# **Python Anesthesia Simulator**

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## SRC.PYTHON\_ANESTHESIA\_SIMULATOR PACKAGE

## 1.1 Submodules

## 1.2 src.python\_anesthesia\_simulator.simulator module

```
class Patient(patient_characteristic: list, co_base: float = 6.5, map_base: float = 90, model_propo: str =

'Schnider', model_remi: str = 'Minto', ts: float = 1, hill_param: Optional[list] = None,

random_PK: bool = False, random_PD: bool = False, co_update: bool = False, save_data_bool:

bool = True)
```

Bases: object

Define a Patient class able to simulate Anesthesia process.

#### **Parameters**

#### Patient characteristic: list

Patient\_characteristic = [age (yr), height(cm), weight(kg), gender(0: female, 1: male)]

## co\_base

[float, optional] Initial cardiac output. The default is 6.5L/min.

## map\_base

[float, optional] Initial Mean Arterial Pressure. The default is 90mmHg.

#### model propo

[str, optional] Name of the Propofol PK Model. The default is 'Schnider'.

## model\_remi

[str, optional] Name of the Remifentanil PK Model. The default is 'Minto'.

ts

[float, optional] Samplling time (s). The default is 1.

#### BIS param

[list, optional] Parameter of the BIS model (Propo Remi interaction) list [C50p\_BIS, C50r\_BIS, gamma\_BIS, beta\_BIS, E0\_BIS, Emax\_BIS]. The default is None.

## random\_PK

[bool, optional] Add uncertainties in the Propodfol and Remifentanil PK models. The default is False.

## random\_PD

[bool, optional] Add uncertainties in the BIS PD model. The default is False.

#### co update

[bool, optional] Turn on the option to update PK parameters thanks to the CO value. The default is False.

## save\_data\_bool

[bool, optional] Save all interns variable at each sampling time in a data frame. The default is True.

#### **Attributes**

#### age

[float] Age of the patient (yr).

## height

[float] Height of the patient (cm).

#### weight

[float] Weight of the patient (kg).

## gender

[bool] 0 for female, 1 for male.

#### co base

[float] Initial cardiac output (L/min).

#### map base

[float] Initial mean arterial pressure (mmHg).

#### ts

[float] Sampling time (s).

#### model\_propo

[str] Name of the propofol PK model.

### model remi

[str] Name of the remifentanil PK model.

#### hill\_param

[list] Parameter of the BIS model (Propo Remi interaction) list [C50p\_BIS, C50r\_BIS, gamma\_BIS, beta\_BIS, E0\_BIS, Emax\_BIS].

## random PK

[bool] Add uncertainties in the Propodfol and Remifentanil PK models.

### random PD

[bool] Add uncertainties in the BIS PD model.

#### co update

[bool] Turn on the option to update PK parameters thanks to the CO value.

#### save\_data\_bool

[bool] Save all interns variable at each sampling time in a data frame.

#### lbm

[float] Lean body mass (kg).

#### propo\_pk

[CompartmentModel] 6-compartments model for Propofol.

#### remi\_pl

[CompartmentModel] 5-comparements model for Remifentanil.

#### nore pk

[CompartmentModel] 1-comparements model for Norepinephrine.

## bis\_pd

[BIS\_model] Surface-response model for bis computation.

## tol\_pd

[TOL\_model] Hierarchical model for TOL computation.

## hemo\_pd

[Hemo\_PD\_model] Hemodynamic model for CO and MAP computation.

#### data

[pd.DataFrame] Dataframe containing all the intern variables at each sampling time.

#### bis

[float] Bispectral index (%).

#### tol

[float] Tolerance of laryngospie probability (0-1).

co

[float] Cardiac output (L/min).

#### man

[float] Mean arterial pressure (mmHg).

## blood\_volume

[float] Blood volume (L).

#### **Methods**

blood_loss([fluid_rate])	Actualize the patient parameters to mimic blood loss.
<pre>find_bis_equilibrium_with_ratio(bis_target)</pre>	Find the input of Propofol and Remifentanil to meet
	the BIS target at the equilibrium with a fixed ratio
	between drugs rates.
<pre>find_equilibrium(bis_target, tol_target,)</pre>	Find the input to meet the targeted outputs at the equi-
	librium.
full_sim([u_propo, u_remi, u_nore])	Simulate the patient model with the given inputs.
<pre>init_dataframe()</pre>	Initilize the dataframe variable.
<pre>initialized_at_given_input([u_propo,])</pre>	Initialize the patient Simulator at the given input as
	an equilibrium point.
<pre>initialized_at_maintenance(bis_target,)</pre>	Initialize the patient model at the equilibrium point
	for the given output value.
one_step([u_propo, u_remi, u_nore,])	Simulate one step time of the patient.
<pre>save_data([inputs])</pre>	Save all current intern variable as a new line in
	self.dataframe.

## $blood_loss(fluid_rate: float = 0)$

Actualize the patient parameters to mimic blood loss.

#### **Parameters**

## fluid\_rate

[float, optional] Fluid rates from blood volume (mL/min), negative is bleeding while positive is a transfusion. The default is 0.

## Returns

None.

 $find\_bis\_equilibrium\_with\_ratio(bis\_target: float, rp\_ratio: float = 2) \rightarrow tuple[float, float]$ 

Find the input of Propofol and Remifentanil to meet the BIS target at the equilibrium with a fixed ratio between drugs rates.

Solve the optimization problem:

$$J = (bis - bis_{target})^2$$

Where bis is the BIS computed from the pharmacodynamic model. And with the constraints:

$$u_{propo} = u_{remi} * rp_{ratio}$$

$$A_{propo} x_{propo} + B_{propo} u_{propo} = 0$$

$$A_{remi} x_{remi} + B_{remi} u_{remi} = 0$$

## **Parameters**

## bis\_target

[float] BIS target (%).

## rp\_ratio

[float] remifentanil over propofol rates ratio. The default is 2.

#### Returns

## $u\_propo$

[float:] Propofol infusion rate (mg/s).

#### u remi

[float:] Remifentanil infusion rate (µg/s).

**find\_equilibrium**( $bis\_target$ : float,  $tol\_target$ : float,  $map\_target$ : float)  $\rightarrow$  tuple[float, float] Find the input to meet the targeted outputs at the equilibrium.

Solve the optimization problem to find the equilibrium input for BIS - TOL:

$$min_{C_{p,es},C_{r,es}} \frac{||BIS_{target} - BIS||^2}{100^2} + ||TOL_{target} - TOL||^2$$

Then compute the concentration of Noradrenaline to meet the MAP target.

Finally, compute the input of Propofol, Remifentanil and Noradrenaline to meet the targeted concentration.

#### **Parameters**

#### bis\_target

[float] BIS target (%).

## tol\_target

[float] TOL target ([0, 1]).

## map\_target:float

MAP target (mmHg).

## Returns

#### u\_propo

[float:] Propofol infusion rate (mg/s).

## u\_remi

[float:] Remifentanil infusion rate ( $\mu$ g/s).

#### u nore

[float:] Norepinephrine infusion rate (µg/s).

```
full_sim(u\_propo: Optional[list] = None, u\_remi: Optional[list] = None, u\_nore: Optional[list] = None) Simulate the patient model with the given inputs.
```

#### **Parameters**

#### u\_propo

[list] Propofol infusion rate (mg/s).

#### u remi

[list] Remifentanil infusion rate (µg/s).

#### u nore

[list] Norepinephrine infusion rate (µg/s).

#### Returns

## pandas.Dataframes

Dataframe with all the data.

#### init\_dataframe()

Initilize the dataframe variable.

```
initialized_at\_given\_input(u\_propo: float = 0, u\_remi: float = 0, u\_nore: float = 0)
```

Initialize the patient Simulator at the given input as an equilibrium point.

For each drug, the equilibrium state is computed from the input. Then this state is used to intitialze each drug pharmacokinetic model.

#### **Parameters**

## u\_propo

[float, optional] Propofol infusion rate (mg/s). The default is 0.

## u remi

[float, optional] Remifentanil infusion rate ( $\mu g/s$ ). The default is 0.

#### u nore

[float, optional] Norepinephrine infusion rate (µg/s). The default is 0.

### Returns

None.

 $\label{loss_target:float} \textbf{initialized\_at\_maintenance}(\textit{bis\_target: float}, \textit{tol\_target: float}, \textit{map\_target: float}) \rightarrow \text{tuple}[\text{float}, \text{float}]$ 

Initialize the patient model at the equilibrium point for the given output value.

#### **Parameters**

```
bis_target
[float] BIS target (%).

rass_target
[float] RASS target ([0, -5]).

map_target:float
MAP target (mmHg).

Returns

u_propo
```

[float:] Propofol infusion rate (mg/s).

```
u remi
                 [float:] Remifentanil infusion rate (µg/s).
              u nore
                 [float:] Norepinephrine infusion rate (µg/s).
one\_step(u\_propo: float = 0, u\_remi: float = 0, u\_nore: float = 0, blood\_rate: float = 0, dist: list = [0, 0, 0],
           noise: bool = True) \rightarrow tuple[float, float, float]
     Simulate one step time of the patient.
          Parameters
              u propo
                 [float, optional] Propofol infusion rate (mg/s). The default is 0.
              u remi
                 [float, optional] Remifentanil infusion rate (\mug/s). The default is 0.
              u nore
                 [float, optional] Norepinephrine infusion rate (\mu g/s). The default is 0.
              blood_rate
                 [float, optional] Fluid rates from blood volume (mL/min), negative is bleeding while posi-
                 tive is a transfusion. The default is 0.
                 [list, optional] Disturbance vector on [BIS (%), MAP (mmHg), CO (L/min)]. The default
                 is [0]*3.
              noise
                 [bool, optional] bool to add measurement noise on the outputs. The default is True.
          Returns
              bis
                 [float] Bispectral index(%).
                 [float] Cardiac output (L/min).
                 [float] Mean arterial pressure (mmHg).
              tol
                 [float] Tolerance of Laringoscopy index (0-1).
```

Save all current intern variable as a new line in self.dataframe.

## 1.3 src.python\_anesthesia\_simulator.pk\_models module

Bases: object

 $save\_data(inputs: list = [0, 0, 0])$ 

PKmodel class modelize the PK model of propofol or remifentanil drug. Simulate the drug distribution in the body.

Use a 6 compartement model for propofol, a 5 compartement model for remifentanil, and a 1 compartement model for norepinephrine. The model is a LTI model. The state vector is the concentration of the drug in each compartement.

## **Parameters**

## Patient\_characteristic: list

Patient characteristic = [age (yr), height(cm), weight(kg), gender(0: female, 1: male)]

#### lbm

[float] lean body mass index.

#### drug

[str] can be "Propofol", "Remifentanil" or "Norepinephrine".

#### model

[str, optional] Could be "Schnider" [1], "Marsh\_initial"[2], "Marsh\_modified"[3], "Shuttler"[4] or "Eleveld"[5\_] for Propofol. "Minto"[6], "Eleveld"[7] for Remifentanil. only "Beloeil"[8] for Norepinephrine. The default is "Minto" for Remifentanil and "Schnider" for Propofol.

ts

[float, optional] Sampling time, in s. The default is 1.

## random

[bool, optional] bool to introduce uncertainties in the model. The default is False.

 $\mathbf{x}$ 

[list, optional] Initial concentration of the compartement model. The default is np.ones([4, 1])\*1e-4.

## opiate

[bool, optional] For Elelevd model for propofol, specify if their is a co-administration of opiate (Remifentantil) in the same time. The default is True.

#### measurement

[str, optional] For Elelevd model for propofol, specify the measuremnt place for blood concentration. Can be either 'arterial' or 'venous'. The default is 'arterial'.

#### References

```
[1], [2], [3], [4], [5], [6], [7], [8]
```

#### **Attributes**

ts

[float] Sampling time, in s.

#### drug

[str] can be "Propofol", "Remifentanil" or "Norepinephrine".

#### A init

[list] Initial value of the matrix A.

## B init

[list] Initial value of the matrix B.

v1

[float] Volume of the first compartement.

## continuous\_sys

[control.StateSpace] Continuous state space model.

#### discrete sys

[control.StateSpace] Discrete state space model.

X

[list] State vector.

y

[list] Output vector (hypnotic effect site concentration).

#### **Methods**

full_sim(u)	Simulate PK model with a given input.
one_step(u)	Simulate one step of PK model.
update_param_CO(CO_ratio)	Update PK coefficient with a linear function of Car-
	diac output value.
update_param_blood_loss(v_ratio)	Update PK coefficient to mimic a blood loss.

## **full\_sim**(u: list) $\rightarrow list$

Simulate PK model with a given input.

#### **Parameters**

u

[list] Infusion rate (mg/s for Propofol,  $\mu$ g/s for Remifentanil and Norepinephrine).

#### Returns

## numpy array

List of the states value during the simulation. ( $\mu g/mL$  for Propofol and ng/mL for Remifentanil and Norepinephrine).

$$one\_step(u: float) \rightarrow list$$

Simulate one step of PK model.

$$x^+ = Ax + Bu$$

## **Parameters**

u

[float] Infusion rate (mg/s for Propofol,  $\mu$ g/s for Remifentanil).

#### Returns

## numpy array

Actual effect site concentration ( $\mu g/mL$  for Propofol and ng/mL for Remifentaniland Nore-pinephrine).

## update\_param\_CO(CO\_ratio: float)

Update PK coefficient with a linear function of Cardiac output value.

#### **Parameters**

 $\mathbf{CO}$ 

[float] Ratio of Current CO relatively to initial CO.

## Returns

None.

## update\_param\_blood\_loss(v\_ratio: float)

Update PK coefficient to mimic a blood loss.

Update the blodd volume compartment

#### **Parameters**

#### v ratio

[float] blood volume as a fraction of init volume, 1 mean no loss, 0 mean 100% loss.

#### Returns

None.

## 1.4 src.python\_anesthesia\_simulator.pd\_models module

 $\textbf{class BIS\_model}(hill\_model: str = 'Bouillon', hill\_param: Optional[list] = None, random: bool = False)$ 

Bases: object

Surface Response model to link Propofol and Remifentanil blood concentration to BIS.

equation:

$$BIS = E0 + Emax * \frac{U^{\gamma}}{1 + U^{\gamma}}$$

$$U = \frac{U_p + U_r}{1 - \beta\theta + \beta\theta^2}$$

$$U_p = \frac{C_{p,es}}{C_{p,50}}$$

$$U_r = \frac{C_{r,es}}{C_{r,50}}$$

$$\theta = \frac{U_p}{U_r + U_p}$$

## **Parameters**

## hill\_model

[str, optional] Only 'Bouillon' [9] is available. Ignored if hill\_param is specified.

#### hill param

[list, optional] Parameter of the Hill model (Propo Remi interaction) list [c50p\_BIS, c50r\_BIS, gamma\_BIS, beta\_BIS, E0\_BIS, Emax\_BIS]:

- c50p\_BIS : Concentration at half effect for propofol effect on BIS (μg/mL)
- c50r\_BIS : Concentration at half effect for remifentanil effect on BIS (ng/mL)
- gamma\_BIS : slope coefficient for the BIS model,
- beta\_BIS : interaction coefficient for the BIS model,
- E0\_BIS: initial BIS,
- Emax\_BIS: max effect of the drugs on BIS.

The default is None.

#### random

[bool, optional] Add uncertainties in the parameters. Ignored if Hill\_cruv is specified. The default is False.

ts

[float, optional] Sampling time, in s. The default is 1.

## References

[9]

#### Attributes

c50p

[float] Concentration at half effect for propofol effect on BIS (µg/mL).

#### c50r

[float] Concentration at half effect for remifentanil effect on BIS (ng/mL).

#### gamma

[float] slope coefficient for the BIS model.

#### beta

[float] interaction coefficient for the BIS model.

**E0** 

[float] initial BIS.

#### **Emax**

[float] max effect of the drugs on BIS.

## hill\_param

[list] Parameter of the Hill model (Propo Remi interaction) list [c50p\_BIS, c50r\_BIS, gamma\_BIS, beta\_BIS, E0\_BIS, Emax\_BIS]

## c50p\_init

[float] Initial value of c50p, used for blood loss modelling.

## **Methods**

compute_bis(c_es_propo, c_es_remi)	Compute BIS function from Propofol and Remifen-
	tanil effect site concentration.
<pre>inverse_hill(BIS[, c_es_remi])</pre>	Compute Propofol effect site concentration from BIS
	and Remifentanil Effect site concentration.
plot_surface()	Plot the 3D-Hill surface of the BIS related to Propofol
	and Remifentanil effect site concentration.
update_param_blood_loss(v_ratio)	Update PK coefficient to mimic a blood loss.

**compute\_bis**( $c\_es\_propo: float, c\_es\_remi: float) \rightarrow float$ 

Compute BIS function from Propofol and Remifentanil effect site concentration.

## **Parameters**

cep

[float] Propofol effect site concentration µg/mL.

cer

[float] Remifentanil effect site concentration ng/mL

#### Returns

#### BIS

[float] Bis value.

**inverse\_hill**(*BIS: float, c\_es\_remi: float* = 0)  $\rightarrow$  float

Compute Propofol effect site concentration from BIS and Remifentanil Effect site concentration.

#### **Parameters**

#### BIS

[float] BIS value.

cer

[float, optional] Effect site Remifentanil concentration (ng/mL). The default is 0.

## Returns

cep

[float] Effect site Propofol concentration (µg/mL).

## plot\_surface()

Plot the 3D-Hill surface of the BIS related to Propofol and Remifentanil effect site concentration.

## update\_param\_blood\_loss(v\_ratio: float)

Update PK coefficient to mimic a blood loss.

Update the c50p parameters thanks to the blood volume ratio.

## **Parameters**

#### v loss

[float] blood volume as a fraction of init volume, 1 mean no loss, 0 mean 100% loss.

## Returns

None.

class Hemo\_PD\_model(nore\_param: Optional[list] = None, propo\_param: Optional[list] = None, remi\_param: Optional[list] = None, random: bool = False,  $co_base$ : float = 6.5,  $map_base$ : float = 90)

Bases: object

Modelize the effect of Propofol, Remifentanil, Norepinephrine on Mean Arterial Pressure and Cardiac Output.

Use the addition of sigmoid curve to model the effect of each drugs on MAP and CO. The following articles are used to define the parameters of the model:

- Norepinephrine to MAP: [10]
- Noepinephrine to CO: [11]
- Propofol to MAP: [12]
- Propofol to CO: [13]
- Remifentanil to MAP: [14]
- Remifentanil to CO: [15]

#### **Parameters**

#### nore\_param

[list, optional] List of hill curve parameters for Norepinephrine action [Emax\_map, c50\_map, gamma\_map, Emax\_co, c50\_co, gamma\_co]. The default is None.

#### propo param

[list, optional] List of hill curve parameters for Propofol action [emax\_SAP, emax\_DAP, c50\_map\_1, c50\_map\_2, gamma\_map\_1, gamma\_map\_2, Emax\_co, c50\_co, gamma\_co]. The default is None.

## remi\_param

[list, optional] List of hill curve parameters for Relifentanil action [Emax\_map, c50\_map, gamma\_map, Emax\_co, c50\_co, gamma\_co]. The default is None.

#### random

[bool, optional] Add uncertainties in the parameters. The default is False.

## co\_base: float, optional

Baseline Cardiac output (L/min). The default is 6.5 L/min.

### map\_base: float, optional

Baseline mean arterial pressure (mmHg). The default is 90mmHg.

#### References

## [10], [11], [12], [13], [14], [15]

#### **Attributes**

#### co base

[float] Baseline cardiac output.

## map\_base

[float] Baseline mean arterial pressure.

### emax\_nore\_map

[float] Maximal effect of Norepinephrine on MAP.

## c50\_nore\_map

[float] Concentration of Norepinephrine that produce half of the maximal effect on MAP.

## gamma\_nore\_map

[float] Slope of the sigmoid curve for Norepinephrine effect on MAP.

## emax\_nore\_co

[float] Maximal effect of Norepinephrine on CO.

## c50\_nore\_co

[float] Concentration of Norepinephrine that produce half of the maximal effect on CO.

#### gamma\_nore\_co

[float] Slope of the sigmoid curve for Norepinephrine effect on CO.

## emax\_propo\_SAP

[float] Maximal effect of Propofol on SAP.

## emax\_propo\_DAP

[float] Maximal effect of Propofol on DAP.

#### emax\_propo\_co

[float] Maximal effect of Propofol on CO.

## c50\_propo\_map\_1

[float] Concentration of Propofol that produce half of the maximal effect on MAP.

## c50\_propo\_map\_2

[float] Concentration of Propofol that produce half of the maximal effect on MAP.

## gamma\_propo\_map\_1

[float] Slope of the sigmoid curve for Propofol effect on MAP.

## gamma\_propo\_map\_2

[float] Slope of the sigmoid curve for Propofol effect on MAP.

## c50\_propo\_co

[float] Concentration of Propofol that produce half of the maximal effect on CO.

#### gamma propo co

[float] Slope of the sigmoid curve for Propofol effect on CO.

## emax\_remi\_map

[float] Maximal effect of Remifentanil on MAP.

#### emax remi co

[float] Maximal effect of Remifentanil on CO.

#### c50\_remi\_map

[float] Concentration of Remifentanil that produce half of the maximal effect on MAP.

#### gamma remi map

[float] Slope of the sigmoid curve for Remifentanil effect on MAP.

## c50\_remi\_co

[float] Concentration of Remifentanil that produce half of the maximal effect on CO.

#### gamma\_remi\_co

[float] Slope of the sigmoid curve for Remifentanil effect on CO.

#### man

[float] Mean arterial pressure.

co

[float] Cardiac output.

## **Methods**

compute\_hemo(c\_es\_propo, c\_es\_remi, c\_es\_nore) Compute current MAP and CO using addition of hill curv, one for each drugs.

 $\textbf{compute\_hemo}(c\_\textit{es\_propo}: \textit{list}, c\_\textit{es\_remi}: \textit{float}, c\_\textit{es\_nore}: \textit{float}) \rightarrow \text{tuple}[\text{float}, \text{float}]$ 

Compute current MAP and CO using addition of hill curv, one for each drugs.

## **Parameters**

#### c\_es\_propo

[list] Propofol concentration on both hemodynamic effect site concentration µg/mL.

#### c es remi

[float] Remifentanil hemodynamic effect site concentration µg/mL.

#### c es nore

[float] Norepinephrine hemodynamic effect site concentration µg/mL.

## Returns

## map

[float] Mean arterial pressure (mmHg), without blood loss.

co

[float] Cardiac output (L/min), without blood loss.

 ${\bf class} \ \ {\bf TOL\_model}(model: \ str = 'Bouillon', model\_param: \ Optional[list] = None, \ random: \ bool = False)$ 

Bases: object

Hierarchical model to link druf effect site concentration to Tolerance of Laringoscopy.

The equation are:

$$\begin{aligned} postopioid &= preopioid * \left(1 - \frac{C_{r,es}^{\gamma_r}}{C_{r,es}^{\gamma_r} + (C_{r,50}preopioid)^{\gamma_r}}\right) \\ TOL &= \frac{C_{p,es}^{\gamma_p}}{C_{p,es}^{\gamma_p} + (C_{p,50}postopioid)^{\gamma_p}} \end{aligned}$$

#### **Parameters**

#### model

[str, optional] Only 'Bouillon'[9] is available. Ignored if model\_param is specified. The default is 'Bouillon'.

### model\_param

[list, optional] Model parameters, model\_param = [c50p, c50p, gammaP, gammaR, Preopioid intensity]. The default is None.

#### random

[bool, optional] Add uncertainties in the parameters. Ignored if model\_param is specified. The default is False.

#### References

[9]

## Attributes

c50p

[float] Concentration at half effect for propofol effect on BIS ( $\mu g/mL$ ).

c50r

[float] Concentration at half effect for remifentanil effect on BIS (ng/mL).

#### gamma\_p

[float] Slope of the Hill function for propofol effect on TOL.

## gamma\_r

[float] Slope of the Hill function for remifentanil effect on TOL.

#### pre intensity

[float] Preopioid intensity.

## **Methods**

compute_tol(c_es_propo, c_es_remi)	Return TOL from Propofol and Remifentanil effect
	site concentration.
plot_surface()	Plot the 3D-Hill surface of the BIS related to Propofol
	and Remifentanil effect site concentration.

**compute\_tol**( $c\_es\_propo: float, c\_es\_remi: float) \rightarrow float$ 

Return TOL from Propofol and Remifentanil effect site concentration.

Compute the output of the Hirarchical model to predict TOL from Propofol and Remifentanil effect site concentration. TOL = 1 mean very relaxed and will tolerate laryngoscopie while TOL = 0 mean fully awake and will not tolerate.

#### **Parameters**

cep

[float] Propofol effect site concentration µg/mL.

cer

[float] Remifentanil effect site concentration ng/mL

#### Returns

TOL

[float] TOL value.

## plot\_surface()

Plot the 3D-Hill surface of the BIS related to Propofol and Remifentanil effect site concentration.

fsig(x, c50, gam)

## 1.5 src.python\_anesthesia\_simulator.disturbances module

compute\_disturbances(time: float, dist\_profil: str = 'realistic',  $start\_step$ : float = 600,  $end\_step$ : float = 1200)  $\rightarrow$  list

Give the value of the distubance profil for a given time.

### **Parameters**

time

[float] Time: in seconde.

## dist\_profil

[str, optional] disturbance profil, can be: 'realistic', 'simple', 'step' or "null". The default is 'realistic'.

#### start step

[float, optional] start time of the step distuebance (seconds). The default is 600s.

### end\_step

[float, optional] End time of the step distuebance (seconds). The default is 1200s.

## Returns

list

dist\_bis, dist\_map, dist\_co: respectively the additive disturbance to add to the BIS, MAP and CO signals.

## 1.6 src.python\_anesthesia\_simulator.metrics module

**compute\_control\_metrics**(time: list, bis: list, phase: str = 'maintenance',  $start\_step$ : float = 600, end\_step: float = 1200)

Compute metrics for closed loop anesthesia.

This function compute the control metrics initially proposed in [1].

#### **Parameters**

#### time

[list] List of time value.

#### bis

[list] List of BIS value over time.

ts

[float, optional] Sampling time in second. The default is 1.

## phase

[str, optional] Control phase, can be "maintenance", 'induction" or "total". The default is 'maintenance'.

## start\_step: float, optional

Start time of the step disturbance, for maintenance and total phase. The default is 600s.

#### end\_step: float, optional

End time of the step disturbance, for maintenance and total phase. The default is 1200s.

## Returns

## TT

[float] Observed time-to-target (in minute) required for reaching first time the target interval of [55,45] BIS values

## BIS\_NADIR: float

for "induction" or "total" phase. The lowest observed BIS value during induction phase

#### ST10: float

for "induction" or "total" phase. Settling time (in minute) on the reference BIS value, defined within  $\pm$  5BIS(i.e., between 45 and 55 BIS)and stay within this BIS range

#### ST20: float

for "induction" or "total" phase. Settling time (in minute) on the reference BIS value, defined within  $\pm$  10BIS(i.e., between 40 and 60 BIS) and stay within this BIS range

#### US: float

for "induction" or "total" phase. Undershoot, defined as the BIS value that exceeds the limit of the defined BIS interval, namely, the 45 BIS value.

## TTp

[float] Time to target (in minute) after the positive step disturbance.

## BIS\_NADIRp: float

for "maintenance" or "total" phase. Minimum BIS vamue after the positive step disturbance.

#### TTpn: float

for "maintenance" or "total" phase. Time to target (in minute) after the negative step disturbance.

#### **BIS\_NADIRn:** float

for "maintenance" or "total" phase. Maximum BIS vamue after the negative step disturbance.

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