. Then equation (46) gives

$$\mathcal{N}^L_a = \{N \in \mathcal{N} \mid -\mathbf{V}(\mathbf{j}) \text{ is } \mathbf{D}\text{-stable for all } \mathbf{j} \in \mathbb{R}^f_+\}\,. \tag{80}$$

The network stability problem is therefore partly the problem of finding necessary and sufficient conditions for $-\mathbf{V}(\mathbf{j})$ to be $\mathbf{D}$-stable for all $\mathbf{j} \in \mathbb{R}^f_+$, when $\mathbf{V}(\mathbf{j})$ has the structure given in Eq. (24). Of course this only determines what we call *linear* asymptotic stability; the nonlinear terms must sometimes be considered to determine whether the current is asymptotically stable.

The *sign stability problem* is closely related to the network stability problem. Each chemical system is associated with the network N that represents a set of systems. Each matrix $\mathbf{U} \in \mathbb{R}^{n\times n}$ will be associated with a set of matrices $\Sigma(\mathbf{U}) \equiv \{\mathbf{M}(\mathbf{p}) \mid \mathbf{p} \in D\}$, called a *sign matrix set*, where $\mathbf{p} \in \mathbb{R}^{n\times n}$ is an $n \times n$ parameter matrix, $\mathbf{D} \equiv \mathbb{R}^{n\times n}_+$, and

$$M_{ij}(\mathbf{p}) \equiv U_{ij}\, p_{ij}\,. \tag{81}$$

The sign matrix set is analogous to a network. Since the sign matrix set depends only on whether each element of $\mathbf{U}$ is positive, negative, or zero, we may assume that $U_{ij} \in \{-1, 0, 1\}$.

Each sign matrix set has domains on which $\mathbf{M}(\mathbf{p})$ on which has various stability properties. These domains are called $D_a, D_m, D_w, D_e, D_{mw}, D_u, D_{\mathrm{semi}}$, and D_s and are defined yet. Similarly, each sign matrix set can be classified according to the most unstable matrix in it. We say that $\Sigma(\mathbf{U})$ is *asymptotically stable, marginally stable, weakly unstable, exponentially unstable, marginally or weakly unstable, unstable, semistable, or stable*, in analogy with the network classification. Then we may define sets of sign matrix sets having various stability classifications as follows. Let $\mathcal{U}$ be the set of all sign matrix sets. The set of *asymptotically stable* sign matrix set is

$$\mathcal{U}_a \equiv \{\Sigma \in \mathcal{U} \mid D_a = D\}\,. \tag{82}$$

The set of *marginally stable* sign matrix set is

$$\mathcal{U}_m \equiv \{\Sigma \in \mathcal{U} \mid D_m \neq \emptyset,\ D_w = D_e = \emptyset\}\,. \tag{83}$$

the set of *weakly unstable* sign matrix set is

$$\mathcal{U}_w \equiv \{\Sigma \in \mathcal{U} \mid D_w \neq \emptyset,\ D_e = \emptyset\}\,. \tag{84}$$

and the set of *exponentially unstable* sign matrix set is

$$\mathcal{U}_e \equiv \{\Sigma \in \mathcal{U} \mid D_e \neq \emptyset\}\,. \tag{85}$$

Then we define the rest sets $\mathcal{U}_s \equiv \mathcal{U}_a \cup \mathcal{U}_m$, $\mathcal{U}_{\text{semi}} \equiv \mathcal{U}_a \cup \mathcal{U}_m \cup \mathcal{U}_w$, and $\mathcal{U}_u \equiv \mathcal{U}_w \cup \mathcal{U}_e$. If $\Sigma(\mathbf{U}) \in \mathcal{U}_a$, we will say that $\mathbf{U}$ is sign asymptotically stable. Similarly, other stability classifications of $\Sigma(\mathbf{U})$ may be ascribed to $\mathbf{U}$ by prefixing the term "sign".

Quirk-Ruppert-Maybee Theorem. An $n \times n$ matrix $\mathcal{U}$ is sign semistable if and only if it satisfies the following three conditions:

(a) $U_{ii} \leqslant 0$ for all i.

(b) $U_{ij}U_{ji} \leqslant 0$ for all $i \neq j$.

(c) $U_{i(1)i(2)} \ldots U_{i(k-1)i(k)}\, U_{i(k)i(1)} = 0$, for each sequence of $k \geqslant 3$ distinct indices $i(1), \ldots, i(k)$.

The stoichiometric network stability problem reduces into the sign stability problem when the effective power function $\underline{\boldsymbol{\kappa}}(\mathbf{p})$ can vary over a suitable range. All the techniques that we apply to the network problem may be applied to the sign stability problem.

Given a matrix $\mathcal{U}$, a cyclic product of k matrix elements $U_{\gamma(1)\gamma(2)}\, U_{\gamma(2)\gamma(3)} \cdots U_{\gamma(k)\gamma(1)}$ is a *matrix feedback k-cycle*, or simply a *k-cycle*. The feedback is *positive* (*negative*), or (the cycle *does not occur*) if the product is *positive* (*negative*), or (*zero*).

6 Network diagrams

The basic concepts concerning diagrams can be presented in a manner that stresses the relationship between diagrams and graph theory. Most problems of graph theory can be generalized to the diagrams. Thus a rich field of mathematics is potentially at hand (Clarke, 1980). We will briefly introduce a graphical representation of the network called a network diagram since it is useful guide for a visual identification of both positive and negative feedbacks in the chemical network.

We now define the *network diagram*. It is equivalent to the *directed set-graph network* (DSG-network) introduced by Clarke (1980). But network diagrams use a more practical notation for chemical networks than the DSG-networks. Each reaction R_j can be represented as a multi-headed multi-tailed arrow which is oriented from the reactants to the products. The number of *feathers* determines the stoichiometric coefficients of reactants. The number of left feathers determines the reaction order of the reacting species. The number of *barbs* determines the stoichiometric coefficients of products.

We simplify the notation of network diagrams by the following way. If $\nu_{ij}^{\mathrm{L}} = \kappa_{ij} = 1$ in the reaction R_j, then we leave the feather on the tail of the arrow corresponding to the ith species out. If external species are present in such surplus so that their concentrations are effectively time invariant, then we may emphasize this fact by drawing of the species into a square.

7 Useful stability criteria

The expression for α_i as polynomials in $\mathbf{h}$ and $\mathbf{j}$, or in $\mathbf{h}$ for fixed $\mathbf{j}$, are called *stability polynomials*. The coefficients in the first case are determined by $-\mathbf{S}^{(1)}, \ldots, -\mathbf{S}^{(f)}$, and in the latter case by $-\mathbf{V}(\mathbf{j})$. Since these matrices are represented by their current matrix diagrams, it is possible to represent any coefficient in these polynomials as a sum of diagrams. Computer studies have shown that networks seem to be linearly exponentially unstable whenever any coefficient is negative. Hence we work toward obtaining necessary and sufficient conditions for the existence of a negative coefficient.

Consider α_i as a polynomial in $\mathbf{h}$ with $\mathbf{j}$ fixed. Write the characteristic equation as

$$\det|\lambda\mathbf{I} + \mathbf{V}(\mathbf{j})\,\mathrm{diag}\,\mathbf{h}| = 0\,, \tag{86}$$

and recall that α_i is the coefficient of λ^{n-i} in this polynomial. The $n-i$ factors of λ come from the diagonal elements of $n-i$ distinct columns. From the remaining i columns come factors of h_k, say $h_{\gamma(1)}, \ldots, h_{\gamma(i)}$. Since the jth column of $\mathbf{V}(\mathbf{j})\,\mathrm{diag}\,\mathbf{h}$ is associated with h_j, these i factors are all different. Hence the general form of α_i is

$$\alpha_i(\mathbf{h},\mathbf{j}) = \sum_{\boldsymbol{\gamma}\in A(n,i)} h_{\gamma(1)}, \ldots, h_{\gamma(i)}\,\beta(\boldsymbol{\gamma},\mathbf{j})\,, \tag{87}$$

where

$$\beta(\boldsymbol{\gamma}, \mathbf{j}) \equiv \begin{vmatrix} V_{\gamma(1)\gamma(1)}(\mathbf{j}) & \dots & V_{\gamma(1)\gamma(i)}(\mathbf{j}) \\ \vdots & & \vdots \\ V_{\gamma(i)\gamma(1)}(\mathbf{j}) & \dots & V_{\gamma(i)\gamma(i)}(\mathbf{j}) \end{vmatrix} . \tag{88}$$

The sum is taken over the $\binom{n}{i}$ ways to choose i distinct integers $\gamma(1), \dots, \gamma(i)$ from the n distinct integers $1, \dots, n$. Let $A(n, i)$ be set of all these $\boldsymbol{\gamma}$. The network is exponentially unstable if there exists i, $\mathbf{j}$ and $\boldsymbol{\gamma} \in A(n, i)$ such that $\beta(\boldsymbol{\gamma}, \mathbf{j}) < 0$. To prove this, choose any $\varepsilon > 0$, let $h_{\gamma(1)} = h_{\gamma(2)} = \dots = h_{\gamma(i)} = \varepsilon^{-1}$, and let all other components of $\mathbf{h}$ be equal to 1. Then $\alpha_i(\mathbf{h}, \mathbf{j})$ is a polynomial in ε^{-1} with $\beta(\boldsymbol{\gamma}, \mathbf{j})$ as the coefficient of the algebraically lowest power term, ε^{-i}. As $\varepsilon \to 0$ this term dominates every other terms and makes α_i negative. The network is exponentially unstable by Eq. (67).

7.1 Sufficient condition for Hopf bifurcation

A sufficient condition for instability of a network $\mathcal{N}$ is that there exists a subnetwork with at least one negative principal minor of $-\mathbf{S}$, that is $\beta(\boldsymbol{\gamma}, \mathbf{j}) < 0$. This condition itself leads to a saddle point (generally giving rise to bistability), while for a Hopf bifurcation an additional condition needs to be fulfilled. Thus Eiswirth *et al.* (1996) have formulated subsequent sufficient and necessary conditions for the occurrence of a Hopf bifurcation in a chemical network.

Sufficient condition for Hopf bifurcation. A network $\mathcal{N}$ contains a Hopf bifurcation if there exists a species $\mathcal{S}_l$ with reciprocal concentration h_l and a natural number $k < d$ such that for some subnetwork:

1. The sum is $\sum_{\boldsymbol{\gamma} \in A(n,k)} h_{\gamma(1)}, \dots, h_{\gamma(k)} \, \beta(\boldsymbol{\gamma}, \mathbf{j}) < 0$ over such $\boldsymbol{\gamma}$s which depend on h_l, i.e. for all $\boldsymbol{\gamma}$ exist a number i, $1 \leqslant i \leqslant k$, such that $\gamma(i) = l$.
2. The sum is $\sum_{\boldsymbol{\gamma} \in A(n,d)} h_{\gamma(1)}, \dots, h_{\gamma(d)} \, \beta(\boldsymbol{\gamma}, \mathbf{j}) > 0$ over such $\boldsymbol{\gamma}$s which depend on h_l, i.e. for all $\boldsymbol{\gamma}$ exist a number i, $1 \leqslant i \leqslant d$, such that $\gamma(i) = l$.

This condition lead to two inequalities for criteria (1.) and (2.). If these do not contradict each other, the existence of a Hopf bifurcation is guaranteed.

Criterion (1.) actually implies that there is a positive feedback loop (autocatalysis) involving k species, which gives rise to an unstable steady state. Criterion (2.) reflects the existence of a negative feedback loop involving at least one additional species $d > k$ and thus (indirectly) also a different time scale. The above condition therefore just represents a precise formulation interplay of a fast autocatalysis and a negative feedback loop occurring on a slower time scale.

7.2 Necessary and sufficient condition for Hopf bifurcation

Condition 7.1 is applicable as long as the mechanism becomes unstable via an autocatalysis. A more general condition for the occurrence of a Hopf bifurcation can be obtained from the Routh–Hurwitz criterion. Recall that the characteristic equation of matrix $\mathbf{M}(\mathbf{p})$ has the form

$$f(\lambda) = \lambda^\rho \sum_{i=0}^{d} \lambda^{d-i}\, \alpha_i(\mathbf{p})\,,$$

where $\rho = n - d$, $\alpha_0(\mathbf{p}) = 1$, and α_i is the sum defined in Eq. (87). A modified Routh scheme can be defined as

$$\begin{array}{cccc} D_{1,0} & D_{1,1} & D_{1,2} & \dots \\ D_{2,0} & D_{2,1} & D_{2,2} & \dots \\ D_{3,0} & D_{3,1} & D_{3,2} & \dots \\ \vdots & \vdots & \vdots & \end{array} \tag{89}$$

with $D_{1,k} = \alpha_{2k}$, $D_{2,k} = \alpha_{2k+1}$ and $D_{m+1,k} = D_{m,0}\, D_{m-1,k+1} - D_{m-1,0}\, D_{m,k+1}$ for $k = 0, 1, \dots$.

Necessary and sufficient condition for Hopf bifurcation. Let $f(\lambda)$ be a polynomial in λ. If (1.) $\alpha_d > 0$ and (2.) $D_{k,0} > 0$ for $k = 1, \dots, d-1$, and (3.) $D_{k,0} = 0$ for $k = [d,\, d+1]$, then $f(\lambda)$ has two roots $\pm\,\omega\mathrm{i}$ and $d-2$ roots with negative real part. We also have to verify that the highest two change sign upon variation of a parameter (which is actually no problem in a complete parameter set). It suffices to check $D_{d,0}$, since $D_{d+1,0}$ has the same sign.

Condition 7.2 is actually needed only for rare cases of nonautocatalytic oscillators. On the other hand, it is also useful to make sure that no Hopf bifurcation can occur in a certain network.

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