Enzyme kinetics: reduction of the chemical Langevin equation (CLE)

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Too many constants obscure a first analysis: so set all $k_i := 1$. The CLE system then is

$$\begin{bmatrix} \dot s \\ \dot c \end{bmatrix} = \begin{bmatrix} sc + c \\ -sc - 2c \end{bmatrix} + e_0 \begin{bmatrix} -s \\ s \end{bmatrix} + \sigma \vec f(t) \tag{1}$$

for some stochastic forcing $\vec f$.

I would phrase it that the manifold $\mathcal{M}_0$ of equilibria is $c = e_0 = 0$ for all s.

Deterministic analysis is basis for forcing Analyse via my web service[1] for deterministic systems via the following input. The variable s_0 denotes the point of analysis on $\mathcal{M}_0$ so $s := s_0 + u_1$ and $c := 0 + u_2$.

```
RHS function = ( (s_0+u1)*u2  +u2 -e_0*(s_0+small*u1)
,-(s_0+u1)*u2-2*u2 +e_0*(s_0+small*u1) )
Invariant eigenvalues = 0
Invariant eigenvectors = (1,0)
Adjoint basis = (1,0)
```

[1] https://tuck.adelaide.edu.au/gencm.php based upon Roberts (1997).

```
Order of error = 3
factor small,e_0
```

The above and the web service then introduces artificial `small` $\equiv \varepsilon$ to actually analyse the system

$$\begin{aligned}\dot u_1 &= (s_0+1+\varepsilon u_1)u_2 - \varepsilon e_0(s_0+\varepsilon u_1),\\ \dot u_2 &= -(s_0+2+\varepsilon u_1)u_2 + \varepsilon e_0(s_0+\varepsilon u_1).\end{aligned}$$

Orders of errors The web service operates to errors $\mathcal{O}(\varepsilon^p)$ for some specified p. Frankly, the simplest way to understand the errors in terms of physical variables is to simply construct to sufficient order in the artificial ε, and then variously truncate the expansions in terms of physical variables (ignoring ε) as best befits the desired use of the model (justified by Li and Roberts (2007) and/or §5.5 by Roberts (2015)).

However, here I think we can give ε a more traditional meaning. Here, multiplying both ODEs by ε shows that variable ε counts the nonlinearity in $\vec u$ and half the number of e_0 factors. So physically (that is, $\varepsilon=1$) a construction to errors $\mathcal{O}(\varepsilon^p)$ is equivalent to physical errors $\mathcal{O}\big(|\vec u|^{p+1}+e_0^{(p+1)/2}\big)$. And these errors are so for every s_0. For simplicity, let's just write errors $\mathcal{O}(p)$ for such errors.

To errors $\mathcal{O}(3)$, the slow manifold is then simply

$$u_1=s_1\,,\quad u_2=\varepsilon\frac{e_0s_0}{2+s_0}+\varepsilon^2\frac{2e_0s_1}{(2+s_0)^2}\,,\quad \dot s_1=-\varepsilon\frac{e_0s_0}{2+s_0}-\varepsilon^2\frac{2e_0s_1}{(2+s_0)^2}\,. \tag{2}$$

Instead of the local variable s_1, phrase in terms of, say, $S(t)=s_0+\varepsilon s_1(t)$:

$$s=s_0+\varepsilon u_1 \quad = s_0+\varepsilon s_1+\mathcal{O}(3) \quad = S+\mathcal{O}(3), \tag{3a}$$

$$c=0+\varepsilon u_2 \quad =\varepsilon^2\frac{e_0s_0}{2+s_0}+\mathcal{O}(3) \quad =\varepsilon^2\frac{e_0S}{2+S}+\mathcal{O}(3), \tag{3b}$$

$$\dot S=0+\varepsilon\dot s_1 \quad =-\varepsilon^2\frac{e_0s_0}{2+s_0}+\mathcal{O}(3) \quad =-\varepsilon^2\frac{e_0S}{2+S}+\mathcal{O}(3). \tag{3c}$$

The leading order forcing The web service (based upon Roberts 2000) gives the projection vector

$$\vec z = \begin{bmatrix} 1-\varepsilon^2\frac{e_0 2(1+S)}{(2+S)^3} \\ \frac{1+S}{2+S}-\varepsilon^2\frac{e_0 S(3+2S)}{(2+S)^4} \end{bmatrix} + \mathcal{O}\big(3\big) \tag{4}$$

Roberts (1989) argued this projection gives the leading order forcing term should be $\vec z\cdot\vec f$ with errors quadratic in the size of the forcing, namely, errors here are $\mathcal{O}\big(\sigma^2\big)$. The leading order term in this projection appears the same as JSE's (4).

JSE appears to ignore ζ_2,ζ_3, so shall I (although they both appear to be $\mathcal{O}\big(1\big)$, the same as ζ_1). So here $\vec f = \sigma\zeta_1\sqrt{k_1(e_0-c)s}(-1,1) \equiv \sigma\zeta_1\sqrt{(\varepsilon^2 e_0-c)S}(-1,1)$ and $\varepsilon^2 e_0 - c = \varepsilon^2(e_0 - e_0\frac{S}{2+S}) + \mathcal{O}\big(3\big) = \varepsilon^2 2e_0/(2+S) + \mathcal{O}\big(3\big)$. So then the forcing of the slow differential equation becomes

$$\vec z\cdot\vec f = -\frac{\sigma\zeta_1\varepsilon}{2+S}\sqrt{\frac{2e_0 S}{2+S}} + \mathcal{O}\big(2,\sigma^2\big). \tag{5}$$

This appears to have many similarities, but also differences, to JSE's version. Need to check the above.

New equation-free non-autonomous construction Unfortunately, as yet the code needs a polynomial expression for the differential equations, so for this system the square-roots in the noise cannot all be dealt with. For an example, let's try this alternative.

```
% Example CLE of Justin Eilertsen
in_tex "slowNonauto.tex"$
on gcd;
factor small,sigma,e_0,ou,w;
let sign(-2-s_0)=>-1;
slownonauto(
    mat(( (s_0+u1)*u2  +u2 -e_0*(s_0+small*u1)
```

```
        ,-(s_0+u1)*u2-2*u2 +e_0*(s_0+small*u1) ))
    +w(1)*mat((-1,1))*sqrt(s_0)*(1+small*u1/s_0/2) ,
    mat((1,0)),
    mat((-2-s_0)),
    mat((-1-s_0,2+s_0)),
    2 )$
write "**** simplifying form with s_1=0";
u_1:=sub(s(1)=0,u_(1,1));
u_2:=sub(s(1)=0,u_(2,1));
dsdt:=sub(s(1)=0,ff(1));
end;
```

That is, here I model (1) with forcing $\vec f := \begin{bmatrix} -\sqrt{s} \\ \sqrt{s} \end{bmatrix} w_1$. Expanding the about each s_0, $\sqrt{s} = \sqrt{s_0}(1 + u_1/s_0/2 + \cdots)$. The procedure then tweaks the above given system to actually analyse the following:

$$\dot u_1 = -1/2\sqrt{s_0}w_1\sigma\varepsilon u_1 s_0^{-1} - \sqrt{s_0}w_1\sigma - e_0\varepsilon^2 u_1 - e_0\varepsilon s_0 + \varepsilon u_2 u_1 + u_2 s_0 + u_2 \tag{6a}$$

$$\dot u_2 = 1/2\sqrt{s_0}w_1\sigma\varepsilon u_1 s_0^{-1} + \sqrt{s_0}w_1\sigma + e_0\varepsilon^2 u_1 + e_0\varepsilon s_0 - \varepsilon u_2 u_1 - u_2 s_0 - 2u_2 \tag{6b}$$

The constructed slow manifold is rather complicated, and maybe only of peripheral interest, but starts[2]

$$u_1 = s_1 - e_0\varepsilon\frac{s_0^2 + s_0}{(2+s_0)^2} - \sigma\frac{(s_0+1)\sqrt{s_0}}{s_0+2}\mathrm{e}^{(-s_0-2)t}\star w_1 + O\big(\varepsilon^2 + \sigma^2\big) \tag{7a}$$

$$u_2 = \frac{e_0\varepsilon s_0}{s_0+2} + \sigma\sqrt{s_0}\mathrm{e}^{(-s_0-2)t}\star w_1 + O\big(\varepsilon^2 + \sigma^2\big) \tag{7b}$$

The emergent slow evolution is then constructed to be

$$\dot S = -\frac{\varepsilon e_0 S}{S+2} - \frac{\sigma\sqrt{S}}{S+2}w_1 + \frac{\sigma^2\varepsilon(1-S)}{2(2+S)^2}\mathrm{e}^{(-S-2)t}\star w_1\, w_1 + O\big(\varepsilon^2, \sigma^3\big). \tag{8}$$

[2] Check where the deterministic $\mathcal{O}(\varepsilon)$ term in u_1 comes from??

Weak modelling of noise-noise interactions The model (8) is a 'strong' pathwise model. Chao and Roberts (1996) [§4.1] first argued that noise-noise interactions $e^{(-S-2)t}\star w_1\, w_1$ could be approximated 'weakly', in distribution, by its differential $\mapsto \frac{1}{2}\,dt + \frac{1}{2\sqrt{S+2}}dW_1'$ for some new independent noise W_1', and causing a drift $\frac{1}{2}$. This weak approximation is valid to errors decaying *algebraically* in time (I recall like $1/\Delta t$ in some sense??, where Δt is 'time step' or 'time resolution' for the slow model). That is, a weak emergent slow manifold model, with noise induced drift, is

$$\dot S = -\frac{\varepsilon e_0 S}{S+2} - \frac{\sigma\sqrt{S}}{S+2}w_1 + \frac{\sigma^2\varepsilon(1-S)}{2(2+S)^2}\left(\frac{1}{2} + \frac{W_1'}{2\sqrt{S+2}}\right) + O\big(\varepsilon^2, \sigma^3, \Delta t^{-1}\big). \tag{9}$$

References

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