

## SBML Model Report

# Model name: “Moore2004 - Chronic Myeloid Leukemic cells and T-lymphocyte interaction”



May 17, 2018

## 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Matthew Grant Roberts<sup>1</sup>, Rahuman Sheriff<sup>2</sup> and Catherine Lloyd<sup>3</sup> at June 25<sup>th</sup> 2010 at 1:18 p.m. and last time modified at June 25<sup>th</sup> 2010 at 1:18 p.m. Table 1 gives an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	5
events	0	constraints	0
reactions	10	function definitions	6
global parameters	12	unit definitions	7
rules	0	initial assignments	0

## Model Notes

Moore2004 - Chronic Myeloid Leukemic cells and T-lymphocytes interactionA mathematical model for the interaction of between cancer cells and immune system, involving CML cancer

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cells, naive and effector T-lymphocytes.

This model is described in the article: [A mathematical model for chronic myelogenous leukemia \(CML\) and T cell interaction](#). Moore H, Li NK.J. Theor. Biol. 2004 Apr; 227(4): 513-523

Abstract:

In this paper, we propose and analyse a mathematical model for chronic myelogenous leukemia (CML), a cancer of the blood. We model the interaction between naive T cells, effector T cells, and CML cancer cells in the body, using a system of ordinary differential equations which gives rates of change of the three cell populations. One of the difficulties in modeling CML is the scarcity of experimental data which can be used to estimate parameters values. To compensate for the resulting uncertainties, we use Latin hypercube sampling (LHS) on large ranges of possible parameter values in our analysis. A major goal of this work is the determination of parameters which play a critical role in remission or clearance of the cancer in the model. Our analysis examines 12 parameters, and identifies two of these, the growth and death rates of CML, as critical to the outcome of the system. Our results indicate that the most promising research avenues for treatments of CML should be those that affect these two significant parameters (CML growth and death rates), while altering the other parameters should have little effect on the outcome.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000662](#).

To cite BioModels Database, please use: [Chelliah V et al. BioModels: ten-year anniversary. Nucl. Acids Res. 2015, 43\(Database issue\):D542-8.](#)

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## 2 Unit Definitions

This is an overview of ten unit definitions of which three are predefined by SBML and not mentioned in the model.

### 2.1 Unit `time`

**Name** `time`

**Definition** 86400 s

### 2.2 Unit `substance`

**Name** `substance`

**Definition** `item`

### 2.3 Unit `unit_0`

**Name**  $1/(11.5741 \cdot 1 \cdot \text{s})$

**Definition**  $(11.5741 \text{ l})^{-1} \cdot \text{s}^{-1}$

### 2.4 Unit `unit_1`

**Name**  $1/(0.0115741 \cdot \text{ms})$

**Definition**  $(0.0115741 \text{ ms})^{-1}$

### 2.5 Unit `unit_2`

**Name** 1

**Definition** dimensionless<sup>0</sup>

### 2.6 Unit `unit_3`

**Name**  $0.0864 \cdot 1/\text{s}$

**Definition**  $0.0864 \text{ l} \cdot \text{s}^{-1}$

### 2.7 Unit `unit_4`

**Name**  $1/\text{Ml}$

**Definition**  $\text{Ml}^{-1}$

### 2.8 Unit `volume`

**Notes** Litre is the predefined SBML unit for volume.

**Definition** 1

### 2.9 Unit `area`

**Notes** Square metre is the predefined SBML unit for area since SBML Level 2 Version 1.

**Definition**  $\text{m}^2$

### 2.10 Unit `length`

**Notes** Metre is the predefined SBML unit for length since SBML Level 2 Version 1.

**Definition** m

### 3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
COMpartment	Blood		3	1	litre	<input checked="" type="checkbox"/>	

#### 3.1 Compartment COMpartment

This is a three dimensional compartment with a constant size of one litre.

**Name** Blood

## 4 Species

This model contains five species. The boundary condition of two of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 8 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
CML	CML	COMpartment	$\text{item} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
T_cell_naive	T_cell_naive	COMpartment	$\text{item} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
T_cell_effector	T_cell_effector	COMpartment	$\text{item} \cdot \text{l}^{-1}$	<input type="checkbox"/>	<input type="checkbox"/>
Source	Source	COMpartment	$\text{item} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Sink	Sink	COMpartment	$\text{item} \cdot \text{l}^{-1}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

## 5 Parameters

This model contains twelve global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
sn	sn		0.071	$(11.5741\text{ l})^{-1} \cdot \text{s}^{-1}$	✓
dn	dn		0.050	$(0.0115741\text{ ms})^{-1}$	✓
alpha_n	alpha_n		0.560	dimensionless <sup>0</sup>	✓
alpha_e	alpha_e		0.530	$(0.0115741\text{ ms})^{-1}$	✓
de	de		0.120	$(0.0115741\text{ ms})^{-1}$	✓
gamma_e	gamma_e		0.008	$0.0864\text{ l} \cdot \text{s}^{-1}$	✓
Cmax	Cmax		190000.000	$\text{Ml}^{-1}$	✓
rc	rc		0.230	$(0.0115741\text{ ms})^{-1}$	✓
dc	dc		0.680	$(0.0115741\text{ ms})^{-1}$	✓
gamma_c	gamma_c		0.047	$0.0864\text{ l} \cdot \text{s}^{-1}$	✓
kn	kn		0.063	$(0.0115741\text{ ms})^{-1}$	✓
eta	eta		43.000	$\text{Ml}^{-1}$	✓

## 6 Function definitions

This is an overview of six function definitions.

### 6.1 Function definition `function_for_naive_activation`

**Name** function for naive activation

**Arguments** naive, [CML], eta, k

**Mathematical Expression**

$$k \cdot \text{naive} \cdot \frac{[\text{CML}]}{[\text{CML}] + \text{eta}} \quad (1)$$

### 6.2 Function definition `function_for_T_cell_effector_death_by_CML`

**Name** function for T\_cell\_effector death by CML

**Arguments** param, [CML], effector

**Mathematical Expression**

$$\text{param} \cdot [\text{CML}] \cdot \text{effector} \quad (2)$$

### 6.3 Function definition `function_for_CML_growth`

**Name** function for CML growth

**Arguments** `r`, `C`, `Cmax`

**Mathematical Expression**

$$r \cdot C \cdot \left( \frac{C_{\max}}{C} \right) \quad (3)$$

### 6.4 Function definition `function_for_CML_death_by_T_cell_effector`

**Name** function for CML death by T\_cell\_effector

**Arguments** `param`, `mod`, `substrate`

**Mathematical Expression**

$$\text{param} \cdot \text{mod} \cdot \text{substrate} \quad (4)$$

### 6.5 Function definition `function_for_T_cell_effector_production_from_T-cell_naive_activation`

**Name** function for T\_cell\_effector production from T\_cell\_naive activation

**Arguments** `alpha`, `k`, `naive`, `[CML]`, `eta`

**Mathematical Expression**

$$\alpha \cdot k \cdot \text{naive} \cdot \frac{[\text{CML}]}{[\text{CML}] + \text{eta}} \quad (5)$$

### 6.6 Function definition `function_for_T_cell_effector_recruitment`

**Name** function for T\_cell\_effector\_recruitment

**Arguments** `alpha`, `effector`, `[CML]`, `eta`

**Mathematical Expression**

$$\alpha \cdot \text{effector} \cdot \frac{[\text{CML}]}{[\text{CML}] + \text{eta}} \quad (6)$$

## 7 Reactions

This model contains ten reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

Nº	Id	Name	Reaction Equation	SBO
1	T_cell_naive- _Source	T_cell_naive Source	Source $\longrightarrow$ T_cell_naive	
2	T_cell_naive- _Natural_Death	T_cell_naive Natural Death	T_cell_naive $\longrightarrow$ Sink	
3	T_cell_naive- _Activation	T_cell_naive Activation	T_cell_naive $\xrightarrow{\text{CML}}$ Sink	
4	T_cell- _effector- _Recruitment	T_cell_effector Recruitment	Source $\xrightarrow{\text{CML}}$ T_cell_effector	
5	T_cell- _effector- _Natural_Death	T_cell_effector Natural Death	T_cell_effector $\longrightarrow$ Sink	
6	T_cell- _effector- _Death_by_CML	T_cell_effector Death by CML	T_cell_effector $\xrightarrow{\text{CML}}$ Sink	
7	CML_Growth	CML Growth	Source $\longrightarrow$ CML	
8	CML_death_by_T- _cell_effector	CML death by T_cell_effector	CML $\xrightarrow{\text{T\_cell\_effector}}$ Sink	
9	CML_natural- _death	CML natural death	CML $\longrightarrow$ Sink	



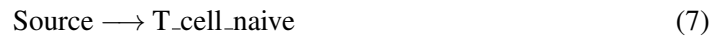
Nº	Id	Name	Reaction Equation	SBO
10	T_cell- _effector- _Production- _from_T- _cell_Naive- _activation	T_cell_effector Production from T_cell_Naive activation	Source $\xrightarrow{\text{T\_cell\_naive, CML}}$ T_cell_effector	

### 7.1 Reaction T\_cell\_naive\_Source

This is an irreversible reaction of one reactant forming one product.

**Name** T\_cell\_naive Source

#### Reaction equation



#### Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
Source	Source	

#### Product

Table 7: Properties of each product.

Id	Name	SBO
T_cell_naive	T_cell_naive	

#### Kinetic Law

**Derived unit**  $\text{s}^{-1} \cdot \text{item} \cdot \text{l}^{-1}$

$$v_1 = \text{vol}(\text{COMpartment}) \cdot \text{sn} \cdot [\text{Source}] \quad (8)$$

### 7.2 Reaction T\_cell\_naive\_Natural\_Death

This is an irreversible reaction of one reactant forming one product.

**Name** T\_cell\_naive Natural Death

#### Reaction equation



#### Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
T_cell_naive	T_cell_naive	

## Product

Table 9: Properties of each product.

Id	Name	SBO
Sink	Sink	

## Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

$$v_2 = \text{vol}(\text{COMpartment}) \cdot \text{dn} \cdot [\text{T\_cell\_naive}] \quad (10)$$

## 7.3 Reaction T\_cell\_naive\_Activation

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

**Name** T\_cell\_naive Activation

## Reaction equation



## Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
T_cell_naive	T_cell_naive	

## Modifier

Table 11: Properties of each modifier.

Id	Name	SBO
CML	CML	

## Product

Table 12: Properties of each product.

Id	Name	SBO
Sink	Sink	

## Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

$$v_3 = \text{vol}(\text{COMpartment}) \cdot \text{function\_for\_naive\_activation}([T\_cell\_naive], [CML], \text{eta}, k_n) \quad (12)$$

$$\text{function\_for\_naive\_activation}(\text{naive}, [CML], \text{eta}, k) = k \cdot \text{naive} \cdot \frac{[CML]}{[CML] + \text{eta}} \quad (13)$$

$$\text{function\_for\_naive\_activation}(\text{naive}, [CML], \text{eta}, k) = k \cdot \text{naive} \cdot \frac{[CML]}{[CML] + \text{eta}} \quad (14)$$

## 7.4 Reaction T\_cell\_effector\_Recruitment

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

**Name** T\_cell\_effector Recruitment

### Reaction equation



## Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
Source	Source	

## Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
CML	CML	

## Product

Table 15: Properties of each product.

Id	Name	SBO
T_cell_effector	T_cell_effector	

## Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

$$v_4 = \text{vol}(\text{COMpartment}) \cdot \text{function\_for\_T\_cell\_effector\_recruitment}(\alpha_e, [\text{T\_cell\_effector}], [\text{CML}], \text{eta}) \quad (16)$$

$$\begin{aligned} & \text{function\_for\_T\_cell\_effector\_recruitment}(\alpha, \text{effector}, [\text{CML}], \text{eta}) \\ &= \alpha \cdot \text{effector} \cdot \frac{[\text{CML}]}{[\text{CML}] + \text{eta}} \end{aligned} \quad (17)$$

$$\begin{aligned} & \text{function\_for\_T\_cell\_effector\_recruitment}(\alpha, \text{effector}, [\text{CML}], \text{eta}) \\ &= \alpha \cdot \text{effector} \cdot \frac{[\text{CML}]}{[\text{CML}] + \text{eta}} \end{aligned} \quad (18)$$

## 7.5 Reaction T\_cell\_effector\_Natural\_Death

This is an irreversible reaction of one reactant forming one product.

**Name** T\_cell\_effector Natural Death

### Reaction equation



### Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
T_cell_effector	T_cell_effector	

### Product

Table 17: Properties of each product.

Id	Name	SBO
Sink	Sink	

### Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

$$v_5 = \text{vol}(\text{COMpartment}) \cdot \text{de} \cdot [\text{T\_cell\_effector}] \quad (20)$$

## 7.6 Reaction T\_cell\_effector\_Death\_by\_CML

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

**Name** T\_cell\_effector Death by CML

### Reaction equation



### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
T_cell_effector	T_cell_effector	

## Modifier

Table 19: Properties of each modifier.

Id	Name	SBO
CML	CML	

## Product

Table 20: Properties of each product.

Id	Name	SBO
Sink	Sink	

## Kinetic Law

**Derived unit**  $\text{s}^{-1} \cdot \text{item}^2$

$$v_6 = \text{vol}(\text{COMpartment}) \cdot \text{function\_for\_T\_cell\_effector\_death\_by\_CML}(\text{gamma\_e}, [\text{CML}], [\text{T\_cell.effector}]) \quad (22)$$

$$\text{function\_for\_T\_cell\_effector\_death\_by\_CML}(\text{param}, [\text{CML}], \text{effector}) = \text{param} \cdot [\text{CML}] \cdot \text{effector} \quad (23)$$

$$\text{function\_for\_T\_cell\_effector\_death\_by\_CML}(\text{param}, [\text{CML}], \text{effector}) = \text{param} \cdot [\text{CML}] \cdot \text{effector} \quad (24)$$

### 7.7 Reaction CML\_Growth

This is an irreversible reaction of one reactant forming one product.

**Name** CML Growth

#### Reaction equation



#### Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
Source	Source	

## Product

Table 22: Properties of each product.

Id	Name	SBO
CML	CML	

## Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

$$v_7 = \text{vol}(\text{COMpartment}) \cdot \text{function\_for\_CML\_growth}(rc, [\text{CML}], C_{\max}) \quad (26)$$

$$\text{function\_for\_CML\_growth}(r, C, C_{\max}) = r \cdot C \cdot \left( \frac{C_{\max}}{C} \right) \quad (27)$$

$$\text{function\_for\_CML\_growth}(r, C, C_{\max}) = r \cdot C \cdot \left( \frac{C_{\max}}{C} \right) \quad (28)$$

## 7.8 Reaction CML\_death\_by\_T\_cell\_effector

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

**Name** CML death by T\_cell\_effector

### Reaction equation



## Reactant



Table 23: Properties of each reactant.

Id	Name	SBO
CML	CML	

## Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
T_cell_effector	T_cell_effector	

## Product

Table 25: Properties of each product.

Id	Name	SBO
Sink	Sink	

## Kinetic Law

**Derived unit**  $\text{s}^{-1} \cdot \text{item}^2$

$$v_8 = \text{vol}(\text{COMpartment}) \cdot \text{function\_for\_CML\_death\_by\_T\_cell\_effector}(\text{gamma\_c}, [\text{T\_cell\_effector}], [\text{CML}]) \quad (30)$$

$$\text{function\_for\_CML\_death\_by\_T\_cell\_effector}(\text{param}, \text{mod}, \text{substrate}) = \text{param} \cdot \text{mod} \cdot \text{substrate} \quad (31)$$

$$\text{function\_for\_CML\_death\_by\_T\_cell\_effector}(\text{param}, \text{mod}, \text{substrate}) = \text{param} \cdot \text{mod} \cdot \text{substrate} \quad (32)$$

### 7.9 Reaction [CML\\_natural\\_death](#)

This is an irreversible reaction of one reactant forming one product.

**Name** CML natural death

### Reaction equation



### Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
CML	CML	

### Product

Table 27: Properties of each product.

Id	Name	SBO
Sink	Sink	

### Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

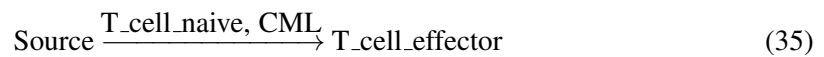
$$v_9 = \text{vol}(\text{COMpartment}) \cdot \text{dc} \cdot [\text{CML}] \quad (34)$$

## 7.10 Reaction `T_cell_effector_Production_from_T_cell_Naive_activation`

This is an irreversible reaction of one reactant forming one product influenced by two modifiers.

**Name** `T_cell_effector Production from T_cell_Naive activation`

### Reaction equation



### Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
Source	Source	

## Modifiers

Table 29: Properties of each modifier.

Id	Name	SBO
T_cell_naive	T_cell_naive	
CML	CML	

## Product

Table 30: Properties of each product.

Id	Name	SBO
T_cell_effector	T_cell_effector	

## Kinetic Law

**Derived unit**  $(0.0115741 \text{ ms})^{-1} \cdot \text{item}$

$$\begin{aligned} v_{10} = & \text{vol}(\text{COMpartment}) \\ & \cdot \text{function\_for\_T\_cell\_effector\_production\_from\_T\_cell\_naive\_activation}(\alpha_n, k_n, \\ & \quad [T\_cell\_naive], [CML], \text{eta}) \end{aligned} \quad (36)$$

$$\begin{aligned} & \text{function\_for\_T\_cell\_effector\_production\_from\_T\_cell\_naive\_activation}(\alpha, \\ & \quad k, \text{naive}, [CML], \text{eta}) = \alpha \cdot k \cdot \text{naive} \cdot \frac{[CML]}{[CML] + \text{eta}} \end{aligned} \quad (37)$$

$$\begin{aligned} & \text{function\_for\_T\_cell\_effector\_production\_from\_T\_cell\_naive\_activation}(\alpha, \\ & \quad k, \text{naive}, [CML], \text{eta}) = \alpha \cdot k \cdot \text{naive} \cdot \frac{[CML]}{[CML] + \text{eta}} \end{aligned} \quad (38)$$

## 8 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML substance per time. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions > 0` for certain species.

## 8.1 Species CML

**Name** CML

**Initial concentration** 10000 item · l<sup>-1</sup>

This species takes part in seven reactions (as a reactant in `CML_death_by_T_cell_effector`, `CML_natural_death` and as a product in `CML_Growth` and as a modifier in `T_cell_naive_Activation`, `T_cell_effector_Recruitment`, `T_cell_effector_Death_by_CML`, `T_cell_effector_Production_from_T_cell_Naive_activation`).

$$\frac{d}{dt}\text{CML} = v_7 - v_8 - v_9 \quad (39)$$

## 8.2 Species T\_cell\_naive

**Name** T\_cell\_naive

**Initial concentration** 1510 item · l<sup>-1</sup>

This species takes part in four reactions (as a reactant in `T_cell_naive_Natural_Death`, `T_cell_naive_Activation` and as a product in `T_cell_naive_Source` and as a modifier in `T_cell_effector_Production_from_T_cell_Naive_activation`).

$$\frac{d}{dt}\text{T\_cell\_naive} = v_1 - v_2 - v_3 \quad (40)$$

## 8.3 Species T\_cell\_effector

**Name** T\_cell\_effector

**Initial concentration** 20 item · l<sup>-1</sup>

This species takes part in five reactions (as a reactant in `T_cell_effector_Natural_Death`, `T_cell_effector_Death_by_CML` and as a product in `T_cell_effector_Recruitment`, `T_cell_effector_Production_from_T_cell_Naive_activation` and as a modifier in `CML_death_by_T_cell_effector`).

$$\frac{d}{dt}\text{T\_cell\_effector} = v_4 + v_{10} - v_5 - v_6 \quad (41)$$

## 8.4 Species Source

**Name** Source

**Initial concentration** 1 item · l<sup>-1</sup>

This species takes part in four reactions (as a reactant in `T_cell_naive_Source`, `T_cell_effector_Recruitment`, `CML_Growth`, `T_cell_effector_Production_from_T_cell_Naive_activation`), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt} \text{Source} = 0 \quad (42)$$

## 8.5 Species Sink

**Name** Sink

**Initial concentration** 1 item · l<sup>-1</sup>

This species takes part in six reactions (as a product in `T_cell_naive_Natural_Death`, `T_cell_naive_Activation`, `T_cell_effector_Natural_Death`, `T_cell_effector_Death_by_CML`, `CML_death_by_T_cell_effector`, `CML_natural_death`), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt} \text{Sink} = 0 \quad (43)$$

SBML2<sup>LaTeX</sup> was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

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