Supplementary Information for "Measuring Retroactivity from Noise in Gene Regulatory Networks"

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We provide the *Mathematica* code for the example "Dimer transcription factor with negative feedback". In this code, the same mathematical notations are used as shown in the main manuscript and the data for Figure 8B is obtained.

Oligomer (dimer, w/ and w/o negative feedback)

Deterministic retroactivity

$$x2 = \frac{k1}{k2 + \gamma 2} x^2;$$

$$\alpha[x\_] := \frac{\alpha 0}{1 + \beta\, x2};$$

$$tau0 = \frac{1 + \frac{4\, k1\, x}{k2+\gamma 2}}{-\text{Evaluate}[D[\alpha[x], x]] + \gamma + \frac{4\, \gamma 2\, k1\, x}{k2+\gamma 2}};$$

$$f[x\_] := \frac{x2}{kd + x2};$$

$$tau[pt\_] := tau0 \left(1 + 2 \frac{\text{Evaluate}[D[f[x], x]]}{1 + \frac{4\, k1\, x}{k2+\gamma 2}} pt\right);$$

$$R[pt\_] := \frac{tau[pt] - tau0NoNeg}{tau[pt]};$$

```
kd = koff / kon;
pb = pt f[x];
```

No negative feedback (β =0.00001)

```
param = {α0 → 20, β → 0.00001, γ → 2, k1 → 20, k2 → 1, γ2 → 2, koff → 10, kon → 10};
```

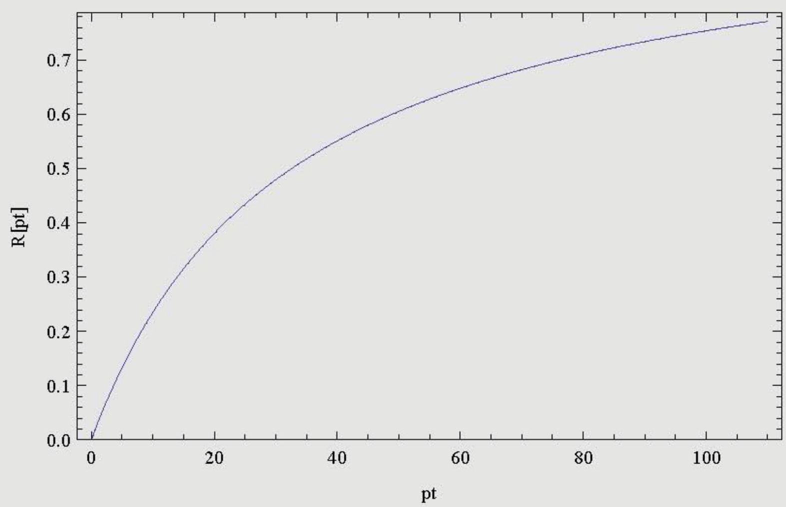
```
xsol = Cases[NSolve[α[x] - γ x - 2 γ2 x2 == 0 /. param, x], {_ → _?Positive}][[1]]
(*Choose the positive real solution of x*)
```

```
{x → 0.829317}
```

```
tau0NoNeg = tau0 /. param /. xsol
```

```
0.499976
```

```
g1 = Plot[R[pt] /. param /. xsol, {pt, 0.1, 110}, Frame → True,
  FrameLabel → {"pt", "R[pt]"}, PlotRange → {Automatic, {0, Automatic}}]
```




```
list1 = Table[{pt, R[pt] /. param /. xsol}, {pt, 0, 110}];
```

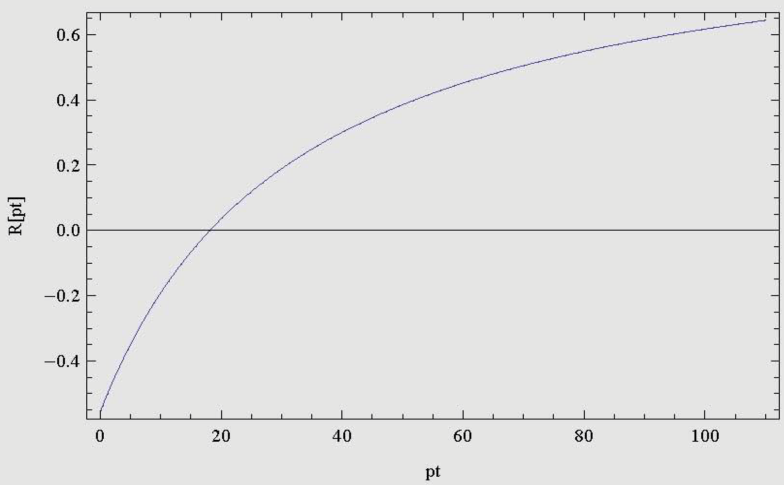
With negative feedback (β = 0.25)

```
param = {α0 → 43, β → 0.25, γ → 2, k1 → 20, k2 → 1, γ2 → 2, koff → 10, kon → 10};
```

```
xsol = Cases[NSolve[α[x] - γ x - 2 γ2 x2 == 0 /. param, x], {_ → _?Positive}][[1]]
```

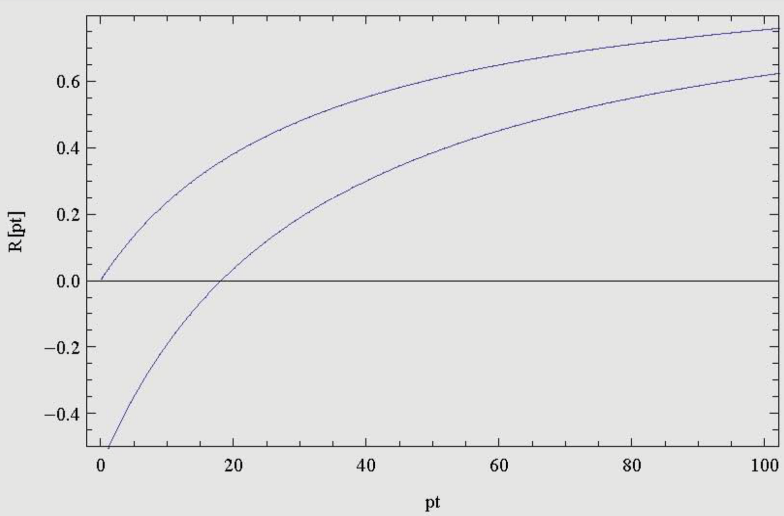
```
{x → 0.829811}
```

```
g2 = Plot[R[pt] /. param /. xsol,
  {pt, 0.1, 110}, Frame → True, FrameLabel → {"pt", "R[pt]"}]
```




```
list2 = Table[{pt, R[pt] /. param /. xsol}, {pt, 0, 110}];
```

```
Show[g1, g2, PlotRange → {{0, 100}, {-0.5, Automatic}}]
```



Stochastic retroactivity -- error bar calculation

```
R = (Tc - T1)/Tc; (*Here, T1 is the correlation time for the case
 without any feedbacka and without any downstream load. *)
dR = Sqrt[(T1/Tc^2)^2 dTc^2 + (1/Tc)^2 dT1^2];
list = {};
```

$$R = \frac{T_c - T_1}{T_c}$$

$$dR = \sqrt{\left(\frac{T_1}{T_c^2}\right)^2 dT_c^2 + \left(\frac{1}{T_c}\right)^2 dT_1^2}$$

without feedback, P_T = 25 for the connected case.

```
{R, dR} /. {T1 → 0.48795, dT1 → 0.03968, Tc → 0.854807, dTc → 0.0709}
```

```
{0.429169, 0.0663059}
```

without feedback, P_T = 50 for the connected case.

```
{R, dR} /. {T1 → 0.48795, dT1 → 0.03968, Tc → 1.30483, dTc → 0.142591}
```

```
{0.626043, 0.050939}
```