Exploring the State of Machine Learning for Biological Data

Edmund Miller

July 26th, 2023

Introduction

About me

- Phd Candidate @ University of Texas at Dallas
- nf-core maintainer

About me

- Phd Candidate @ University of Texas at Dallas
- nf-core maintainer
- Been Machine Learning curious since around 2017

About me

- Phd Candidate @ University of Texas at Dallas
- nf-core maintainer
- Been Machine Learning curious since around 2017
- Never took Linear Algebra

About me

- Phd Candidate @ University of Texas at Dallas
- nf-core maintainer
- Been Machine Learning curious since around 2017
- Never took Linear Algebra
- I had some questions

About me

- Phd Candidate @ University of Texas at Dallas
- nf-core maintainer
- Been Machine Learning curious since around 2017
- Never took Linear Algebra
- I had some questions
- What are the trade offs of all these packages?

About me

- Phd Candidate @ University of Texas at Dallas
- nf-core maintainer
- Been Machine Learning curious since around 2017
- Never took Linear Algebra
- I had some questions
- What are the trade offs of all these packages?
- How do we load biological data? (Personal interest in genomics)

Exploring the State of Machine Learning for Biological Data

Be the PR you want to see in the repo

- Michael Lingelbach

Exploring the State of Machine Learning for Biological Data

Be the ~~PR~~ Talk you want to see ~~in the repo~~ at Juliacon

Goal of *most* Biologists

- We're not trying to create novel machine-learning models
- We're trying to apply these models in novel ways
- Then make biological inferences

Old overview

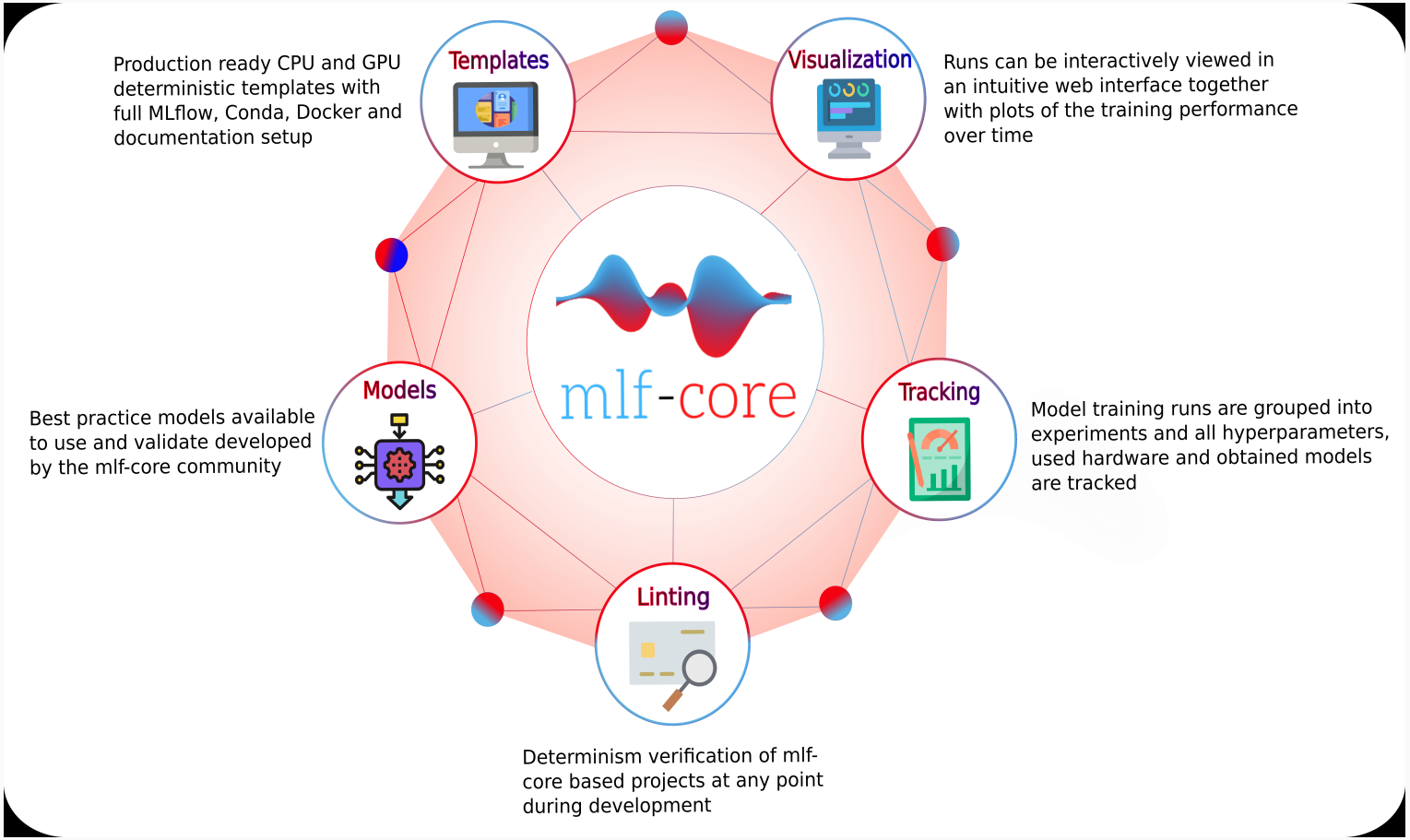
- Ability to call Python and R packages
- What are all of these different ML Packages?
- Loading biological file formats
- Some pretty basic toy examples

Then I had a thought...

Then I had a thought...

What if I reproduce some analyses and recount what I learned along the way?

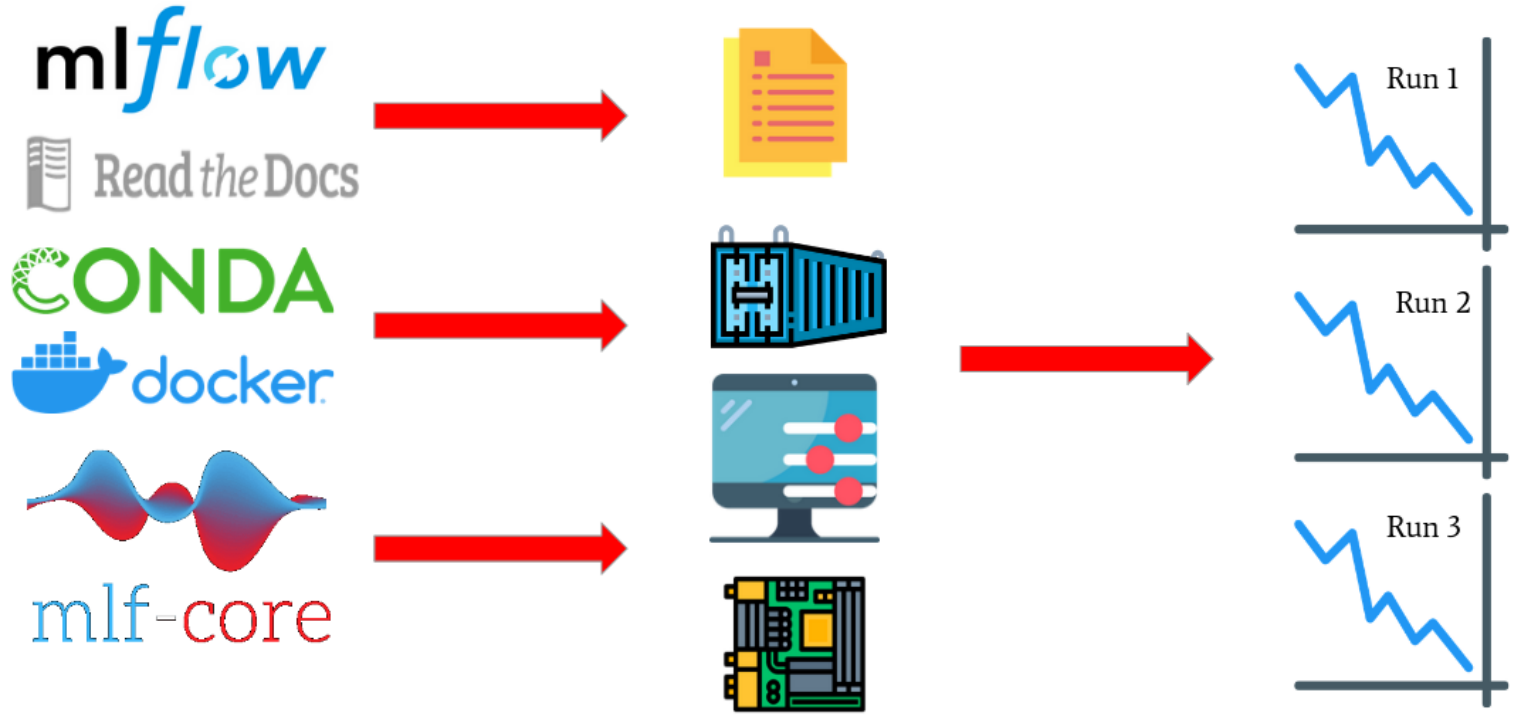
mlf-core - Overview



1

[1] https://doi.org/10.1093/bioinformatics/btad164

mlf-core - Summary



mlf-core - Concept

```
# Install mlf-core
$ pip install mlf-core

# Get an overview of all commands
$ mlf-core --help

# Check out all available templates
$ mlf-core list

# Get started and create your first project
$ mlf-core create
```

mlf-core - Why do we care about Reproducibility?

- why does reproducibility mater in science?
  - compared to selling ads, chatbots
- Lives are at stake

lcep

lcep - Overview

- Classifying cancerous liver samples from gene expression data.
- RNA-seq data
- Nice warm up, purpose was to demonstrate creating a python package using mlf-core, and using the package in a Nextflow pipeline
- Repo Link

lcep - Dataloading - mlf-core

```
def load_train_test_data(train_data, test_data):
    X_train, y_train, train_gene_names,
     ↪  train_sample_names =
     ↪  parse_tpm_table(train_data)

    # Convert to Numpy Arrays
    X_train_np = np.array(X_train)

    # Convert from Numpy Arrays to XGBoost Data
     ↪  Matrices
    dtrain = xgb.DMatrix(X_train_np,
     ↪  label=y_train)

    training_data = Dataset(X_train_np, y_train,
     ↪  dtrain, train_gene_names,
     ↪  train_sample_names)
```

lcep - Dataloading

```
train_url =
 ↪  "https://github.com/mlf-core/lcep/raw/master/data/t
test_url =
 ↪  "https://github.com/mlf-core/lcep/raw/master/data/t

train_data =
 ↪  DataFrame(CSV.File(download(train_url)))
test_data =
 ↪  DataFrame(CSV.File(download(test_url)))
```

- Note the lack of need to dance around with np arrays and XGBoost Data Matrices
  - The Julia XGBoost wrapper handles the conversion from DataFrames to DMatrix

lcep - Dataloading

Gene ID	Gene Name	0_SRR143622	1_bce80114-27
ENSG00000004975	missing	14.2893	18.7965
ENSG00000005339	missing	83.0387	78.4725
ENSG00000005884	missing	2.70558	11.0217
ENSG00000006451	missing	17.5549	34.9154

lcep - Data Cleaning - python

- Probably could have used pandas

```
def parse_tpm_table(input):
    X_train = []
    y_train = []
    gene_names = []
    sample_names = []
```

lcep - Data Cleaning - python

```
with open(input, "r") as file:
    all_runs_info =
     ↪  next(file).split("\n")[0].split("\t")[2:]
    for run_info in all_runs_info:
        split_info = run_info.split("_")
        y_train.append(int(split_info[0]))
        sample_names.append(split_info[1])
    for line in file:
        splitted =
         ↪  line.split("\n")[0].split("\t")
        X_train.append([float(x) for x in
         ↪  splitted[2:]])
        gene_names.append(splitted[:2])

X_train = [list(i) for i in zip(*X_train)]
```

lcep - Data Cleaning - Julia

```
function clean_data(input)
    # Drop any rows that are 0s
    input_zeros = input[findall(x -> x != 0,
    ↪  names(input)), :]
    # Drop Gene Name col
    input_id = input_zeros[!, Not(2)]
    # Flip the dataframe
    input_flip = rename(permutedims(input_id,
    ↪  "Gene ID"), "Gene ID" => :status)

    # The 1_s(cancer) and 0_s(normal) are the
    ↪  labels
    # Split status column by _ and take the first
    transform(input_flip, :status => ByRow(x ->
    ↪  parse(Float64, split(x, "_")[1])) =>
    ↪  :status)
end
```

lcep - Training

```
booster = xgb.train(param, training_data.DM,
 ↪  dict_args['max_epochs'],
 ↪  evals=[(test_data.DM, 'test')],
 ↪  evals_result=results)

test_predictions =
 ↪  np.round(booster.predict(test_data.DM))
```

```
train = (clean_train_data[:, 2:end],
 ↪  clean_train_data.status)
bst = xgboost(train; num_round=1000, param...)

test_predictions = predict(bst, clean_test_data)
```

GPUs

```
using CUDA
X = cu(randn(1000, 3))
y = randn(1000)

dm = DMatrix(X, y)
XGBoost.isgpu(dm)  # true

xgboost((X, y), num_rounds=10)  # no need to use
 ↪  `DMatrix`
```

- ageron Julia notebooks Template
- Automatically downloads the CUDA toolkit for you

sc-autoencoder

sc-autoencoder - Overview

- 3000 Peripheral blood mononuclear cells (PBMCs) from 10x Genomics
- This time however they started from `h5ad`
- However they used scanpy to load and clean the data

Dataloading - Attempt to replicate scanpy functionality in Julia

```
using Muon

pbmc3k_url =
↪  "https://raw.githubusercontent.com/chanzuckerberg/c
pmbc3k = readh5ad(download(pbmc3k_url))
```

- Muon is a part of scverse, the same group that wrote scanpy
- But it threw an error

```
ERROR: MethodError: no method matching
↪  read_dataframe(::HDF5.Dataset)
```

Hacking on a package

```
pkg> develop --local Muon
```

- Then there's a repo cloned at **dev/Muon**!
- And added to the Project.toml for tracking

Hacking on a package

```
pkg> develop --local Muon
```

- Then there's a repo cloned at **dev/Muon**!
- And added to the Project.toml for tracking
- You can do this in python but here it's Julia all the way down

Loading Data using PythonCall - CondaPkg.jl

```
julia> using CondaPkg
pkg> conda add_channel conda-forge
pkg> conda add scanpy python-igraph leidenalg
```

CondaPkg.toml

```
channels = ["conda-forge"]

[deps]
leidenalg = ""
scanpy = ""
python-igraph = ""
```

PythonCall and Pycall are different

- Doesn't have to support as much legacy
  - PythonCall supports Julia 1.6.1+ and Python 3.7+
  - PyCall supports Julia 0.7+ and Python 2.7+.
- Uses CondaPkg by default
- You can use them both at the same time if you needed to for some reason

Loading Data using PythonCall

```
using PythonCall

sc = pyimport("scanpy")

function preprocessing(adata)
    sc.pp.filter_cells(adata, min_genes=200)
    sc.pp.filter_genes(adata, min_cells=3)

    # Normalization and scaling:
    sc.pp.normalize_total(adata, target_sum=1e4)
    sc.pp.log1p(adata)
```

Loading Data using PythonCall

```
    # Identify highly-variable genes
    sc.pp.highly_variable_genes(adata,
     ↪  min_mean=0.0125, max_mean=3,
     ↪  min_disp=0.5, subset=true)
    sc.pp.scale(adata, zero_center=true,
     ↪  max_value=3)
    x = adata.X
    # We don't need Tensorflow because Julia is
     ↪  fast enough I think?
    # data =
     ↪  tf.data.Dataset.from_tensor_slices((x,
     ↪  x))
    x = pyconvert(Array{Float32}, x)

    return [x, x], x
end
```

TensorFlow Dataset Loading

```
data = tf.data.Dataset.from_tensor_slices((x, x))
```

- Realized once again there's no need to learn yet another library, can just use built-in Julia types

DataToolkit

- Conda doesn't work well on NixOS
- Exported the **x** Matrix

```
pkg> add DataToolkit
# }
(.)> init
(sc-autoencoder) data> add pbmc3k
 ↪  https://huggingface.co/datasets/emiller/pbmc3k/reso
```

DataToolkit

- Conda doesn't work well on NixOS
- Exported the `x` Matrix

```
pkg> add DataToolkit
# }
(.)> init
(sc-autoencoder) data> add pbmc3k
 ↪  https://huggingface.co/datasets/emiller/pbmc3k/reso
```

- Better practice would be to use the Julia loader

DataToolkit

```toml
[[pbmc3k]]
uuid = "2c0e014e-eea8-49e2-9916-6ab5d2df08b3"
description = "Preprocessed pmbc3k Single Cell
 ↪  dataset"

    [[pbmc3k.storage]]
    driver = "web"
    url =
     ↪  "https://huggingface.co/datasets/emiller/pbmc3k/

    [[pbmc3k.loader]]
    driver = "delim"
    delim = "\t"
    dtype = "Float32"
```

DataToolkit

```
using DataToolkit

dataset = d"pbmc3k"
```

DataToolkit - Want to learn more?

Robust data management made simple: Introducing DataToolkit

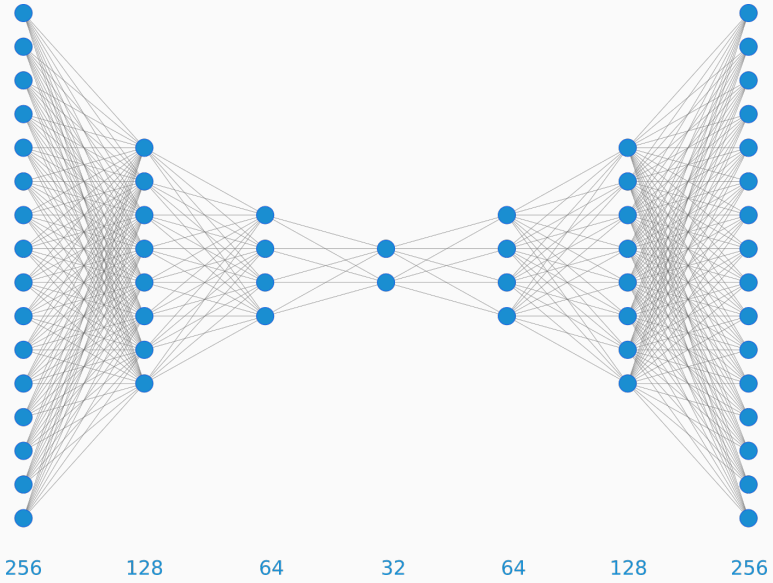
Timothy Chapman

Friday, 07-28, 16:00–16:30 (US/Eastern), 32-123

Flux

The *Elegant* Machine Learning Stack

Flux - Model



- Autoencoders are common in scRNA-seq data
  - Denoising of single cell data
  - predict perturbation responses
- mlf-core purpose was to show that non-deterministic operations can lead to significant differences in latent space embeddings

Flux - DataLoader

```
train_set = Flux.DataLoader((dataset, dataset),
↪  batchsize=256)
```

Flux - Experiment Setup

```
device = cpu # where will the calculations be
 ↪  performed?
L1, L2, L3 = 256, 128, 64 # layer dimensions
η = 0.01 # learning rate for ADAM optimization
 ↪  algorithm
batch_size = 100; # batch size for optimization
```

Autoencoders blog post by wildart

Flux - Build the Model

```
enc1 = Dense(d, L1, relu)
enc2 = Dense(L1, L2, relu)
enc3 = Dense(L2, L3, relu)
dec4 = Dense(L3, L2, relu)
dec5 = Dense(L2, L1, relu)
dec6 = Dense(L1, d)
model = Chain(enc1, enc2, enc3, dec4, dec5, dec6)
 ↪   |> device
```

Autoencoders blog post by wildart

Flux - Training

```
opt_state = Flux.setup(Adam(0.001), model)
for data in train_set
  # Unpack this element (for supervised
  ↪  training):
  input, label = data
  # Calculate the gradient of the objective
  # with respect to the parameters within the
  ↪  model:
  loss(A, B) = Flux.mae(model(A),B)
  grads = Flux.gradient(model) do m
      result = m(input)
      loss(result, label)
  end

  Flux.update!(opt_state, model, grads[1])
end
```

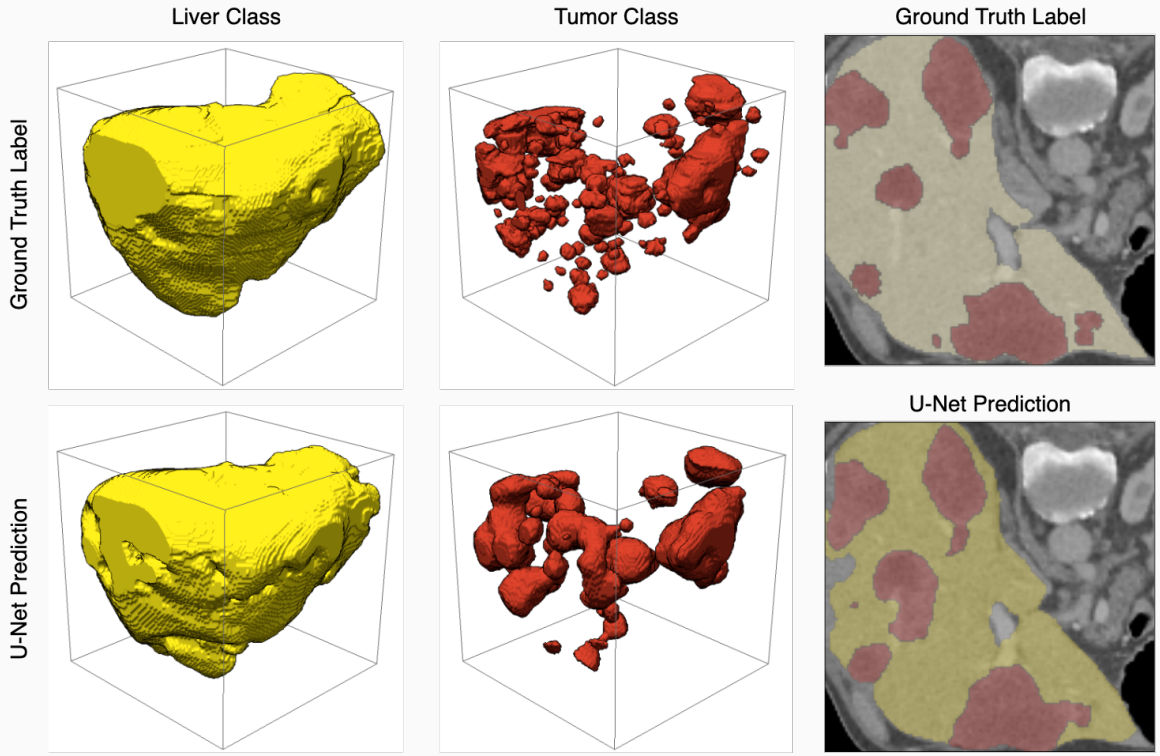
Flux - train!

```
opt_state = Flux.setup(Adam(0.001), model)

loss(A, B) = Flux.mae(model(A),B)

@withprogress Flux.train!(model, train_set,
 ↪  opt_state) do m, x, y
  loss(m(x), y)
end
```

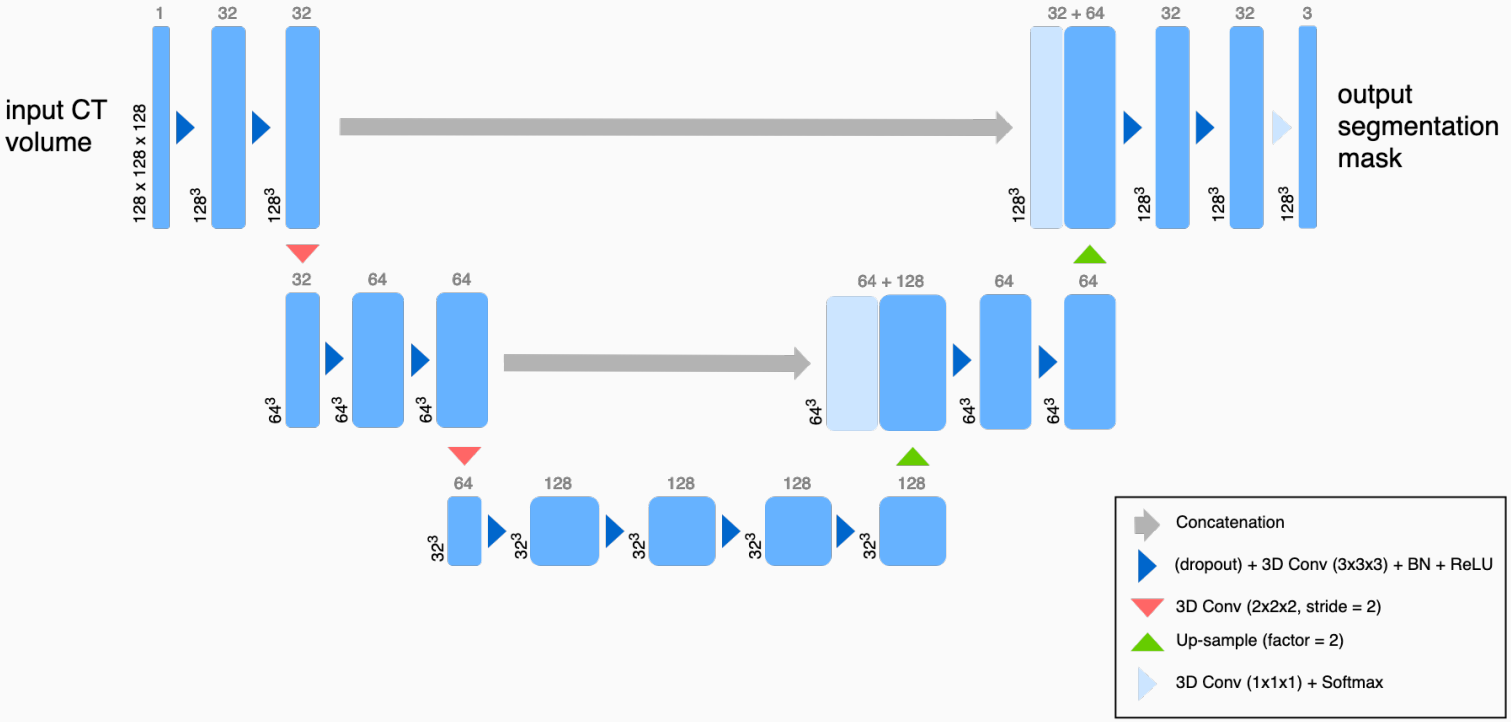
liver-ct-segmentation

liver-ct-segmentation - Overview

- Liver-tumor segmentation of computed tomography scans using a U-Net model.
- The data in this challenge contains abdomen CT scans with contrast enhancement for liver lesions.



liver-ct-segmentation - 3D U-Net architecture



liver-ct-segmentation - Dataset

The data set for LiTS was collected from 6 medical centres. The CT scans as well as the segmentations are provided as Nifti .nii files.

- Of course there's a package for that JuliaNeuroscience/NIfTI.jl (It's 9 years old!)

liver-ct-segmentation - model

- UNet · Julia Packages
  - Written in Flux

```
julia> u = Unet()
UNet:
  ConvDown(64, 64)
  ConvDown(128, 128)
  ConvDown(256, 256)
  ConvDown(512, 512)
  UNetConvBlock(1, 3)
  ...
  UNetConvBlock(1024, 1024)
  UNetUpBlock(1024, 512)
  ...
  UNetUpBlock(256, 64)
```

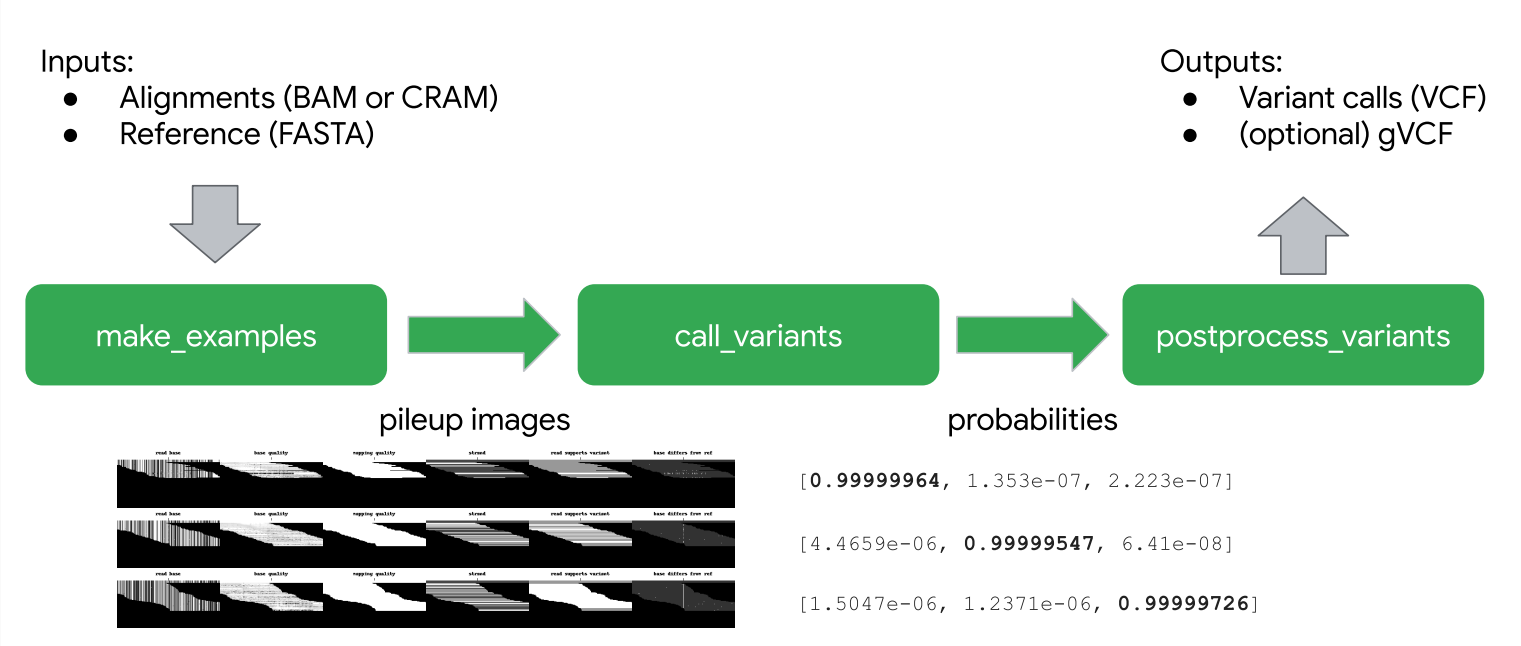
Conclusion

Things we touched upon along the way

- Simplicity of Dataloading
- Hacking on dependencies live
- Calling python packages from Julia
- DataToolkit
- Flux
- There’s plenty of packages

Things I didn’t get answers to

- What would loading up BAMs like Deepvariant look like?



Things I didn't get answers to

- What would FunctionLab/selene look like?
- More Determinism
  - `Lux.jl`?

Links

Slides

link.edmundmiller.dev