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.

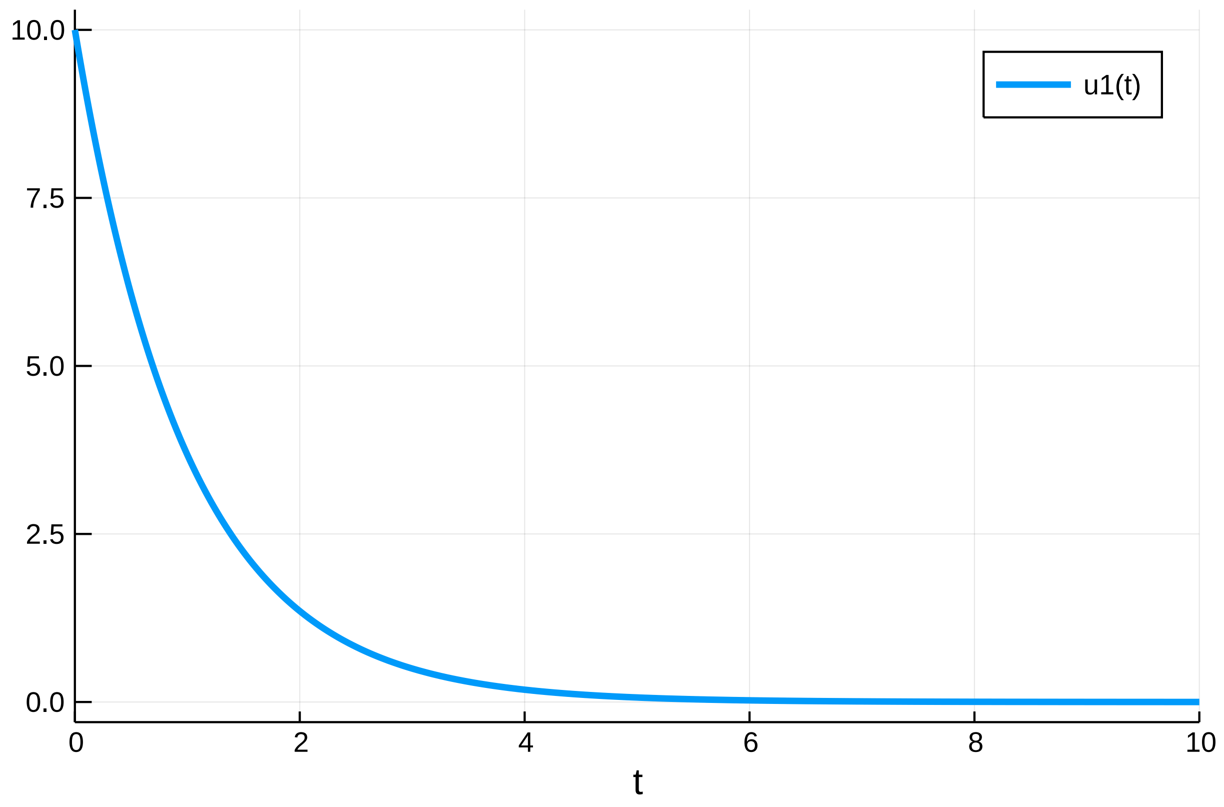
For our model, we will use the simple decay equation. We will write this in the in-place form to make it easy to extend to more complicated examples:

```
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))
```

```
ODEProblem with uType Array{Float64,1} and tType Float64. In-place: true
timespan: (0.0, 10.0)
u0: [10.0]
```

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

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



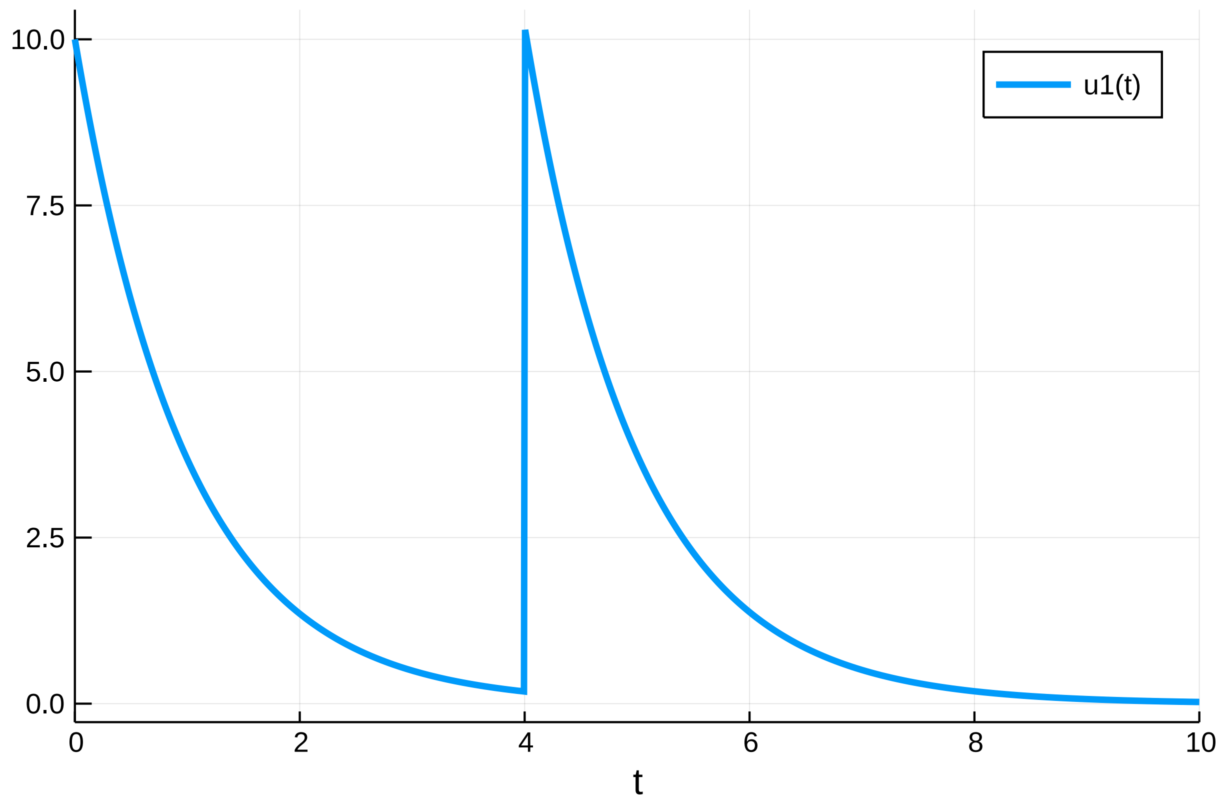
We see that at time `t=4`, the patient should receive a dose. Let's code up that event. We need to check at `t=4` if the concentration `u[1]/4` is `<4`, and if so, add `10` to `u[1]`. We do this with the following:

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

```
DiffEqBase.DiscreteCallback{typeof(Main.WeaveSandBox19.condition),typeof(Ma
in.WeaveSandBox19.affect!),typeof(DiffEqBase.INITIALIZE_DEFAULT)}(Main.Weav
eSandBox19.condition, Main.WeaveSandBox19.affect!, DiffEqBase.INITIALIZE_DE
FAULT, Bool[true, true])
```

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))
```

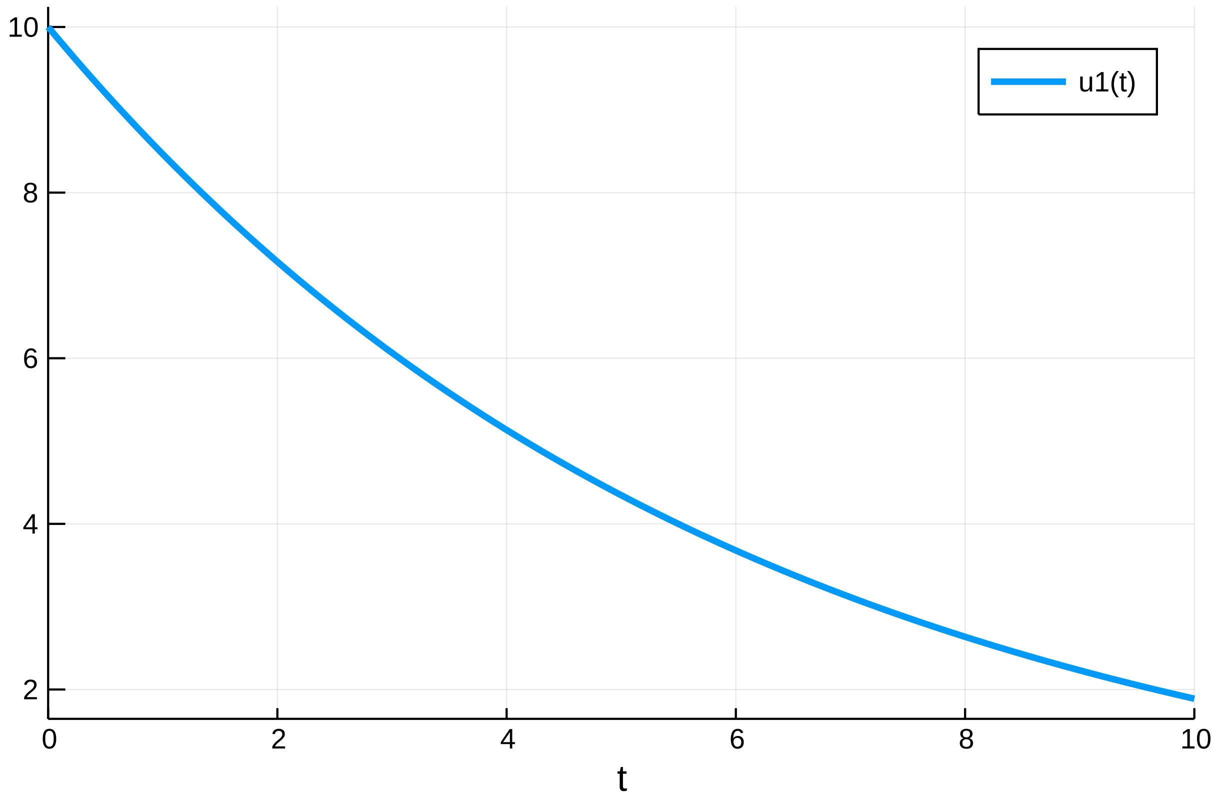
```
[10.1832]
```

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))
```

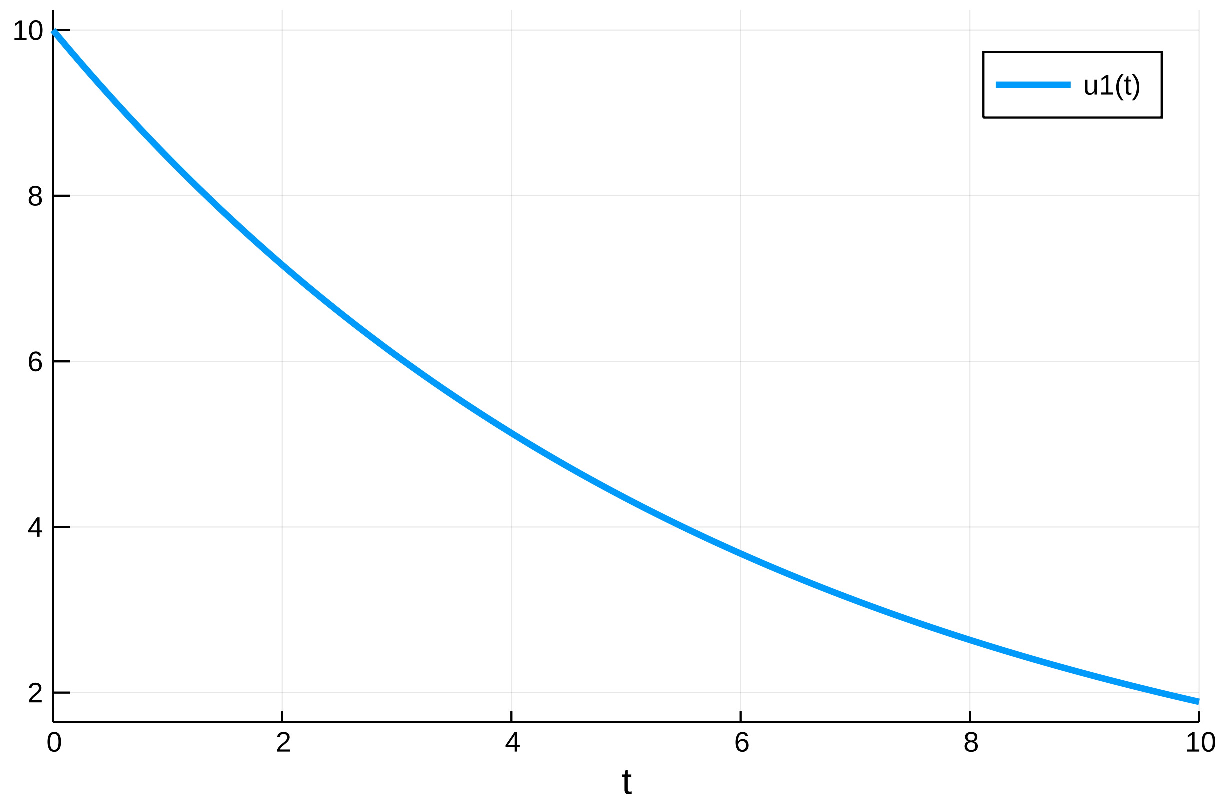
```
ODEProblem with uType Array{Float64,1} and tType Float64. In-place: true
timespan: (0.0, 10.0)
u0: [10.0]
```

```
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

This tutorial is part of the DiffEqTutorials.jl repository, found at: https://github.com/JuliaDiffEq/DiffEq

To locally run this tutorial, do the following commands:

```
using DiffEqTutorials
DiffEqTutorials.weave_file("models","02-conditional_dosing.jmd")
```

Computer Information:

```
Julia Version 1.1.1
Commit 55e36cc308 (2019-05-16 04:10 UTC)
Platform Info:
  OS: Linux (x86_64-pc-linux-gnu)
  CPU: Intel(R) Core(TM) i7-3770 CPU @ 3.40GHz
  WORD_SIZE: 64
  LIBM: libopenlibm
  LLVM: libLLVM-6.0.1 (ORCJIT, ivybridge)
```

Package Information:

```
Status `~/.julia/environments/v1.1/Project.toml`
[7e558dbc-694d-5a72-987c-6f4ebed21442] ArbNumerics 0.5.4
```

```
[6e4b80f9-dd63-53aa-95a3-0cdb28fa8baf] BenchmarkTools 0.4.2
[be33ccc6-a3ff-5ff2-a52e-74243cff1e17] CUDAnative 2.2.0
[3a865a2d-5b23-5a0f-bc46-62713ec82fae] CuArrays 1.0.2
[55939f99-70c6-5e9b-8bb0-5071ed7d61fd] DecFP 0.4.8
[abce61dc-4473-55a0-ba07-351d65e31d42] Decimals 0.4.0
[ebbdde9d-f333-5424-9be2-dbf1e9acfb5e] DiffEqBayes 1.1.0
[eb300fae-53e8-50a0-950c-e21f52c2b7e0] DiffEqBiological 3.8.2
[459566f4-90b8-5000-8ac3-15dfb0a30def] DiffEqCallbacks 2.5.2
[f3b72e0c-5b89-59e1-b016-84e28bfd966d] DiffEqDevTools 2.9.0
[1130ab10-4a5a-5621-a13d-e4788d82bd4c] DiffEqParamEstim 1.6.0
[055956cb-9e8b-5191-98cc-73ae4a59e68a] DiffEqPhysics 3.1.0
[6d1b261a-3be8-11e9-3f2f-0b112a9a8436] DiffEqTutorials 0.1.0
[0c46a032-eb83-5123-abaf-570d42b7fbaa] DifferentialEquations 6.4.0
[31c24e10-a181-5473-b8eb-7969acd0382f] Distributions 0.20.0
[497a8b3b-efae-58df-a0af-a86822472b78] DoubleFloats 0.9.1
[f6369f11-7733-5829-9624-2563aa707210] ForwardDiff 0.10.3
[c91e804a-d5a3-530f-b6f0-dfbca275c004] Gadfly 1.0.1
[7073ff75-c697-5162-941a-fcdaad2a7d2a] IJulia 1.18.1
[4138dd39-2aa7-5051-a626-17a0bb65d9c8] JLD 0.9.1
[23fbe1c1-3f47-55db-b15f-69d7ec21a316] Latexify 0.8.2
[eff96d63-e80a-5855-80a2-b1b0885c5ab7] Measurements 2.0.0
[961ee093-0014-501f-94e3-6117800e7a78] ModelingToolkit 0.2.0
[76087f3c-5699-56af-9a33-bf431cd00edd] NLopt 0.5.1
[2774e3e8-f4cf-5e23-947b-6d7e65073b56] NLsolve 4.0.0
[429524aa-4258-5aef-a3af-852621145aeb] Optim 0.18.1
[1dea7af3-3e70-54e6-95c3-0bf5283fa5ed] OrdinaryDiffEq 5.8.1
[65888b18-ceab-5e60-b2b9-181511a3b968] ParameterizedFunctions 4.1.1
[91a5bcdd-55d7-5caf-9e0b-520d859cae80] Plots 0.25.1
[d330b81b-6aea-500a-939a-2ce795aea3ee] PyPlot 2.8.1
[731186ca-8d62-57ce-b412-fbd966d074cd] RecursiveArrayTools 0.20.0
[90137ffa-7385-5640-81b9-e52037218182] StaticArrays 0.11.0
[f3b207a7-027a-5e70-b257-86293d7955fd] StatsPlots 0.11.0
[c3572dad-4567-51f8-b174-8c6c989267f4] Sundials 3.6.1
[1986cc42-f94f-5a68-af5c-568840ba703d] Unitful 0.15.0
[44d3d7a6-8a23-5bf8-98c5-b353f8df5ec9] Weave 0.9.0
[b77e0a4c-d291-57a0-90e8-8db25a27a240] InteractiveUtils
[37e2e46d-f89d-539d-b4ee-838fcccc9c8e] LinearAlgebra
[44cfe95a-1eb2-52ea-b672-e2afdf69b78f] Pkg
```