

Data Generation for PuMaS

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1 Introduction

This introduction to data generation for PuMaS will cover how to specify subjects and populations to use with PuMaS. You will learn how to read data, specify dosage regimens, covariates, observations, and generate populations to use with the software.

1.1 Installation

Because PuMaS is still unregistered, you will need to give the Git repository in order to add the package. To do this, use the command `]add https://github.com/UMCTM/PuMaS.jl`. Doing it this way, PuMaS and its dependencies will install automatically. If one cannot authenticate for this command (since the repository is currently private!), then first clone the repository how you please, use `]add path/to/PuMaS.jl`, then then do `]build PuMaS`. Using the build command will download and install the dependencies.

1.2 Subjects

PuMaS' unit of observation are subjects.

Each `Subject` is an individual composed of:

- `id`: an unique identifier
- `cvs`: covariates
- `obs`: observations
- `evs`: events

1.3 Population

A `Population` is a collection of subjects.

1.4 NMTRAN data format

The [NMTRAN schema](#) uses a single tabular representation to describe a Population

Consider a NMTRAN text file. We can read the data using the CSV package to read it, and the DataFrames package to work with the tabular representation.

Load the packages through using

```
using CSV, DataFrames, PuMaS
using DataFrames: head
```

We'll be working with an example NMTRAN data set in PuMaS

```
nmtran_data = example_nmtran_data("data1")
show(nmtran_data)
```

```
"C:\\Users\\Chris\\.julia\\dev\\PuMaS\\src\\...\\examples\\data1.csv"
```

We can read the text file using the CSV and DataFrames packages

```
data = DataFrame(CSV.File(nmtran_data)) # Make a DataFrame from the text file.
head(data) # Show the first six rows
```

	id	time	mdv	evid	dv	amt	sex	wt	etn
1	1	0.0	1	1	0.0	10000.0	1	51.6	1
2	1	0.0	0	0	1.2161	0.0	1	51.6	1
3	1	0.25	0	0	12.565	0.0	1	51.6	1
4	1	0.5	0	0	11.218	0.0	1	51.6	1
5	1	0.75	0	0	17.709	0.0	1	51.6	1
6	1	1.0	0	0	21.925	0.0	1	51.6	1

One can obtain a Population from a NMTRAN table through the `process_nmtran` function.

```
using PuMaS
@doc process_nmtran
```

```
process_nmtran(filename, cvs=[], dvs=[:dv])
process_nmtran(data, cvs=[], dvs=[:dv])
```

Import NMTRAN-formatted data.

- `cvs` covariates specified by either names or column numbers
- `dvs` dependent variables specified by either names or column numbers

Based on the documentation for `process_nmtran` it takes a `DataFrame`, an optional list of covariates, and a list of dependent variables which `[:dv]` as the default value. In our case, we want to specify `sex` and `wt` as covariates.

```
population = process_nmtran(data, [:sex, :wt])
show(population)
```

```
Population
Subjects: 40
Covariates: sex, wt
Observables: dv
```

Just like that we have read NMTRAN data and ready it for analysis using PuMaS.

1.5 Interactive

PuMaS offers an alternative to the NMTRAN schema is to generate data

Let us simulate the some values for glucose as out observations

```
using Distributions
distribution = Normal(5.5, 1.5)
show(distribution)

Distributions.Normal{Float64}(μ=5.5, σ=1.5)

glucose = rand(distribution, 5) # Five draws from the distribution

obs = DataFrame(time = 0:8:32, # Makes a sequence starting at 0 by 8 until 32
                glucose = glucose)
head(obs)
```

	time	glucose
1	0	3.97181
2	8	3.24783
3	16	5.50259
4	24	5.60595
5	32	4.53703

Next we generate the covariates for our subject

```
cvs = (sex = "male", age = 25)
show(cvs)

(sex = "male", age = 25)
```

Lastly, we can generate a series of dosage events through a `DosageRegimen`

The first argument is an amount. `addl` specifies additional dosages and `ii` the interdose interval.

```
evs = DosageRegimen(5, addl = 3, ii = 8u"hr")
head(evs.data)
```

	time	cmt	amt	evid	ii	addl	rate	ss
1	0.0	1	5.0	1	8.0	3	0.0	0

This regimen specifies 4 dosage events of five milligrams starting at `time = 0` with an interdose interval of 8 hours

We can now fully specify a subject bringing the covariates, observations, and regimen

```
subject = Subject(cvs = cvs, obs = obs, evs = evs)
show(subject)
```

```
Subject
Events: 4
Observations: 5
Covariates:
  sex: male
  age: 25
Observables: glucose
```

We can inspect the observations through

```

for obs in subject.observations
  println(obs)
end

```

```

Observation
  time of measurement = 0.0
  compartment = 1
  measurements
    glucose = 3.9718062445016495

```

```

Observation
  time of measurement = 8.0
  compartment = 1
  measurements
    glucose = 3.2478313302706123

```

```

Observation
  time of measurement = 16.0
  compartment = 1
  measurements
    glucose = 5.502585187693575

```

```

Observation
  time of measurement = 24.0
  compartment = 1
  measurements
    glucose = 5.605948455664502

```

```

Observation
  time of measurement = 32.0
  compartment = 1
  measurements
    glucose = 4.537029542501786

```

Likewise for the dosage events

```

for evs in subject.events
  println(evs)
end

```

```

Dose event
  dose amount = 5.0
  dose time = 0.0
  compartment = 1
  instantaneous
  interdose interval = 8.0
  infusion start time = 0.0

```

```

Dose event
  dose amount = 5.0
  dose time = 8.0
  compartment = 1
  instantaneous
  interdose interval = 8.0
  infusion start time = 8.0

```

```

Dose event
  dose amount = 5.0
  dose time = 16.0
  compartment = 1

```

```

instantaneous
interdose interval = 8.0
infusion start time = 16.0

```

```

Dose event
dose amount = 5.0
dose time = 24.0
compartment = 1
instantaneous
interdose interval = 8.0
infusion start time = 24.0

```

We can build more complex regimens by passing a collection of arguments

```

regimens = DosageRegimen([0.005u"g", 0.0025u"g"], time = [0, 90u"minute"])
head(regimens.data)

```

	time	cmt	amt	evid	ii	addl	rate	ss
1	0.0	1	5.0	1	0.0	0	0.0	0
2	1.5	1	2.5	1	0.0	0	0.0	0

Given that we have specified the amount in grams, these are converted to milligrams

Likewise, for time which was specified in minutes, these are converted to hours.

```

subject2 = Subject(id = 2,
                    evs = regimens)
show(subject2)

```

```

Subject
Events: 2
Observations: 0
Covariates:

```

This Subject does not have any observations or covariates.

The dosage regimen can be inspected through

```

for evs in subject2.events
    println(evs)
end

```

```

Dose event
dose amount = 5.0
dose time = 0.0
compartment = 1
instantaneous
interdose interval = 0.0
infusion start time = 0.0

```

```

Dose event
dose amount = 2.5
dose time = 1.5
compartment = 1
instantaneous
interdose interval = 0.0
infusion start time = 1.5

```

One may construct a Population by passing a collection of subjects

```

@doc Population

```

```
Population(::AbstractVector{<:Subject})
```

A Population is a set of Subjects. It can be instanced passing a collection or Subject.

There will be six subjects

```
ids = 1:6 # There will be 6 subject 1, 2, 3, 4, 5, 6
```

We will simulate the covariates for these six subjects

```
choose_sex_age() = (sex = rand(["male", "female"]),  
                    age = rand(21:25))
```

choose_sex_age will randomly choose a sex and an age between 21-25 years

We can make a list with covariates for six subjects through a list comprehension

```
cvs = [ choose_sex_age() for i in 1:6 ]  
show(cvs)
```

```
NamedTuple{(:sex, :age),Tuple{String,Int64}}[(sex = "female", age = 22), (s  
ex = "female", age = 25), (sex = "male", age = 21), (sex = "male", age = 25  
) , (sex = "male", age = 23), (sex = "male", age = 23)]
```

We can generate a table with the time and observations for the dependent variable for each of the six subjects

```
obs = [ DataFrame(time = 0:4:8, dv = rand(3)) for id in 1:6 ]  
head.(obs[1:2])
```

```
2-element Array{DataFrames.DataFrame,1}:
```

```
3×2 DataFrames.DataFrame
```

```
Row   time   dv  
      Int64  Float64
```

```
1      0      0.792888  
2      4      0.754819  
3      8      0.207981
```

```
3×2 DataFrames.DataFrame
```

```
Row   time   dv  
      Int64  Float64
```

```
1      0      0.440787  
2      4      0.364492  
3      8      0.131323
```

We will assign one regimen to the first three and another to the last three

```
regimen1 = DosageRegimen(15, addl = 3, ii = 4)  
regimen2 = DosageRegimen(10, addl = 4, ii = 3)  
regimens = vcat(repeat([regimen1], 3),  
                 repeat([regimen2], 3))
```

We can now generate the six subjects using a

```
subjects = Subject[]  
for (id, cvs, evs) in zip(ids, cvs, regimens)  
    push!(subjects, Subject(id = id, cvs = cvs, evs = evs))  
end  
show(subjects)
```

```

PuMaS.Subject[Subject
  Events: 4
  Observations: 0
  Covariates:
    sex: female
    age: 22
, Subject
  Events: 4
  Observations: 0
  Covariates:
    sex: female
    age: 25
, Subject
  Events: 4
  Observations: 0
  Covariates:
    sex: male
    age: 21
, Subject
  Events: 5
  Observations: 0
  Covariates:
    sex: male
    age: 25
, Subject
  Events: 5
  Observations: 0
  Covariates:
    sex: male
    age: 23
, Subject
  Events: 5
  Observations: 0
  Covariates:
    sex: male
    age: 23
]

```

Lastly, we can make a population with comprised of these subjects

```

population = Population(subjects)
show(population)

```

```

Population
  Subjects: 6
  Covariates: sex, age

```

```

for subject in population
  println(subject)
end

```

```

Subject
  Events: 4
  Observations: 0
  Covariates:
    sex: female
    age: 22

```

```

Subject
  Events: 4

```

Observations: 0
Covariates:
sex: female
age: 25

Subject
Events: 4
Observations: 0
Covariates:
sex: male
age: 21

Subject
Events: 5
Observations: 0
Covariates:
sex: male
age: 25

Subject
Events: 5
Observations: 0
Covariates:
sex: male
age: 23

Subject
Events: 5
Observations: 0
Covariates:
sex: male
age: 23