

Package ‘RLescalation’

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Type Package

Title Optimal Dose Escalation Using Deep Reinforcement Learning

Version 1.0.2

Description An implementation to compute an optimal dose escalation rule using deep reinforcement learning in phase I oncology trials (Matsuura et al. (2023) <[doi:10.1080/10543406.2023.2170402](https://doi.org/10.1080/10543406.2023.2170402)>). The dose escalation rule can directly optimize the percentages of correct selection (PCS) of the maximum tolerated dose (MTD).

URL <https://github.com/MatsuuraKentaro/RLescalation>

BugReports <https://github.com/MatsuuraKentaro/RLescalation/issues>

VignetteBuilder knitr

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Collate 'timer.R' 'train_algo.R' 'utils.R' 'escalation_rule.R'
'rl_dnn_config.R' 'rl_config_set.R' 'compute_rl_scenarios.R'
'learn_escalation_rule.R' 'setup_python.R' 'zzz.R'
'simulate_one_trial.R'

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clean_python_settings	<i>Clean the Python Virtual Environment</i>
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Description

Clean the Python Virtual Environment

Usage

```
clean_python_settings(envname = "r-RLescalation")
```

Arguments

envname Python virtual environment name.

compute_rl_scenarios	<i>Compute DLT Probability Scenarios for Reinforcement Learning</i>
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Description

Compute the scenarios described in Sect. 2.2 of the original paper.

Usage

```
compute_rl_scenarios(J, target, epsilon, delta, lower = 0.1, upper = 0.8)
```

Arguments

J	A positive integer value. The number of doses.
target	A positive numeric value. The target DLT probability.
epsilon	A positive numeric value. The acceptable range of target DLT probabilities is defined as [target - epsilon, target + epsilon].
delta	A positive numeric value. The unacceptable ranges of target DLT probabilities are defined as [0, target - delta] and [target + delta, 1].
lower	A positive numeric value. Values lower than lower are clipped. Default is 0.1, which is modified from Sect. 2.2 of the original paper.
upper	A positive numeric value. Values higher than upper are clipped. Default is 0.8.

Value

A named list of three elements: - prob: a list of DLT probability scenarios - MTD: a list of true MTD indices (Note that -1 means "no MTD") - weight: a vector of weights for each scenario

Examples

```
scenarios <- compute_rl_scenarios(J = 6, target = 0.25, epsilon = 0.04, delta = 0.1)
print(scenarios)
```

EscalationRule	<i>EscalationRule Class</i>
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Description

This class represents an escalation rule that generates a next escalation.

Public fields

policy The RLlib policy that is a Python object.
 dir Directory path of the escalation rule (policy).
 dirpath Full path to the directory of the escalation rule.
 created_at Created time of this object.
 info Information when learning the escalation rule.
 input Inputs for learning the escalation rule.
 log The log of scores during the learning of the escalation rule.
 checkpoints The integer vector of iteration counts for checkpoints.
 checkpoints_paths The paths to the directories where each checkpoint is stored.

Methods

Public methods:

- [EscalationRule\\$new\(\)](#)
- [EscalationRule\\$opt_action\(\)](#)
- [EscalationRule\\$resume_learning\(\)](#)
- [EscalationRule\\$set_info\(\)](#)
- [EscalationRule\\$print\(\)](#)
- [EscalationRule\\$clone\(\)](#)

Method `new()`: Create a new `EscalationRule` object.

Usage:

```
EscalationRule$new(dir = "latest", base_dir = "escalation_rules")
```

Arguments:

`dir` A character value. A directory name or path where an escalation rule is outputted. By default, the latest escalation rule is searched in 'base_dir'.

`base_dir` A character value. A directory path that is used as the parent directory if the 'dir' argument is a directory name and is not used otherwise.

Method `opt_action()`: Compute optimal action probabilities using the obtained escalation rule for data of N and DLT.

Usage:

```
EscalationRule$opt_action(current_dose, data_Ns, data_DLTs)
```

Arguments:

`current_dose` An integer value. This is the current dose index, which is within 1:J.

`data_Ns` A numeric vector. The cumulative number of patients assigned to each dose in your clinical trial.

`data_DLTs` A numeric vector. The cumulative number of DLTs corresponding to each dose for the 'data_Ns' argument.

Returns: A character that represents the optimal action. One of the followings: down, stay, up, MTD_1, ..., MTD_J, no_MTD

Method `resume_learning()`: Resume learning the escalation rule. This function updates the original `EscalationRule` object.

Usage:

```
EscalationRule$resume_learning(iter)
```

Arguments:

`iter` A number of additional iterations.

Returns: An updated [EscalationRule](#) object.

Method `set_info()`: Set information when learning the escalation rule.

Usage:

```
EscalationRule$set_info(info, input, log, checkpoints)
```

Arguments:

info Information when learning the escalation rule.

input Inputs for learning the escalation rule.

log The log of scores during the learning of the escalation rule.

checkpoints The paths to the directories where each checkpoint is stored.

Method print(): Print function for EscalationRule object

Usage:

```
EscalationRule$print()
```

Method clone(): The objects of this class are cloneable with this method.

Usage:

```
EscalationRule$clone(deep = FALSE)
```

Arguments:

deep Whether to make a deep clone.

learn_escalation_rule *Build an Optimal Dose Escalation Rule using Reinforcement Learning*

Description

Build an Optimal Dose Escalation Rule using Reinforcement Learning

Usage

```
learn_escalation_rule(
  J,
  target,
  epsilon,
  delta,
  N_total,
  N_cohort,
  seed = NULL,
  rl_config = rl_config_set(),
  rl_scenarios = NULL,
  output_dir = format(Sys.time(), "%Y%m%d_%H%M%S"),
  output_base_dir = "escalation_rules",
  checkpoint_dir = "checkpoints"
)
```

Arguments

J	A positive integer value. The number of doses.
target	A positive numeric value. The target DLT probability.
epsilon	A positive numeric value. The acceptable range of target DLT probabilities is defined as [target - epsilon, target + epsilon].
delta	A positive numeric value. The unacceptable ranges of target DLT probabilities are defined as [0, target - delta] and [target + delta, 1].
N_total	A positive integer value. The total number of patients.
N_cohort	A positive integer value. The number of patients for each cohort.
seed	An integer value. Random seed for reinforcement learning.
rl_config	A list. Other settings for reinforcement learning. See rl_config_set for details.
rl_scenarios	A list. Scenarios used for reinforcement learning. Default is NULL (use scenarios in the Sect. 2.2 of the original paper). See compute_rl_scenarios for details.
output_dir	A character value. Directory name or path to store the built escalation rule. Default is the current datetime.
output_base_dir	A character value. Parent directory path where the built escalation rule will be stored. Valid only if 'output_dir' does not contain '/'. Default is "escalation_rules".
checkpoint_dir	A character value. Parent directory path to save checkpoints. It enables you to resume learning from that point onwards. Default is "checkpoints".

Value

An [EscalationRule](#) object.

Examples

```
library(RLescalation)

# We obtain an optimal dose escalation rule by executing `learn_escalation_rule()`.
## Not run:
escalation_rule <- learn_escalation_rule(
  J = 6, target = 0.25, epsilon = 0.04, delta = 0.1,
  N_total = 36, N_cohort = 3, seed = 123,
  rl_config = rl_config_set(iter = 1000)
)
## End(Not run)
```

rl_config_set	<i>Configuration of Reinforcement Learning</i>
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Description

Mainly settings for the arguments of the training() function. Not compatible with the new API stack introduced in Ray 2.10.0.

Usage

```
rl_config_set(
    iter = 1000L,
    save_start_iter = NULL,
    save_every_iter = NULL,
    cores = 4L,
    gamma = 1,
    lr = 5e-05,
    train_batch_size = 10000L,
    model = rl_dnn_config(),
    sgd_minibatch_size = 200L,
    num_sgd_iter = 20L,
    ...
)
```

Arguments

iter	A positive integer value. Number of iterations.
save_start_iter, save_every_iter	An integer value. Save checkpoints every 'save_every_iter' iterations starting from 'save_start_iter' or later.
cores	A positive integer value. Number of CPU cores used for learning.
gamma	A positive numeric value. Discount factor of the Markov decision process. Default is 1.0 (not discount).
lr	A positive numeric value. Learning rate (default 5e-5). You can set a learning schedule instead of a learning rate.
train_batch_size	A positive integer value. Training batch size. Deprecated on the new API stack.
model	A list. Arguments passed into the policy model. See rl_dnn_config for details.
sgd_minibatch_size	A positive integer value. Total SGD batch size across all devices for SGD. Deprecated on the new API stack.
num_sgd_iter	A positive integer value. Number of SGD iterations in each outer loop.
...	Other settings for training(). See the arguments of the training() function in the source code of RLlib. https://github.com/ray-project/ray/blob/master/rllib/algorithms/algorithm_config.py https://github.com/ray-project/ray/blob/master/rllib/algorithms/ppo/ppo.py

Value

A list of reinforcement learning configuration parameters

Examples

```
## Not run:
escalation_rule <- learn_escalation_rule(
  J = 6, target = 0.25, epsilon = 0.04, delta = 0.1,
  N_total = 36, N_cohort = 3, seed = 123,
  # We change `iter` to 200 and `cores` for reinforcement learning to 2
  rl_config = rl_config_set(iter = 200, cores = 2)
)
## End(Not run)
```

rl_dnn_config

DNN Configuration for Reinforcement Learning

Description

DNN (deep neural network) configuration for reinforcement learning. For detail, see Section 3.1 of the original paper.

Usage

```
rl_dnn_config(
  fcnet_hiddens = c(256L, 256L),
  fcnet_activation = c("relu", "tanh", "swish", "silu", "linear"),
  ...
)
```

Arguments

fcnet_hiddens A positive integer vector. Numbers of units of the intermediate layers.

fcnet_activation

A character value specifying the activation function. Possible values are "ReLU" (default), "tanh", "Swish" (or "SiLU"), or "linear".

...

Other configurations. See source code of RLLib. <https://github.com/ray-project/ray/blob/master/rllib/models>

Value

A list of DNN configuration parameters

Examples

```
## Not run:
escalation_rule <- learn_escalation_rule(
  J = 6, target = 0.25, epsilon = 0.04, delta = 0.1,
  N_total = 36, N_cohort = 3, seed = 123,
  rl_config = rl_config_set(
    iter = 1000,
    # We change the DNN model
    model = rl_dnn_config(fcnet_hiddens = c(512L, 512L), fcnet_activation = "tanh")
  )
)
## End(Not run)
```

setup_python

*Setting up a Python Virtual Environment***Description**

Setting up a Python virtual environment for the Ray package, which includes the RLLib library for reinforcement learning.

Usage

```
setup_python(envname = "r-RLescalation")
```

Arguments

envname Python virtual environment name.

simulate_one_trial

*Simulate One Trial Using an Obtained Optimal Dose Escalation Rule***Description**

Simulate One Trial Using an Obtained Optimal Dose Escalation Rule

Usage

```
simulate_one_trial(escalation_rule, prob_true, seed = NULL)
```

Arguments

escalation_rule An object of class [EscalationRule](#) specifying an obtained optimal dose escalation rule.

prob_true A numeric vector specifying the true DLT probabilities.

seed An integer value. Random seed for data generation in this trial.

Value

A data frame which contains the cohort ID, the assigned dose, the number of assigned patients, the number of DLTs, and the recommended action including down, stay, up, MTD_1, ..., MTD_J, no_MTD, and fail to determine MTD.

Examples

```
library(RLescalation)

## Not run:
escalation_rule <- learn_escalation_rule(
  J = 6, target = 0.25, epsilon = 0.04, delta = 0.1,
  N_total = 36, N_cohort = 3, seed = 123,
  rl_config = rl_config_set(iter = 1000)
)
## End(Not run)

prob_true <- c(0.03, 0.13, 0.17, 0.19, 0.26, 0.31)

# Simulate one trial using the obtained `escalation_rule`
## Not run:
sim_one <- simulate_one_trial(escalation_rule, prob_true, seed = 123)
## End(Not run)
```

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