Conditional Dosing Pharmacometric Example

Chris Rackauckas

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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))
```

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

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

```julia
sol = solve(prob,Tsit5())
using Plots; gr()
plot(sol)
```
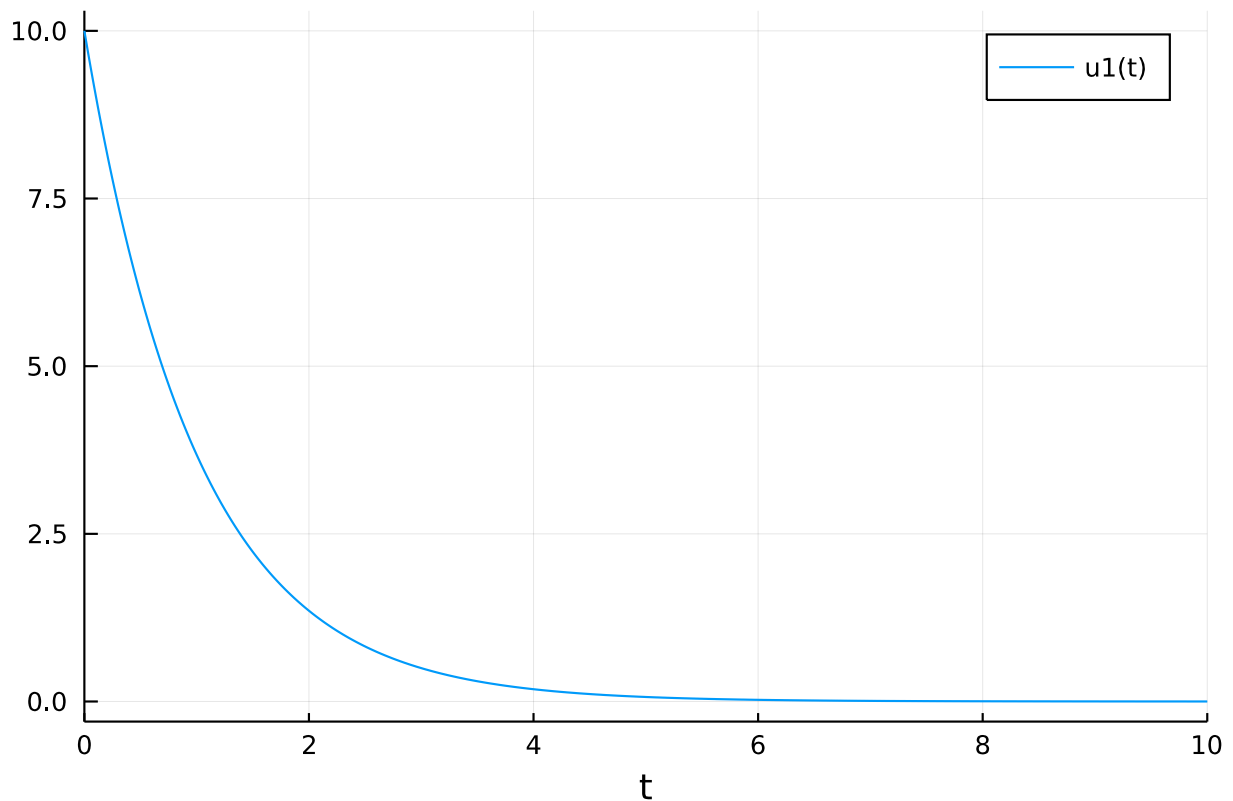
We see that at time `t=4`, the patient should receive a dose. Let's code up that event. We need to check at `t=4` if the concentration `u[1]/4` is `<4`, and if so, add `10` to `u[1]`. We do this with the following:

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

DiffEqBase.DiscreteCallback{typeof(Main.##WeaveSandBox#5436.condition), typ
eof(Main.##WeaveSandBox#5436.affect!), typeof(DiffEqBase.INITIALIZE_DEFAULT
), typeof(DiffEqBase.FINALIZE_DEFAULT)}(Main.##WeaveSandBox#5436.condition,
 Main.##WeaveSandBox#5436.affect!, DiffEqBase.INITIALIZE_DEFAULT, DiffEqBas
e.FINALIZE_DEFAULT, Bool[1, 1])
```

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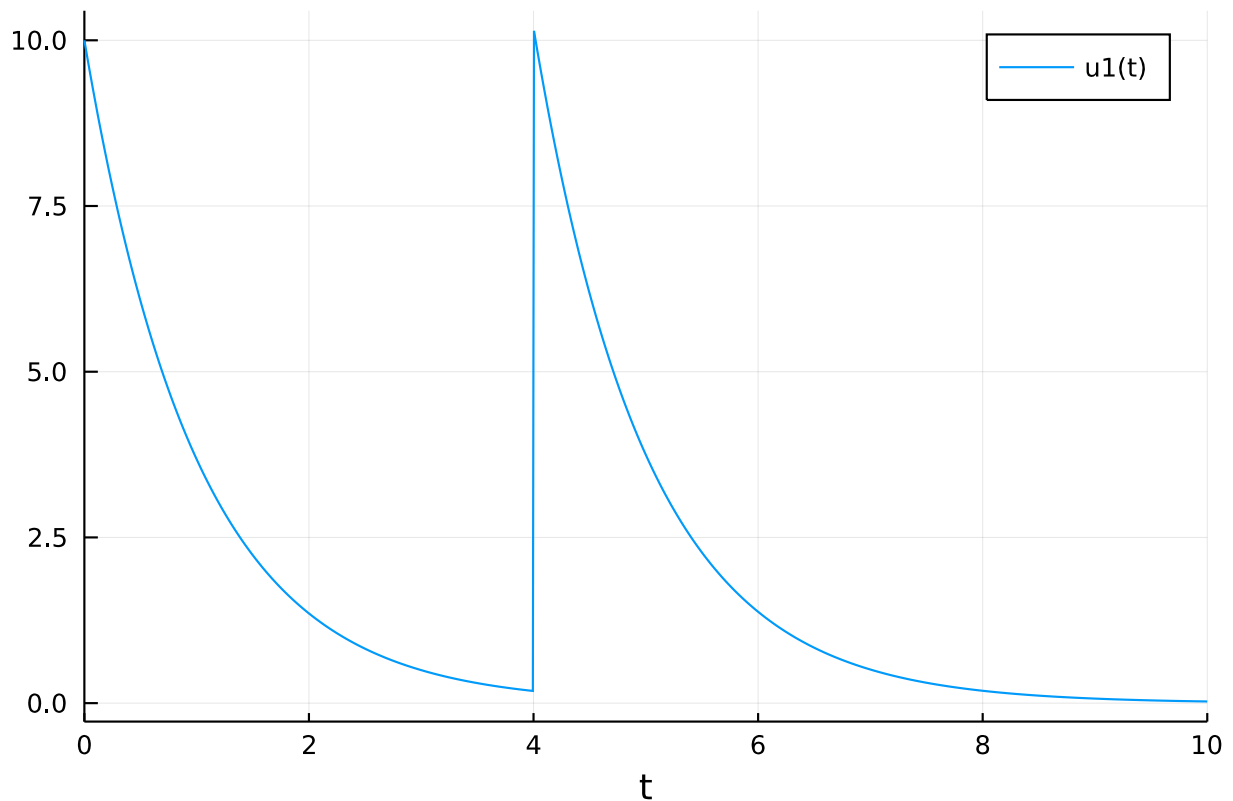
Let's show that it actually added 10 instead of setting the value to 10. We could have set the value using `affect!(integrator) = integrator.u[1] = 10`

```
println(sol(4.00000))
println(sol(4.000000000001))
```
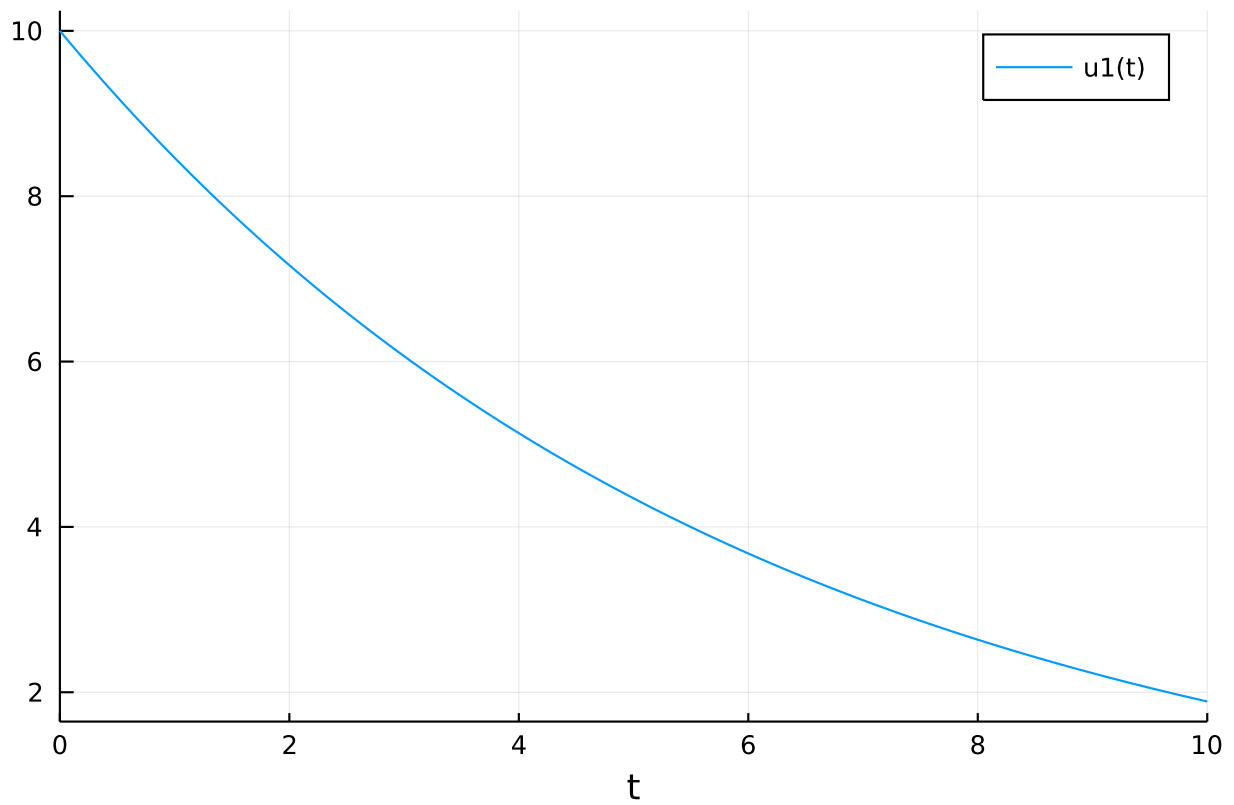
```
[0.18316389222022983]
[10.183163892210045]
```

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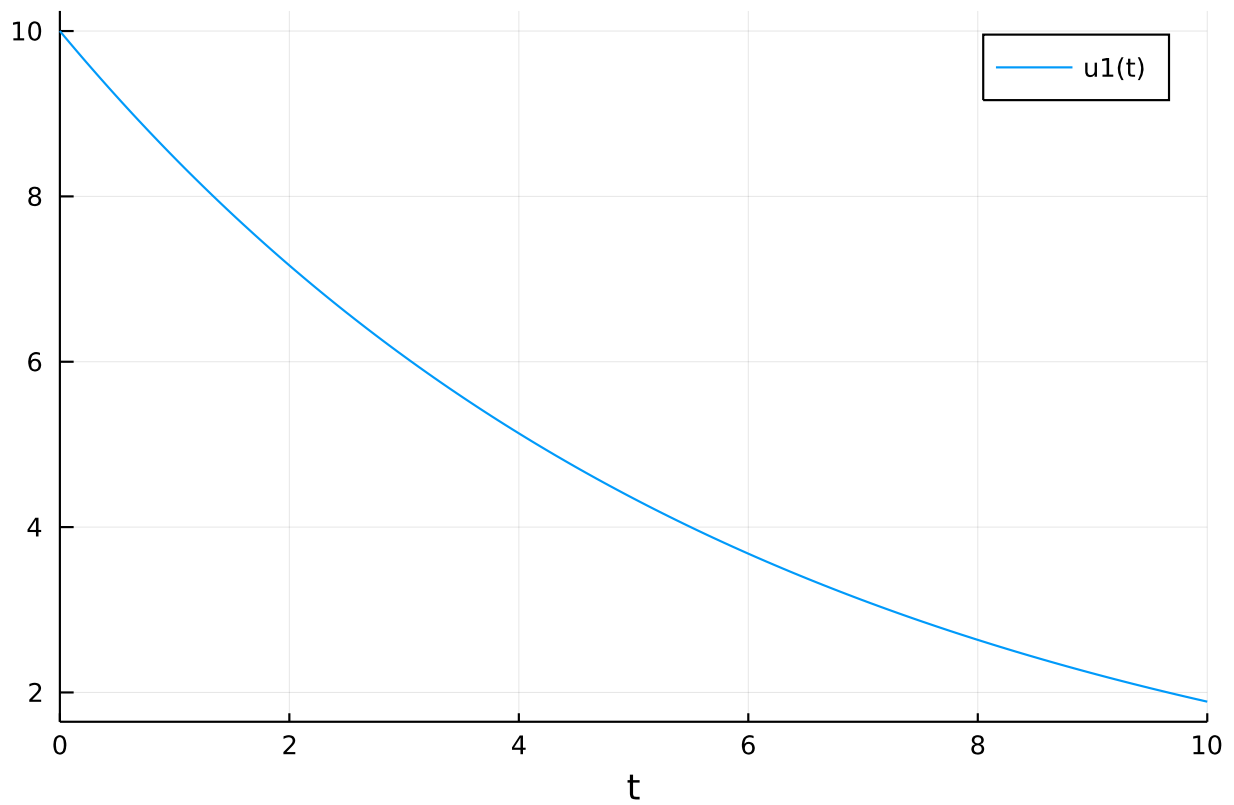
```
ODEProblem with uType Vector{Float64} and tType Float64. In-place: true
timespan: (0.0, 10.0)
u0: 1-element Vector{Float64}:
 10.0
```

```
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

These tutorials are a part of the SciMLTutorials.jl repository, found at: https://github.com/SciML/SciML
For more information on high-performance scientific machine learning, check out the SciML
Open Source Software Organization https://sciml.ai.

To locally run this tutorial, do the following commands:

```
using SciMLTutorials
SciMLTutorials.weave_file("tutorials/models","02-conditional_dosing.jmd")
```

Computer Information:

```
Julia Version 1.6.2
Commit 1b93d53fc4 (2021-07-14 15:36 UTC)
Platform Info:
  OS: Linux (x86_64-pc-linux-gnu)
  CPU: AMD EPYC 7502 32-Core Processor
  WORD_SIZE: 64
  LIBM: libopenlibm
  LLVM: libLLVM-11.0.1 (ORCJIT, znver2)
Environment:
  JULIA_DEPOT_PATH = /root/.cache/julia-buildkite-plugin/depots/a6029d3a-f78b-41ea-bc97
  JULIA_NUM_THREADS = 16
```

Package Information:

```
      Status `/var/lib/buildkite-agent/builds/1-amdci4-julia-csail-mit-edu/julialang/sc
  [479239e8] Catalyst v6.12.1
  [459566f4] DiffEqCallbacks v2.16.1
  [f3b72e0c] DiffEqDevTools v2.27.2
  [055956cb] DiffEqPhysics v3.9.0
  [0c46a032] DifferentialEquations v6.17.1
  [31c24e10] Distributions v0.24.18
  [587475ba] Flux v0.12.1
  [f6369f11] ForwardDiff v0.10.18
  [23fbe1c1] Latexify v0.15.5
  [961ee093] ModelingToolkit v5.17.3
  [2774e3e8] NLsolve v4.5.1
  [315f7962] NeuralPDE v3.10.1
  [429524aa] Optim v1.3.0
  [1dea7af3] OrdinaryDiffEq v5.56.0
  [91a5bcdd] Plots v1.15.2
  [731186ca] RecursiveArrayTools v2.11.4
  [30cb0354] SciMLTutorials v0.9.0
  [789caeaf] StochasticDiffEq v6.34.1
  [37e2e46d] LinearAlgebra
  [2f01184e] SparseArrays
```

And the full manifest:

```
     Status `/var/lib/buildkite-agent/builds/1-amdci4-julia-csail-mit-edu/julialang/so
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  [1520ce14] AbstractTrees v0.3.4
  [79e6a3ab] Adapt v3.3.0
  [ec485272] ArnoldiMethod v0.1.0
  [4fba245c] ArrayInterface v3.1.15
  [4c555306] ArrayLayouts v0.7.0
  [13072b0f] AxisAlgorithms v1.0.0
  [ab4f0b2a] BFloat16s v0.1.0
  [aae01518] BandedMatrices v0.16.9
  [764a87c0] BoundaryValueDiffEq v2.7.1
  [fa961155] CEnum v0.4.1
  [00ebfdb7] CSTParser v2.5.0
  [052768ef] CUDA v2.6.3
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  [082447d4] ChainRules v0.7.65
  [d360d2e6] ChainRulesCore v0.9.44
  [b630d9fa] CheapThreads v0.2.5
  [944b1d66] CodecZlib v0.7.0
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  [3da002f7] ColorTypes v0.11.0
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  [38540f10] CommonSolve v0.2.0
  [bbf7d656] CommonSubexpressions v0.3.0
  [34da2185] Compat v3.30.0
  [8f4d0f93] Conda v1.5.2
  [88cd18e8] ConsoleProgressMonitor v0.1.2
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  [a8cc5b0e] Crayons v4.0.4
  [8a292aeb] Cuba v2.2.0
  [667455a9] Cubature v1.5.1
  [9a962f9c] DataAPI v1.6.0
  [82cc6244] DataInterpolations v3.3.1
  [864edb3b] DataStructures v0.18.9
  [e2d170a0] DataValueInterfaces v1.0.0
  [bcd4f6db] DelayDiffEq v5.31.0
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  [5a0ffddc] DiffEqFinancial v2.4.0
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  [77a26b50] DiffEqNoiseProcess v5.7.3
```

```
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[7bc98958] Cubature_jll v1.0.4+0
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[2e619515] Expat_jll v2.2.10+0
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[f5851436] FFTW_jll v3.3.9+7
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[c5fb5394] Xorg_xtrans_jll v1.4.0+3
[8f1865be] ZeroMQ_jll v4.3.2+6
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[f638f0a6] libfdk_aac_jll v0.1.6+4
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[a9144af2] libsodium_jll v1.0.20+0
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[f43a241f] Downloads
```

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[4af54fe1] LazyArtifacts
[b27032c2] LibCURL
[76f85450] LibGit2
[8f399da3] Libdl
[37e2e46d] LinearAlgebra
[56ddb016] Logging
[d6f4376e] Markdown
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[ca575930] NetworkOptions
[44cfe95a] Pkg
[de0858da] Printf
[9abbd945] Profile
[3fa0cd96] REPL
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[ea8e919c] SHA
[9e88b42a] Serialization
[1a1011a3] SharedArrays
[6462fe0b] Sockets
[2f01184e] SparseArrays
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[a4e569a6] Tar
[8dfed614] Test
[cf7118a7] UUIDs
[4ec0a83e] Unicode
[e66e0078] CompilerSupportLibraries_jll
[deac9b47] LibCURL_jll
[29816b5a] LibSSH2_jll
[c8ffd9c3] MbedTLS_jll
[14a3606d] MozillaCACerts_jll
[4536629a] OpenBLAS_jll
[bea87d4a] SuiteSparse_jll
[83775a58] Zlib_jll
[8e850ede] nghttp2_jll
[3f19e933] p7zip_jll
```