Conditional Dosing Pharmacometric Example

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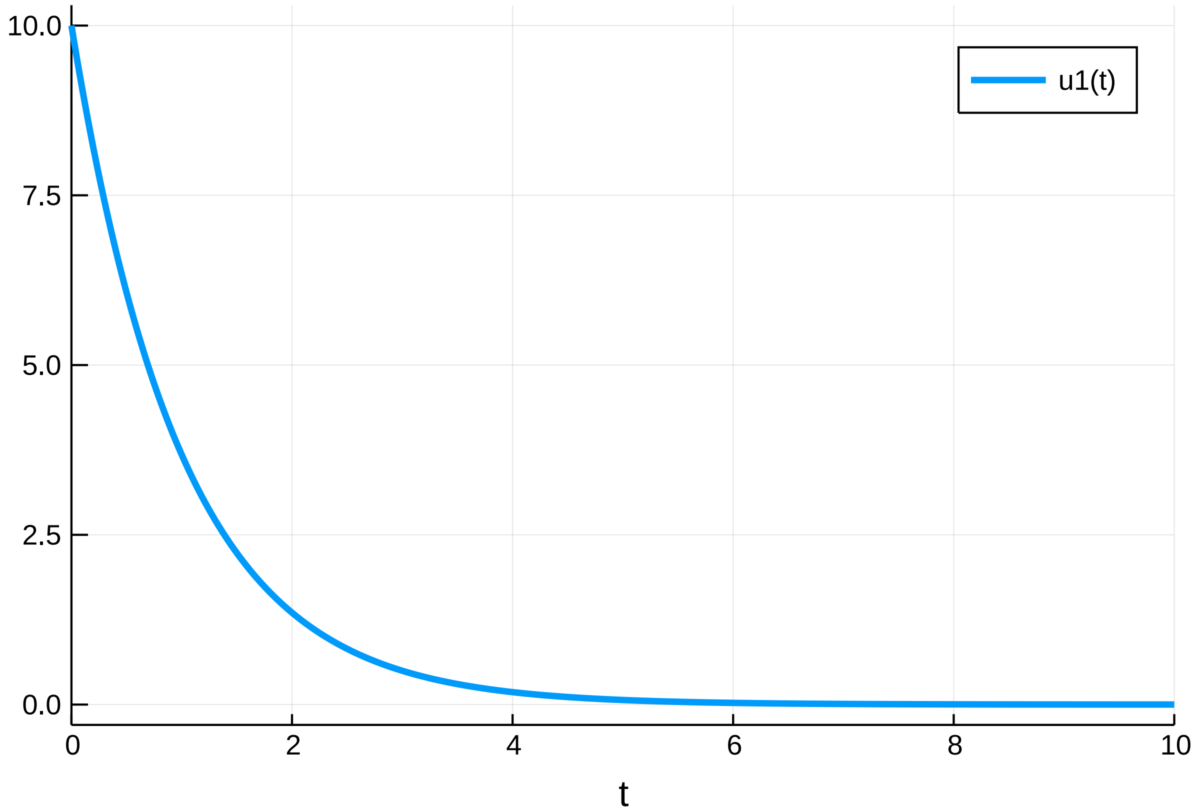
In this example we will show how to model a conditional dosing using the `DiscreteCallbacks`. The problem is as follows. The patient has a drug `A(t)` in their system. The concentration of the drug is given as `C(t)=A(t)/V` for some volume constant `V`. At `t=4`, the patient goes to the clinic and is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

```julia
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.

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

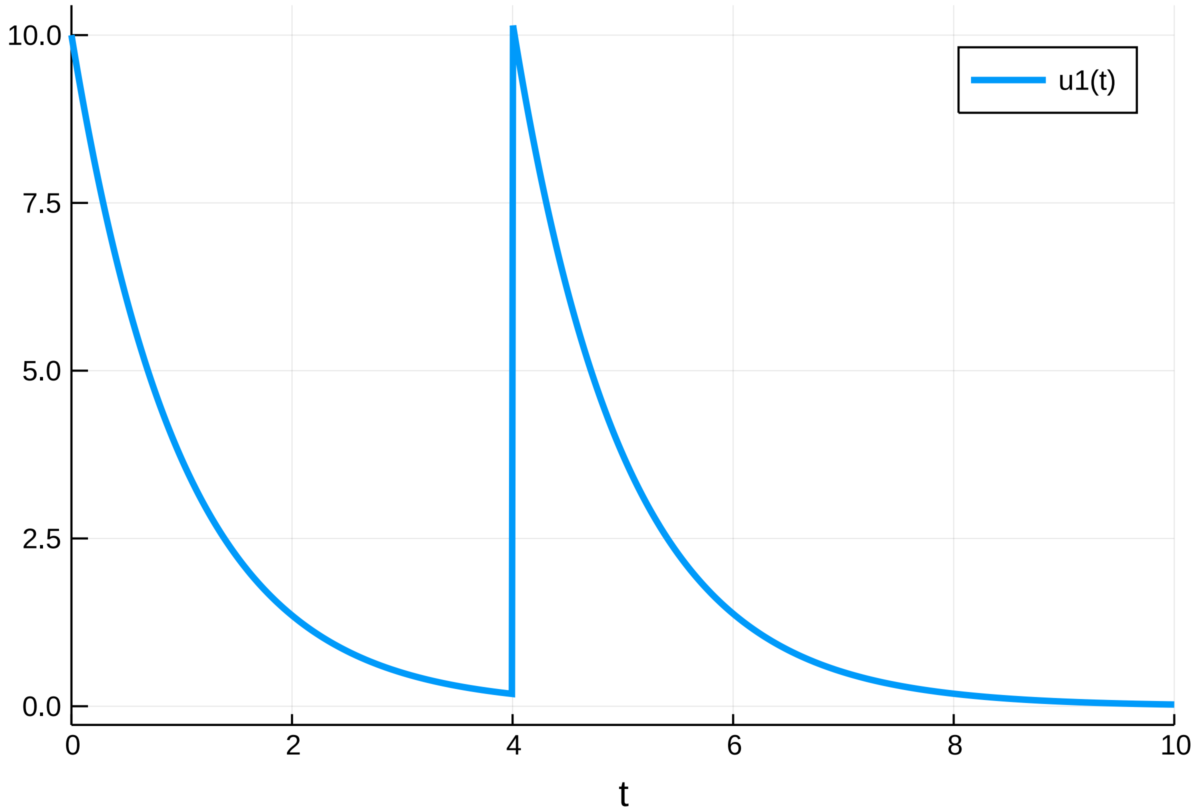


We see that at time t=4, the patient should receive a dose. Let's code up that event. We need to check at t=4 if the concentration u[1]/4 is <4, and if so, add 10 to u[1]. We do this with the following:

```
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]
```

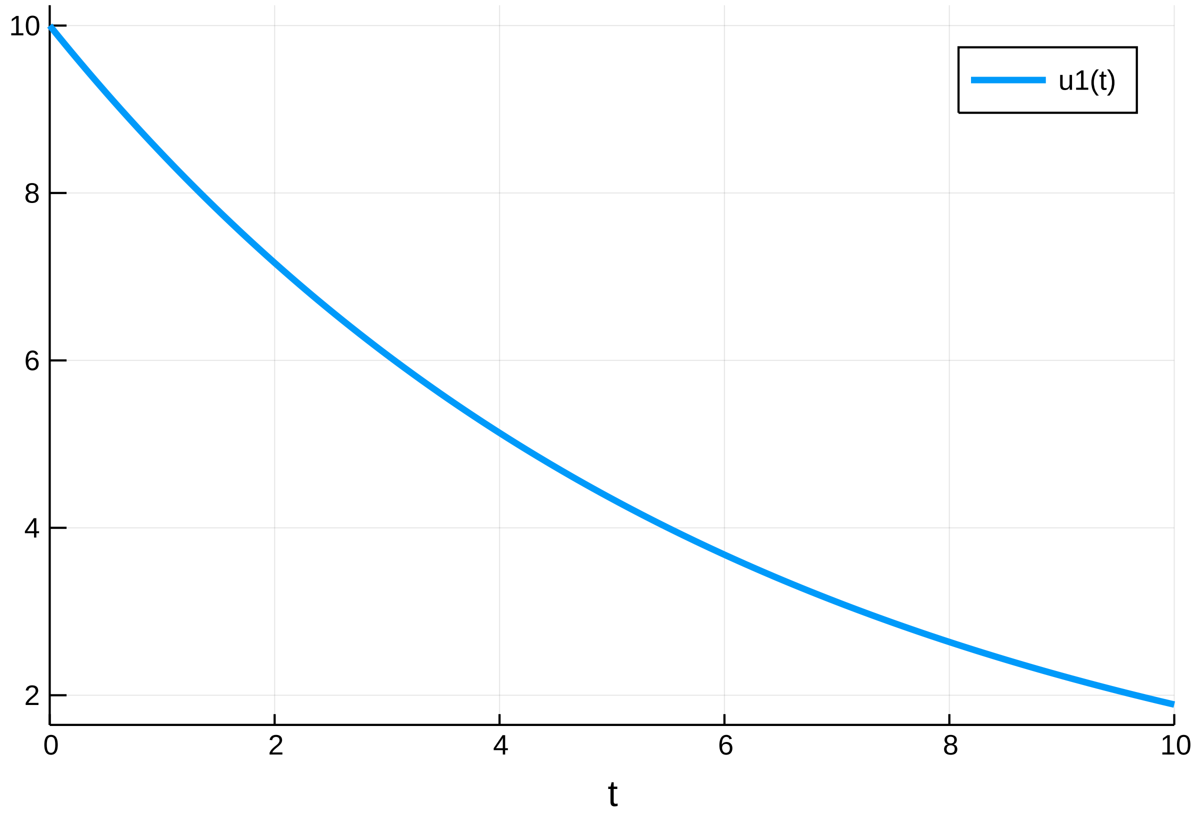
```
println(sol(4.000000000001))
```

```
[10.1832]
```

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

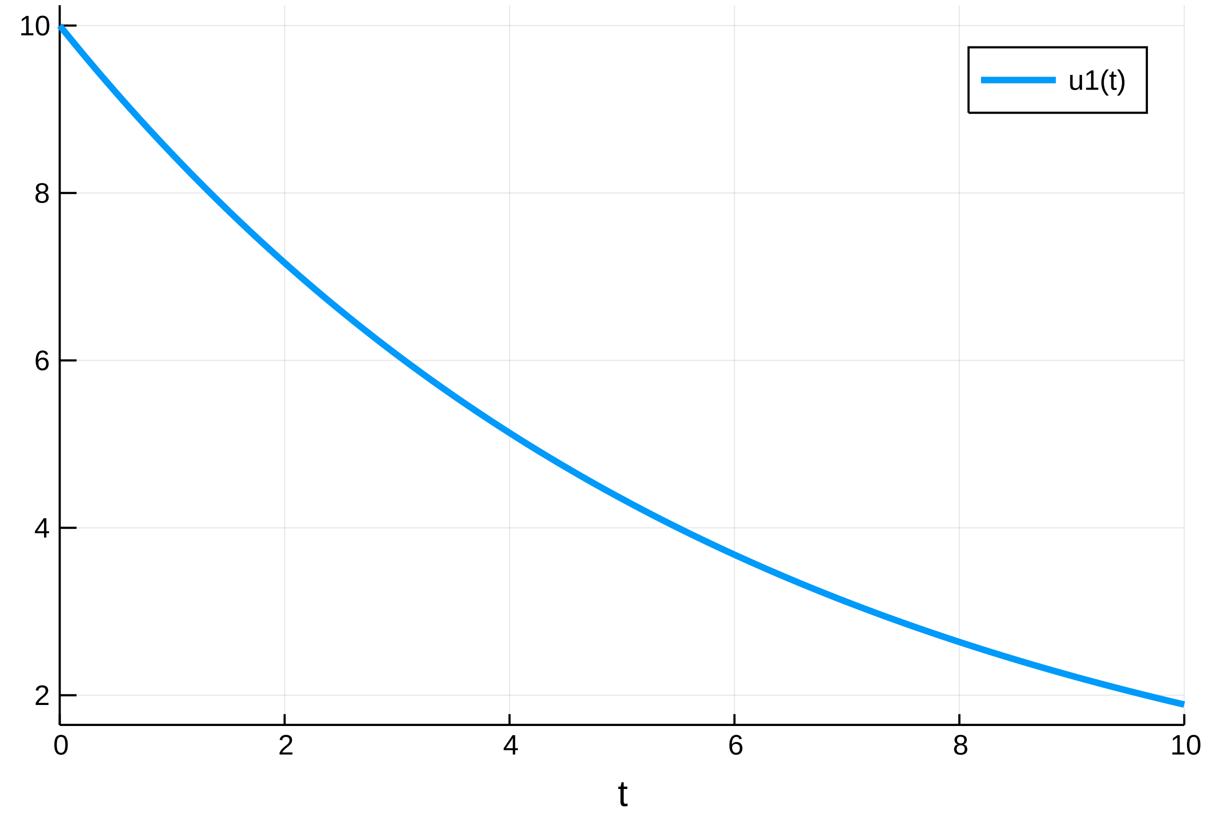
```
function f(du,u,p,t)
    du[1] = -u[1]/6
end
u0 = [10.0]
const V = 1
prob = ODEProblem(f,u0,(0.0,10.0))
```

```
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`
  [7e558dbc] ArbNumerics v0.3.6
  [c52e3926] Atom v0.7.14
  [6e4b80f9] BenchmarkTools v0.4.2
  [336ed68f] CSV v0.4.3
  [3895d2a7] CUDAapi v0.5.4
  [be33ccc6] CUDAnative v1.0.1
  [3a865a2d] CuArrays v0.9.1
  [a93c6f00] DataFrames v0.17.1
  [55939f99] DecFP v0.4.8
  [abce61dc] Decimals v0.4.0
  [39dd38d3] Dierckx v0.4.1
  [bb2cbb15] DiffEqBenchmarks v0.0.0 [`C:\Users\accou\.julia\external\DiffE
qBenchmarks.jl`]
  [459566f4] DiffEqCallbacks v2.5.2
  [f3b72e0c] DiffEqDevTools v2.6.1
  [aae7a2af] DiffEqFlux v0.2.0
  [c894b116] DiffEqJump v6.1.0+ [`C:\Users\accou\.julia\dev\DiffEqJump`]
  [1130ab10] DiffEqParamEstim v1.6.0+ [`C:\Users\accou\.julia\dev\DiffEqPar
amEstim`]
  [055956cb] DiffEqPhysics v3.1.0
  [a077e3f3] DiffEqProblemLibrary v4.1.0
  [225cb15b] DiffEqTutorials v0.0.0 [`C:\Users\accou\.julia\external\DiffEq
Tutorials.jl`]
  [0c46a032] DifferentialEquations v6.3.0
  [497a8b3b] DoubleFloats v0.7.5
  [587475ba] Flux v0.7.3
  [f6369f11] ForwardDiff v0.10.3+ [`C:\Users\accou\.julia\dev\ForwardDiff`]
  [28b8d3ca] GR v0.38.1
  [7073ff75] IJulia v1.17.0
  [c601a237] Interact v0.9.1
  [b6b21f68] Ipopt v0.5.4
  [4076af6c] JuMP v0.19.0
  [e5e0dc1b] Juno v0.5.4
  [7f56f5a3] LSODA v0.4.0
  [eff96d63] Measurements v2.0.0
  [76087f3c] NLopt v0.5.1
  [c030b06c] ODE v2.4.0
  [54ca160b] ODEInterface v0.4.5+ [`C:\Users\accou\.julia\dev\ODEInterface`
]
  [09606e27] ODEInterfaceDiffEq v3.0.0
  [429524aa] Optim v0.17.2
  [1dea7af3] OrdinaryDiffEq v5.2.1+ [`C:\Users\accou\.julia\dev\OrdinaryDif
fEq`]
  [65888b18] ParameterizedFunctions v4.1.1
  [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
  [1986cc42] Unitful v0.14.0
  [2a06ce6d] UnitfulPlots v0.0.0 #master (https://github.com/ajkeller34/Uni
tfulPlots.jl)
  [44d3d7a6] Weave v0.7.1 [`C:\Users\accou\.julia\dev\Weave`]
```