

Conditional Dosing Pharmacometric Example

Chris Rackauckas

February 23, 2019

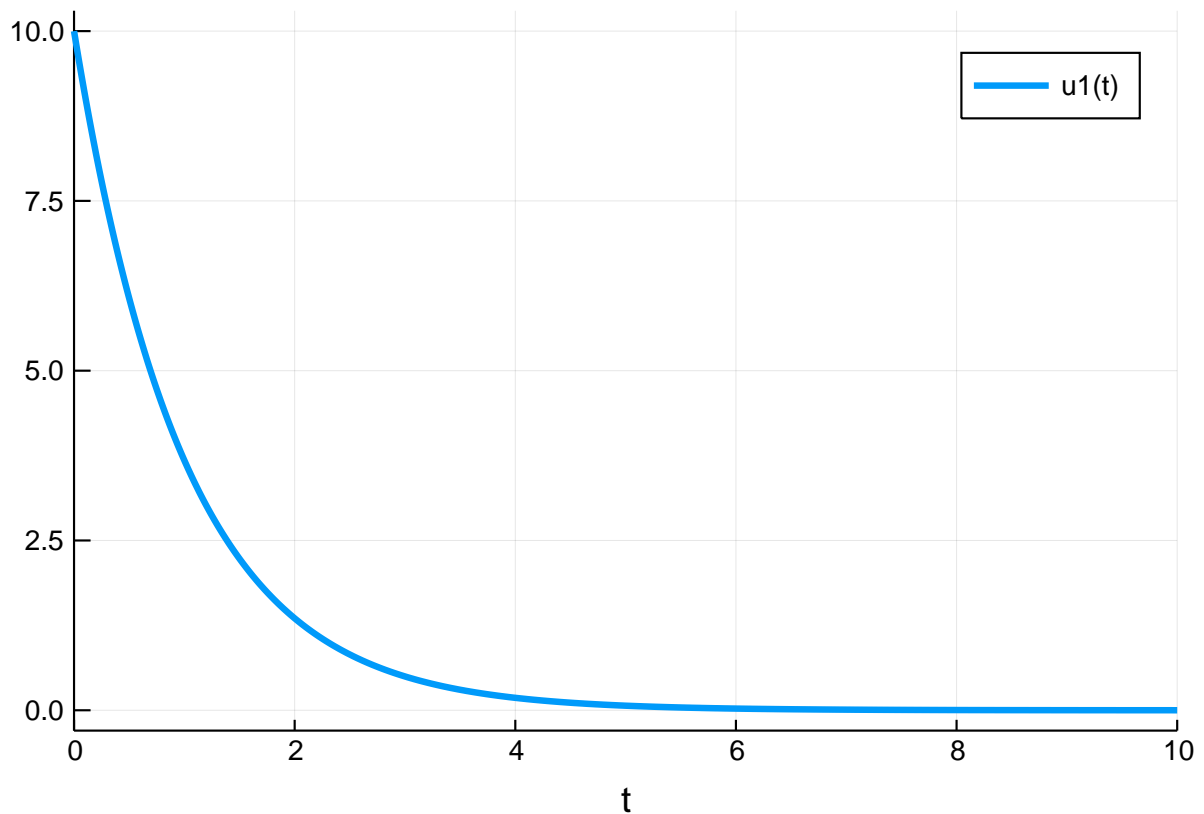
In this example we will show how to model a conditional dosing using the `DiscreteCallbacks`. The problem is as follows. The patient has a drug $A(t)$ in their system. The concentration of the drug is given as $C(t)=A(t)/V$ for some volume constant V . At $t=4$, the patient goes to the clinic and is checked. If the concentration of the drug in their body is below 4, then they will receive a new dose.

For our model, we will use the simple decay equation. We will write this in the in-place form to make it easy to extend to more complicated examples:

```
using DifferentialEquations
function f(du,u,p,t)
    du[1] = -u[1]
end
u0 = [10.0]
const V = 1
prob = ODEProblem(f,u0,(0.0,10.0))
```

Let's see what the solution looks like without any events.

```
sol = solve(prob,Tsit5())
using Plots; gr()
plot(sol)
```

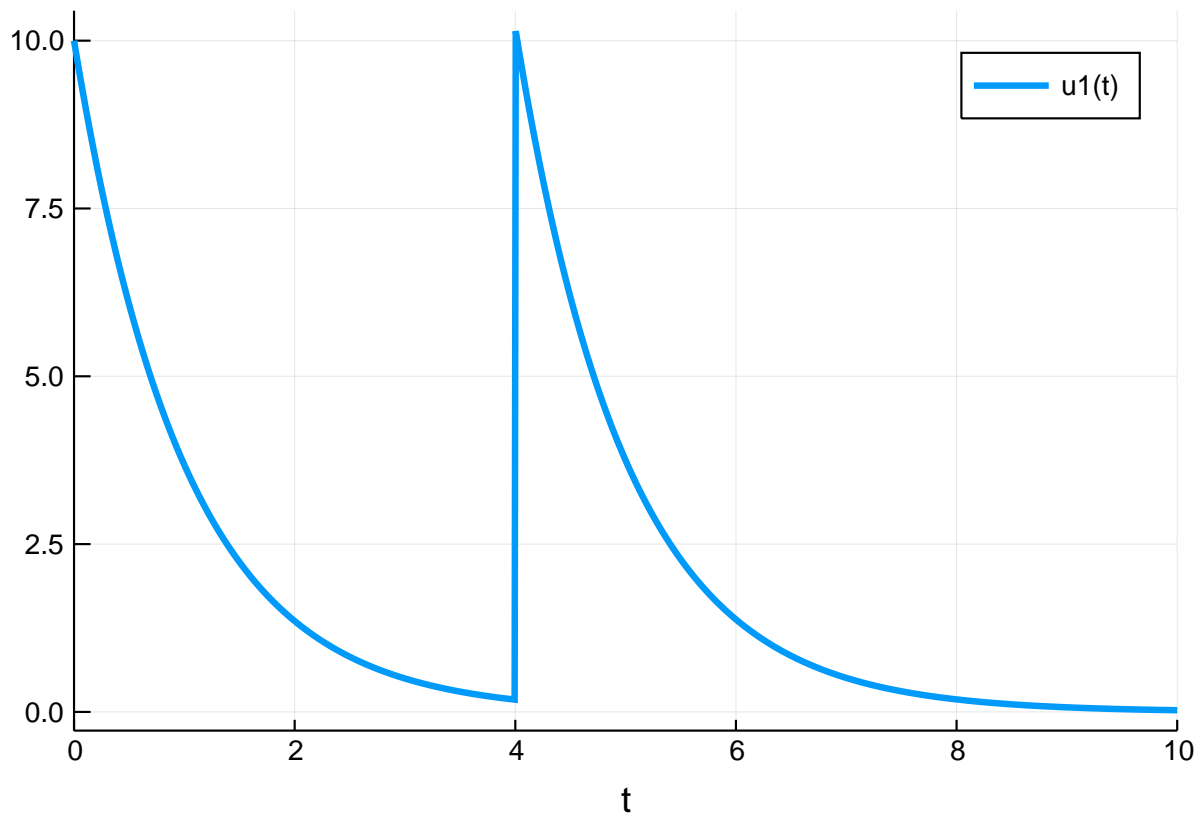


We see that at time $t=4$, the patient should receive a dose. Let's code up that event. We need to check at $t=4$ if the concentration $u[1]/4$ is <4 , and if so, add 10 to $u[1]$. We do this with the following:

```
condition(u,t,integrator) = t==4 && u[1]/V<4
affect!(integrator) = integrator.u[1] += 10
cb = DiscreteCallback(condition,affect!)
```

Now we will give this callback to the solver, and tell it to stop at $t=4$ so that way the condition can be checked:

```
sol = solve(prob,Tsit5(),tstops=[4.0],callback=cb)
using Plots; gr()
plot(sol)
```



Let's show that it actually added 10 instead of setting the value to 10. We could have set the value using `affect!(integrator) = integrator.u[1] = 10`

```
println(sol(4.00000))
```

```
[0.183164]
```

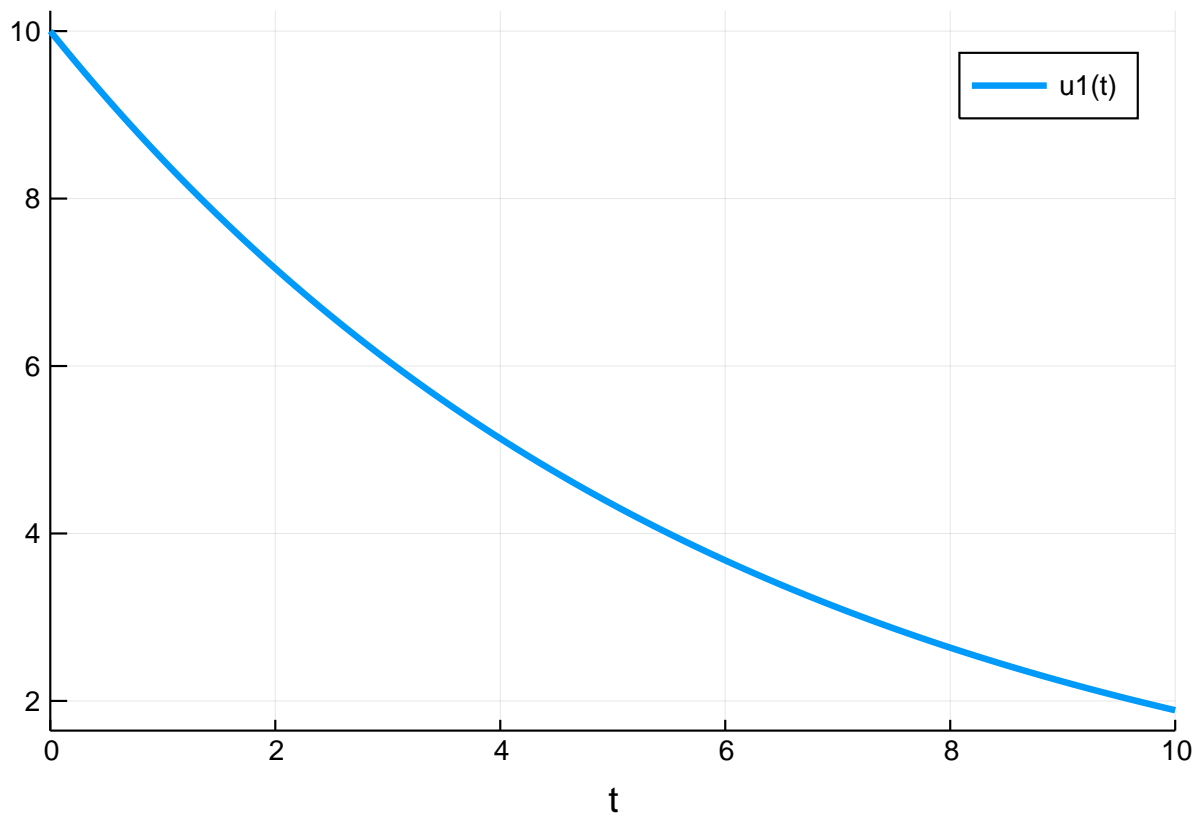
```
println(sol(4.000000000000001))
```

```
[10.1832]
```

Now let's model a patient whose decay rate for the drug is lower:

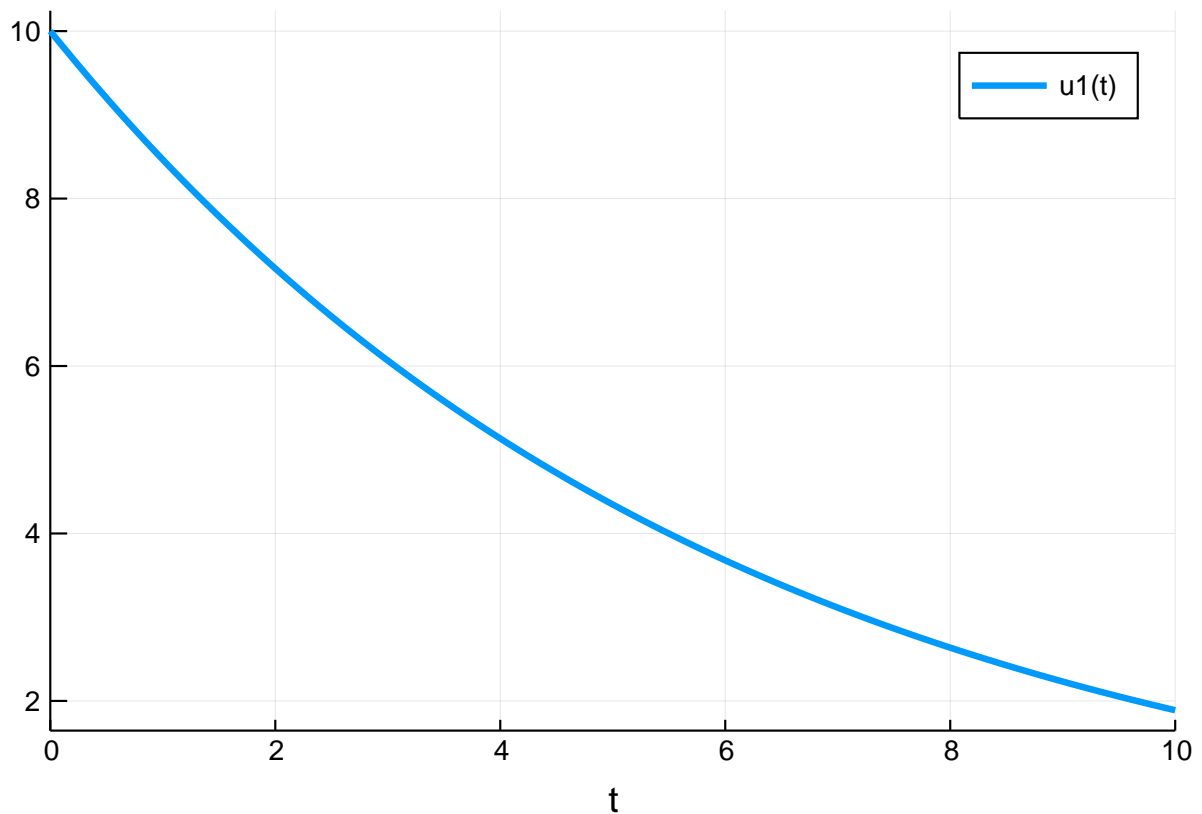
```
function f(du,u,p,t)
    du[1] = -u[1]/6
end
u0 = [10.0]
const V = 1
prob = ODEProblem(f,u0,(0.0,10.0))
```

```
sol = solve(prob,Tsit5())
using Plots; gr()
plot(sol)
```



Under the same criteria, with the same event, this patient will not receive a second dose:

```
sol = solve(prob, Tsit5(), tstops=[4.0], callback=cb)
using Plots; gr()
plot(sol)
```



0.1 Appendix

```
using DiffEqTutorials
DiffEqTutorials.tutorial_footer(WEAVE_ARGS[:folder],WEAVE_ARGS[:file])
```

These benchmarks are part of the DiffEqTutorials.jl repository, found at:

<https://github.com/JuliaDiffEq/DiffEqTutorials.jl>

To locally run this tutorial, do the following commands:

```
using DiffEqTutorials
DiffEqTutorials.weave_file(".", "models/conditional_dosing.jmd")
```

Computer Information:

```
Julia Version 1.1.0
Commit 80516ca202 (2019-01-21 21:24 UTC)
Platform Info:
  OS: Windows (x86_64-w64-mingw32)
  CPU: Intel(R) Core(TM) i7-8700 CPU @ 3.20GHz
  WORD_SIZE: 64
  LIBM: libopenlibm
  LLVM: libLLVM-6.0.1 (ORCJIT, skylake)
Environment:
  JULIA_EDITOR = "C:\Users\accou\AppData\Local\atom\app-1.34.0\atom.exe" -a
  JULIA_NUM_THREADS = 6
```

Package Information:

```
Status `C:\Users\accou\.julia\environments\v1.1\Project.toml`
[c52e3926] Atom v0.7.14
[6e4b80f9] BenchmarkTools v0.4.2
[336ed68f] CSV v0.4.3
[be33ccc6] CUDAnative v1.0.1
[3a865a2d] CuArrays v0.9.1
[a93c6f00] DataFrames v0.17.1
[39dd38d3] Dierckx v0.4.1
[459566f4] DiffEqCallbacks v2.5.2
[aae7a2af] DiffEqFlux v0.2.0
[c894b116] DiffEqJump v6.1.0+ [C:\Users\accou\.julia\dev\DiffEqJump`]
[1130ab10] DiffEqParamEstim v1.5.1
[055956cb] DiffEqPhysics v3.1.0
[225cb15b] DiffEqTutorials v0.0.0 [C:\Users\accou\.julia\external\DiffEq
Tutorials.jl`]
[0c46a032] DifferentialEquations v6.3.0
[587475ba] Flux v0.7.3
[f6369f11] ForwardDiff v0.10.3+ [C:\Users\accou\.julia\dev\ForwardDiff`]
[7073ff75] IJulia v1.17.0
[c601a237] Interact v0.9.1
[b6b21f68] Ipopt v0.5.4
[4076af6c] JuMP v0.18.5
[e5e0dc1b] Juno v0.5.4
[76087f3c] NLOpt v0.5.1
[429524aa] Optim v0.17.2
[1dea7af3] OrdinaryDiffEq v5.1.4+ [C:\Users\accou\.julia\dev\OrdinaryDif
fEq`]
[65888b18] ParameterizedFunctions v4.1.0
[91a5bcdd] Plots v0.23.0
[71ad9d73] PuMaS v0.0.0 [C:\Users\accou\.julia\dev\PuMaS`]
[d330b81b] PyPlot v2.7.0
[731186ca] RecursiveArrayTools v0.20.0
[90137ffa] StaticArrays v0.10.2
[789caeaf] StochasticDiffEq v6.1.1+ [C:\Users\accou\.julia\dev\Stochasti
cDiffEq`]
[c3572dad] Sundials v3.0.0
[44d3d7a6] Weave v0.7.1
```