## Mathematical Oncology

2x2 system of ODEs

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We will consider the homogenous 2x2 system of ODEs with constant coefficients:

$$\mathbf{y}'(t) = \mathbf{A}\mathbf{y}(t), \quad \mathbf{A} = \left(a_{ij}\right)_{i,j=1,2} \in \mathbb{R}^{2x^2}$$
 (1)

**Remark 1.** The treatment of non-linear systems extends beyond the scope of these notes. Still, if needed, a non-linear system could be linearised around the a specific state.

The solution of the system of ODEs (1) depends on the type of eigenvalues of the matrix A—to be more precise, the solution depends of the diagonalization of the matrix A; hence on the eigenvalues and eigenvectors.

Question: Why do the eigenvalues and eigenvectors of A provide a solution to the system (1)?

Answer: Consider an eigenvalue  $\lambda \in \mathbb{R}$  of **A** and  $\mathbf{v} \in \mathbb{R}^2$  the corresponding eigenvector. Since **A** is a matrix of constants,  $\lambda$  and  $\mathbf{v}$  are constants as well. By the definition of eigenvalues/-vectors it holds:

$$\mathbf{A}\mathbf{v} = \lambda\mathbf{v}$$
.

Consider now the function of  $t \geq 0$  given by the specific eigenvalue  $\lambda$  and eigenvector  $\mathbf{v}$ 

$$\mathbf{y}(t) = e^{\lambda t} \mathbf{v},$$

and note that the time derivative of y reads (since  $\lambda$  and v constants)

$$\frac{d}{dt}\mathbf{y}(t) = \frac{d}{dt}\left(e^{\lambda t}\mathbf{v}\right) = \lambda e^{\lambda t}\mathbf{v} = e^{\lambda t}\mathbf{A}\mathbf{v} = \mathbf{A}\mathbf{y}.$$

This implies that  $\mathbf{y}(t) = e^{\lambda t}\mathbf{v}$  is indeed a solution of the ODE system (1).

The fundamental theorem of Algebra states that  $\mathbf{A}$  has exactly two eigenvalues, calculated by e.g. solving the characteristic equation

$$\lambda^2 - \operatorname{tr}(\mathbf{A})\lambda + \det(\mathbf{A}) = 0 \implies \lambda_{1,2} = \frac{\operatorname{tr}(\mathbf{A}) \pm \sqrt{\operatorname{tr}(\mathbf{A})^2 - 4\det(\mathbf{A})}}{2} = \frac{\operatorname{tr}(\mathbf{A}) \pm \sqrt{\Delta}}{2}$$

where  $tr(\mathbf{A})$ ,  $det(\mathbf{A})$  are the trace and determinant of  $\mathbf{A}$  and where  $\Delta = tr(\mathbf{A})^2 - 4 det(\mathbf{A})$  is the discriminant of the quadratic equation above. The eigenvalues  $\lambda_{1,2}$  can either be

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real and distinct  $\lambda_1, \lambda_2 \in \mathbb{R}$ ,  $\lambda_1 \neq \lambda_2$ , or real and equal  $\lambda_1 = \lambda_2 \in \mathbb{R}$ , or complex conjugate  $\lambda_1 = \bar{\lambda}_2 \in \mathbb{C}$ . As the dimension of the solution space of the ODE (1) is 2, it suffices that we found 2 linearly independent solutions,  $\mathbf{y}_1$ ,  $\mathbf{y}_2$ . Then, their linear combination constitutes the general solution

$$\mathbf{y}_{\text{ho}} = c_1 \mathbf{y}_1 + c_2 \mathbf{y}_2$$

of the (homogenous) ODE (1). In more detail:

Case 1: A has two real eigenvalues  $\lambda_1$ ,  $\lambda_2$  with the corresponding eigenvectors  $\mathbf{v}_1, \mathbf{v}_2$  (refresh your method of calculating eigenvectors).

The functions  $\mathbf{y}_1 = e^{\lambda_1 t} \mathbf{v}_1$ ,  $\mathbf{y}_2 = e^{\lambda_2 t} \mathbf{v}_2$  are linearly independent solutions of the problem and, hence, the general solution of (1) reads

$$\mathbf{y}_{\text{ho}} = c_1 e^{\lambda_1 t} \mathbf{v}_1 + c_2 e^{\lambda_2 t} \mathbf{v}_2, \quad c_1, c_2 \in \mathbb{R}.$$

Case 2: A has one double real eigenvalue  $\lambda$  with eigenvector v. One special solution of the ODE system is

$$\mathbf{y}_1(t) = e^{\lambda t} \mathbf{v}.$$

A second special solution, linearly independent to  $y_1$ , is

$$\mathbf{y}_2 = te^{\lambda t}\mathbf{v} + e^{\lambda t}\mathbf{u}$$

where **u** is the solution of  $(\mathbf{A} - \lambda \mathbf{I}) \mathbf{u} = \mathbf{v}$ . The general solution of the ODE system (1) is then given as before by:

$$\mathbf{y}_{\text{ho}} = c_1 \mathbf{y}_1 + c_2 \mathbf{y}_2$$

Case 3: A has two conjugate complex eigenvalues  $\lambda$ ,  $\bar{\lambda}$  with eigenvectors that are also conjugate  $\mathbf{v}$ ,  $\bar{\mathbf{v}}$ . The generic solution is

$$\mathbf{y}_{\text{ho}} = c_1 e^{\lambda t} \mathbf{v} + c_2 e^{\bar{\lambda} t} \bar{\mathbf{v}}, \quad c_1, c_2 \in \mathbb{C}, \quad (\text{YES, complex coefficients!})$$

**Note:** The imaginary part of  $\mathbf{y}_{ho}$  can be avoided by selecting conjugate constants, i.e.  $c_2 = \bar{c}_1 \in \mathbb{C}$ . Namely, for  $c_1 = c_1^R + ic_1^I$ ,  $\lambda = \lambda^R + i\lambda^I$ , and  $\mathbf{v} = \mathbf{v}^R + i\mathbf{v}^I$ ,  $\mathbf{y}_{ho}$  reads

$$\mathbf{y}_{\text{ho}} = \left(c_{1}^{R} + ic_{1}^{I}\right) e^{\lambda^{R}t + i\lambda^{I}t} \left(\mathbf{v}^{R} + i\mathbf{v}^{I}\right) + \left(c_{1}^{R} - ic_{1}^{I}\right) e^{\lambda^{R}t - i\lambda^{I}t} \left(\mathbf{v}^{R} - i\mathbf{v}^{I}\right)$$

$$\stackrel{\text{Euler}}{=} \left(c_{1}^{R} + ic_{1}^{I}\right) e^{\lambda^{R}t} \left(\cos(\lambda^{I}t) + i\sin(\lambda^{I}t)\right) \left(\mathbf{v}^{R} + i\mathbf{v}^{I}\right)$$

$$+ \left(c_{1}^{R} - ic_{1}^{I}\right) e^{\lambda^{R}t} \left(\cos(\lambda^{I}t) - i\sin(\lambda^{I}t)\right) \left(\mathbf{v}^{R} - i\mathbf{v}^{I}\right)$$

$$= \cdots \left(\text{some algebraic manipulations}\right) \cdots$$

$$= e^{\lambda^{R}t} \left(2c_{1}^{R}\cos(\lambda^{I}t)\mathbf{v}^{R} - 2c_{1}^{R}\sin(\lambda^{I}t)\mathbf{v}^{I} - 2c_{1}^{I}\cos(\lambda^{I}t)\mathbf{v}^{I} - 2c_{1}^{I}\sin(\lambda^{I}t)\mathbf{v}^{R}\right)$$

$$= 2e^{\lambda^{R}t} \left(\left(c_{1}^{R}\mathbf{v}^{R} - c_{1}^{I}\mathbf{v}^{I}\right)\cos(\lambda^{I}t) - \left(c_{1}^{R}\mathbf{v}^{I} + c_{1}^{I}\mathbf{v}^{R}\right)\sin(\lambda^{I}t)\right)$$

**NOTE:** The last relation indicates that the dynamics of  $\mathbf{y}_{\text{ho}}$  are "elliptical"! This is due to the trigonometry with either a converging (if  $\lambda^R < 0$ ), or diverging (if  $\lambda^R > 0$ ), or neutral (if  $\lambda^R = 0$ ) character. Confer at this point the Linear Stability Analysis appendix of our lecture notes.

**Remark 2.** In the case of a non-homogenous system of ODEs, e.g.  $\mathbf{y}' = \mathbf{A}\mathbf{y} + \mathbf{R}$ , then in addition to the general solution  $\mathbf{y}_{ho}$  of homogenous, we need to identify one special solution  $\mathbf{y}_{sp}$  of the non-homogenous problem (just one suffices and we usually "guess"). Together, they provide the general solution of the non-homogenous:

$$\mathbf{y} = \mathbf{y}_{ho} + \mathbf{y}_{sp}$$