

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.

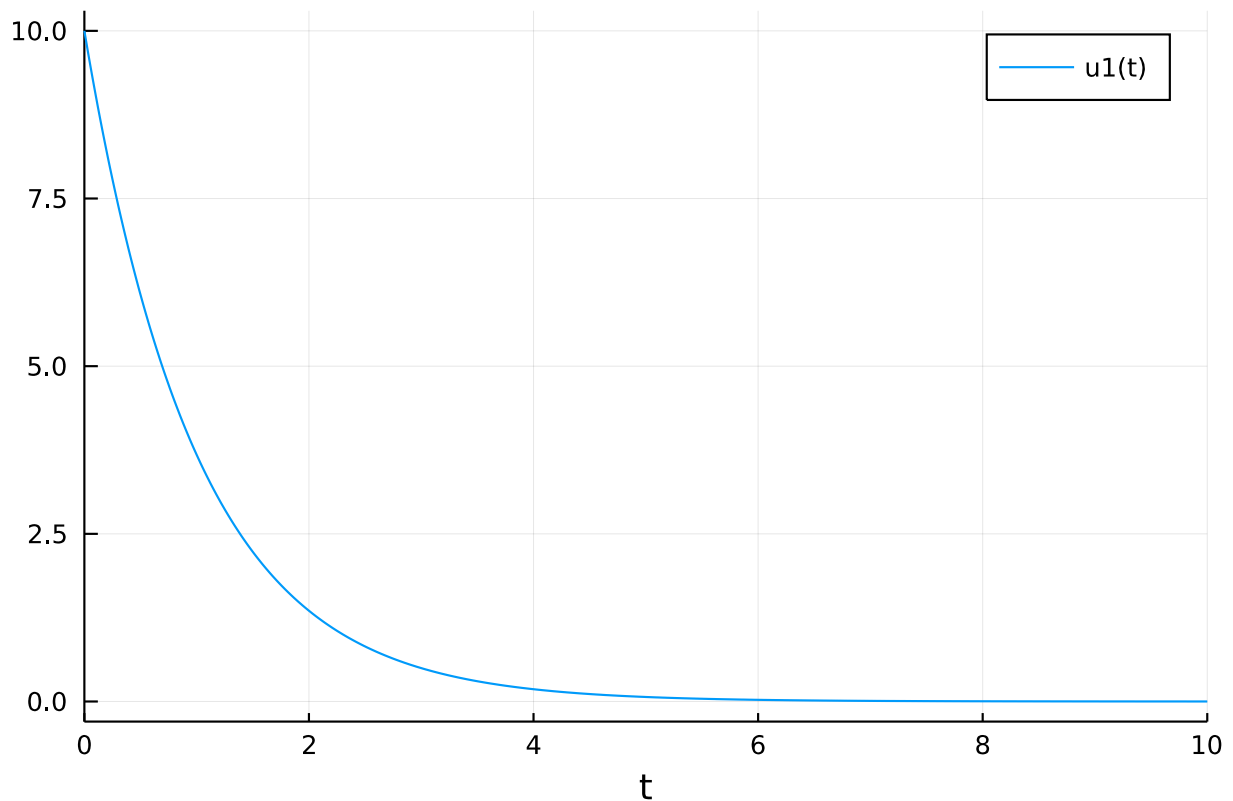
For our model, we will use the simple decay equation. We will write this in the in-place form to make it easy to extend to more complicated examples:

```
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 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.

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



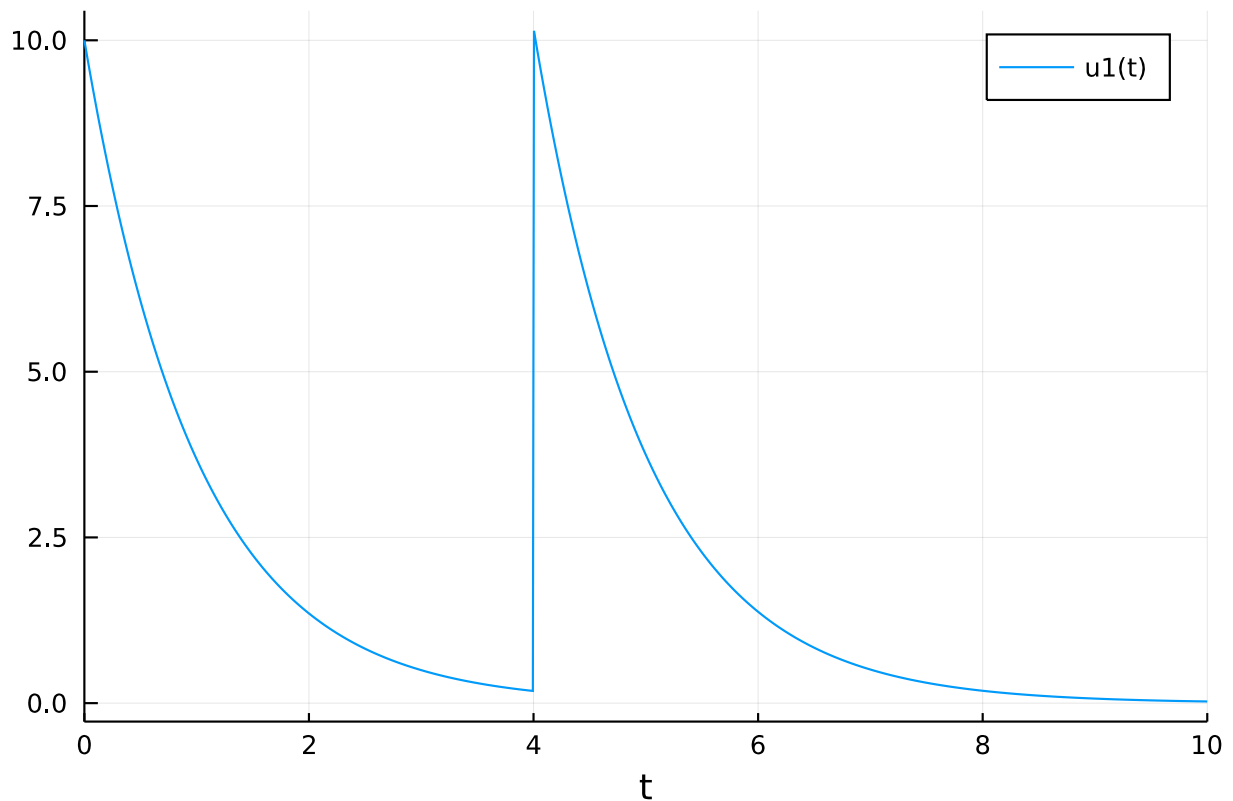
We see that at time $t=4$, the patient should receive a dose. Let's code up that event. We need to check at $t=4$ if the concentration $u[1]/4$ is <4 , and if so, add 10 to $u[1]$. We do this with the following:

```
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), typeof(Main.##WeaveSandBox#5436.affect!), typeof(DiffEqBase.INITIALIZE_DEFAULT), typeof(DiffEqBase.FINALIZE_DEFAULT)}(Main.##WeaveSandBox#5436.condition, Main.##WeaveSandBox#5436.affect!, DiffEqBase.INITIALIZE_DEFAULT, DiffEqBase.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(4.000000000000001))
```

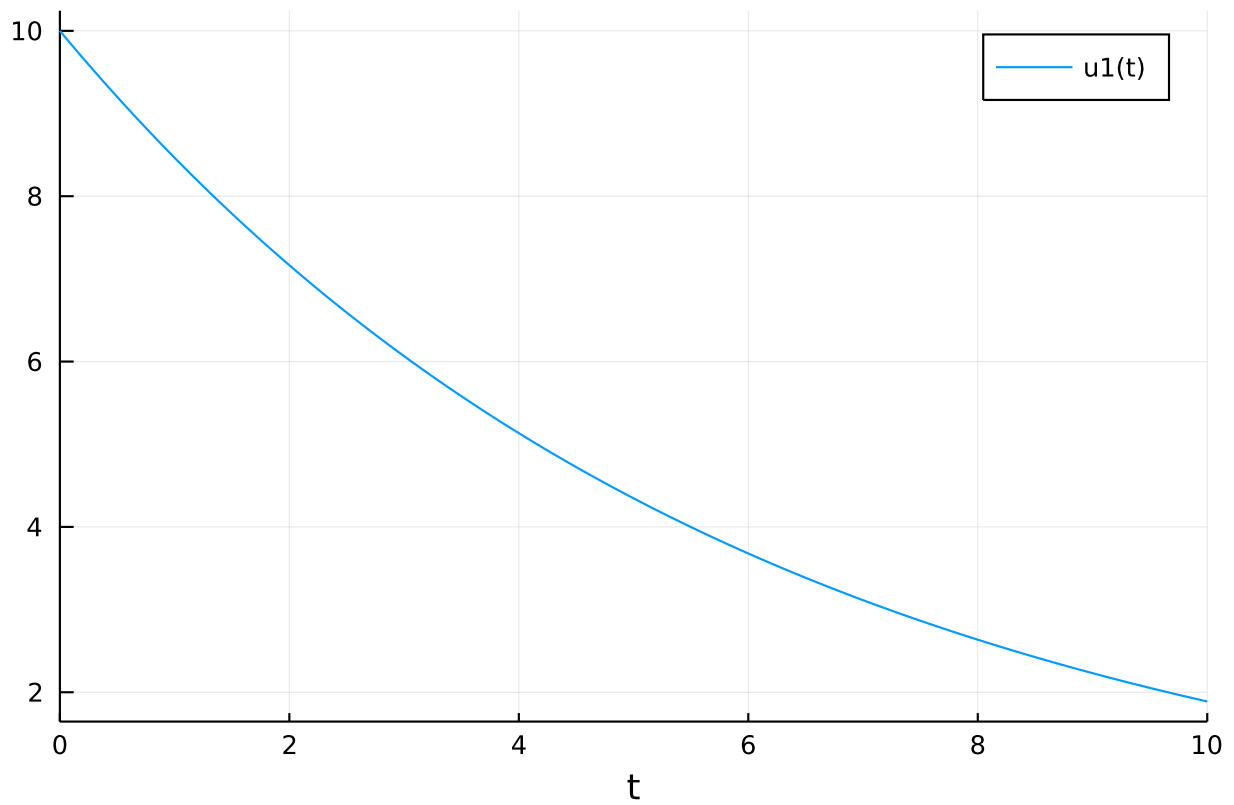
```
[0.18316389222022983]
[10.183163892210045]
```

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))
```

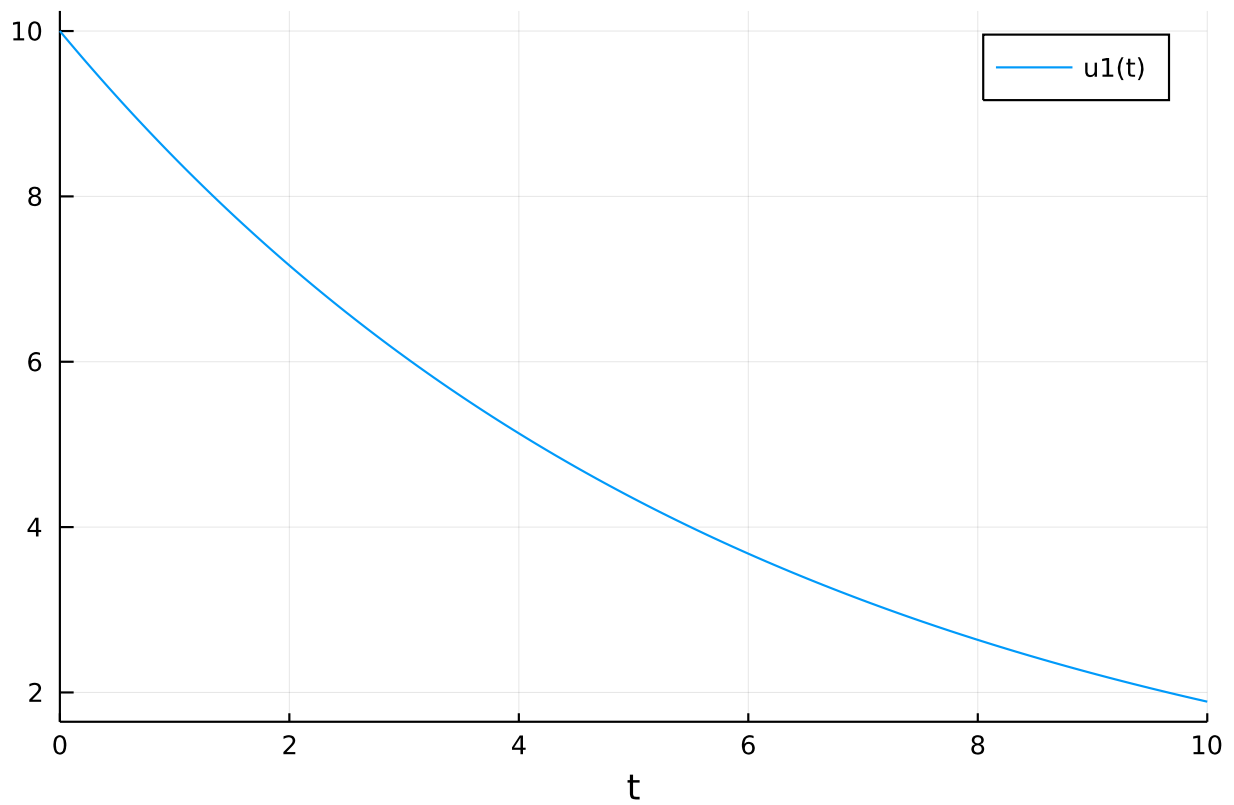
```
ODEProblem with uType Vector{Float64} and tType Float64. In-place: true
timespan: (0.0, 10.0)
u0: 1-element Vector{Float64}:
 10.0
```

```
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/SciMLTutorials.jl>
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-bc9f-4a1a1a1a1a1a
  JULIA_NUM_THREADS = 16
```

Package Information:

```
Status `~/var/lib/buildkite-agent/builds/7-amdci4-julia-csail-mit-edu/julia-lang/status.jl`
[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
[91a5bcd] 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/7-amdci4-julia-csail-mit-edu/julialang/s
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[621f4979] AbstractFFTs v1.0.1
[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
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[944b1d66] CodecZlib v0.7.0
[35d6a980] ColorSchemes v3.12.1
[3da002f7] ColorTypes v0.11.0
[5ae59095] Colors v0.12.8
[861a8166] Combinatorics v1.0.2
[a80b9123] CommonMark v0.8.1
[38540f10] CommonSolve v0.2.0
[bbf7d656] CommonSubexpressions v0.3.0
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[8f4d0f93] Conda v1.5.2
[88cd18e8] ConsoleProgressMonitor v0.1.2
[187b0558] ConstructionBase v1.2.1
[d38c429a] Contour v0.5.7
[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
[2b5f629d] DiffEqBase v6.62.2
[459566f4] DiffEqCallbacks v2.16.1
[f3b72e0c] DiffEqDevTools v2.27.2
[5a0ffddc] DiffEqFinancial v2.4.0
[aae7a2af] DiffEqFlux v1.37.0
[c894b116] DiffEqJump v6.14.2
[77a26b50] DiffEqNoiseProcess v5.7.3
```

[055956cb] DiffEqPhysics v3.9.0
[41bf760c] DiffEqSensitivity v6.45.0
[163ba53b] DiffResults v1.0.3
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[c619ae07] DimensionalPlotRecipes v1.2.0
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[d4d017d3] ExponentialUtilities v1.8.4
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[c87230d0] FFMPEG v0.4.0
[7a1cc6ca] FFTW v1.4.1
[7034ab61] FastBroadcast v0.1.8
[9aa1b823] FastClosures v0.3.2
[1a297f60] FillArrays v0.11.7
[6a86dc24] FiniteDiff v2.8.0
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[0c68f7d7] GPUArrays v6.4.1
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[5c1252a2] GeometryBasics v0.3.12
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[42e2da0e] Grisu v1.0.2
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[3bed1096] Cuba_jll v4.2.1+0
[7bc98958] Cubature_jll v1.0.4+0
[5ae413db] EarCut_jll v2.1.5+1
[2e619515] Expat_jll v2.2.10+0
[b22a6f82] FFMPEG_jll v4.3.1+4
[f5851436] FFTW_jll v3.3.9+7
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[0656b61e] GLFW_jll v3.3.4+0
[d2c73de3] GR_jll v0.57.2+0
[78b55507] Gettext_jll v0.21.0+0
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[e33a78d0] Hwloc_jll v2.4.1+0
[1d5cc7b8] IntelOpenMP_jll v2018.0.3+2
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[c1c5ebd0] LAME_jll v3.100.0+3
[dd4b983a] LZ0_jll v2.10.1+0
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[e9f186c6] Libffi_jll v3.2.2+0
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[94ce4f54] Libiconv_jll v1.16.1+0
[4b2f31a3] Libmount_jll v2.35.0+0
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[38a345b3] Libuuid_jll v2.36.0+0
[856f044c] MKL_jll v2021.1.1+1
[e7412a2a] Ogg_jll v1.3.4+2
[458c3c95] OpenSSL_jll v1.1.1+6

[efe28fd5] OpenSpecFun_jll v0.5.4+0
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 [fb77eaff] Sundials_jll v5.2.0+1
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 [02c8fc9c] XML2_jll v2.9.12+0
 [aed1982a] XSLT_jll v1.1.34+0
 [4f6342f7] Xorg_libX11_jll v1.6.9+4
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 [a51aa0fd] Xorg_libXi_jll v1.7.10+4
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 [35661453] Xorg_xkbcomp_jll v1.4.2+4
 [33bec58e] Xorg_xkeyboard_config_jll v2.27.0+4
 [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
 [b53b4c65] libpng_jll v1.6.38+0
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 [1270edf5] x264_jll v2020.7.14+2
 [dfaa095f] x265_jll v3.0.0+3
 [d8fb68d0] xkbcommon_jll v0.9.1+5
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 [56f22d72] Artifacts
 [2a0f44e3] Base64
 [ade2ca70] Dates
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 [8ba89e20] Distributed
 [f43a241f] Downloads

[7b1f6079] FileWatching
[9fa8497b] Future
[b77e0a4c] InteractiveUtils
[4af54fe1] LazyArtifacts
[b27032c2] LibCURL
[76f85450] LibGit2
[8f399da3] Libdl
[37e2e46d] LinearAlgebra
[56ddb016] Logging
[d6f4376e] Markdown
[a63ad114] Mmap
[ca575930] NetworkOptions
[44cfe95a] Pkg
[de0858da] Printf
[9abbd945] Profile
[3fa0cd96] REPL
[9a3f8284] Random
[ea8e919c] SHA
[9e88b42a] Serialization
[1a1011a3] SharedArrays
[6462fe0b] Sockets
[2f01184e] SparseArrays
[10745b16] Statistics
[4607b0f0] SuiteSparse
[fa267f1f] TOML
[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