## RIWAYAT KORESPONDENSI ARTIKEL DI JURNAL OF APPLIED MATHEMATICS (JAM) (PENERBIT HINDAWI)

# 1. Artikel di submid melalui sistem OJS pada 28 Juni 2018

	2983138: Acknowledging Receipt (Edama) D (BOOK H			0
J	Journal of Applied Mathematics «maryam.nazem@hindawi.com+ to me, maryam.hazem, r_adikusumo, lina, dialibudiyarito +	Thu, Jun 28, 2018, 2-35 PM	☆	÷
	Dear Dr. Adi,			
	The Research Article titled "A Dynamic of PI3K/AKT Pathways in Acute Myeloid Leukemia," by Yudi Adi, Fajar Adi-Kus received and assigned the number 2983138.	iumo, Lina Aryati and Mardiah Hard	iant) ha	s been
	All authors will receive a copy of all the correspondences regarding this manuscript.			
	Thank you for submitting your work to Journal of Applied Mathematics.			
	Best regards,			
	Marvam Hazem			
	Editorial Office			
	Hindawi			
	http://www.hindawi.com			

#### 2. Pada 16 Juli 2018 Editor meminta mnyertakan ID ORCID

2983138: Open Researcher and Contributor ID (Etense) > Induced MIRAN	×	0	2
Journal of Applied Mathematics +maryem hazern@hindawi.com+ to me *	*	47	1
Dear Dr. Adi.			
This is regarding your manuscript titled "A Dynamic of PI3K/AKT Pathways in Acute Myeloid Leukemia" in Journal of Applied Mathematics. Please registe Researcher and Contributor ID (ORCID) and link it to your Manuscript Tracking System (MTS) account, as we need to include authors' ORCID IDs in the that we submit to various indexing services.	r an ID article n	with O netada	ipen ta
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Please make sure to use the name format that is on the MTS when creating your ORCID ID, since it is highly preferred that you use the same format in al dealing with your professional activities. However, if your name on the MTS is not currently correct, let me know the format you prefer, and I will update it in the same format is and the same format in all so the same format is and the same format in all update it is a same format in all update it is a same format in all update it is not same	l of the accordin	systen ngly:	18
Tlook forward to your cooperation:			
Best regards.			
Maryam Hazem			
Editorial Office			
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3. Hasil review dengan kategori revisi Mayor diperoleh pada 1 Oktober 2018



Komentar dan tanggapan seperti dalam Revision report seperti terlampir

Revision Report: "A Dynamics of PI3K/AKT Pathways in Acute Myeloid Leukemia"

#### Dear Editor:

Thank you for the opportunity to revise our manuscript, *A Dynamics of PI3K/AKT Pathways in Acute Myeloid Leukemia*. We thank the review panel for their critical but insightful comments. Addressing those comments resulted in an improved paper. We thank all reviewers for their kind words and positive comments on our paper.

In the table below, we document how we have addressed the comments from the three reviewers. We do hope that you will find the revisions meet the quality standard required by the journal.

Thank you for your consideration.

Sincerely,

Yudi Ari Adi.

#### **REVIEW #1**

No.	The reviewer's comments	Our responses
1	The title looks incomplete	We have changed the title to <b>A Dynamic Model of</b>
	and/or unclear. It should rather	PI3K/AKT Pathways in Acute Myeloid Leukemia
	read like <b>Dynamics of</b>	
	PI3K/AKT pathways in Acute	
	Myeloid Leukemia or A	
	Dynamic Model of PI3K/AKT	
	pathways in Acute Myeloid	
	Leukemia	
-		
2	The grammar and typography	We have improved the Grammar and typography.
	in the article need to be	In page 1, last line, we have changed
	improved.	"Untreated AML patient leading to fatal infection,
		bleeding or organ inflitration within 1-year diagnosis,
		10 "I lutaneted AMI meticant acculta in fatal infaction blooding.
		on organ infiltration within 1 year of diamonia."
		or organ minutation within 1-year of diagnosis,
		In page 2, second paragraph, line 11, we have changed
		"suppression" to "supressing"
		In page 2, third paragraph, line 5, we have changed "
		there no" to "there are no known"
		In page 3, first paragraph, line 2, we have changed "
		extension" to "extended"
		In page 3, first paragraph, line 14, we have changed
		"reserved" to "reversed"
		In page 4, we have not changed "coefficient 3" to "a
		cubic of power", because
		for the Hill's Equation $\frac{X^n}{K^n + X^n}$ , the exponent <i>n</i> ,
		called the <i>Hill coeficient</i> , so we use the term
		coefficient instead of a power

3	There exists some dimensional	According to th	e references, som	e dimensions of the
	inconsistencies in the model.	parameters pres	sented in table 2 an	re incorrect. Therefore, we
	For instance k0 is said to have	make correction	ns as follows	
	units µM	Parameter	Unit	Unit
	which is inconsistent with the		(Before)	(After correction)
	expected dimension ( $\mu M/min$ )	$k_0$	$\mu M$	$\mu Mmin^{-1}$
	$of \frac{dx_1}{dt}$ . Considering the	b	$min^{-1}$	min <sup>-1</sup>
	dimensions of k4 and K4, the	$k_1$	$\mu Mmin^{-1}$	$\mu Mmin^{-1}$
	term $\frac{k_3 x_3^2}{2}$ will have	$d_1$	$min^{-1}$	$min^{-1}$
	$K_3^2 + x_3^2$	<i>a</i> <sub>2</sub>	$min^{-1}$	$\mu Mmin^{-1}$
	dimension of $(\mu M)^2 min^{-1}$ ,	<i>k</i> <sub>2</sub>	$\mu Mmin^{-1}$	$min^{-1}$
	which is inconsistent with that $dx_{A}$ is a particular of $dx_{A}$	<i>k</i> <sub>3</sub>	$\mu Mmin^{-1}$	$\mu Mmin^{-1}$
	of $\frac{d}{dt}$ . If the dimensions of the	$d_2$	$min^{-1}$	$min^{-1}$
	parameters are correct, then	$d_3$	$min^{-1}$	$min^{-1}$
	the model needs to be	p	$\mu Mmin^{-1}$	$min^{-1}$
	reformulated. Authors should	m	$\mu Mmin^{-1}$	$\mu M^{-1}min^{-1}$
	consider the definitions and/or	$k_4$	$\mu Mmin^{-1}$	$min^{-1}$
	in Ta	$k_{5}$	$\mu Mmin^{-1}$	$\mu Mmin^{-1}$
	hle 2.	$d_5$	$\mu Mmin^{-1}$	$min^{-1}$
		$K_1$	μΜ	μM
		K <sub>2</sub>	μΜ	μM
		<i>K</i> <sub>2</sub>	μΜ	μM
		$K_{4}$	иM	иM
		4 Kr	иM	иM
4	Authors should consider doing	We also correct dephosphorylat The complete o The model is	description $d_5$ , " ion" to "FOXO3a <u>f Tabel 2 is presen</u> not sufficiently a	Constant rate of FOXO3a p degradation rate". nted in the paper. accessible to allow us to
	some basic mathematical analysis of the model, like biological and mathematical and/or possessedness of the model before the simulation.	conduct the r complexity of t use of the Hill's number of prote binding sites s	nathematical ana the model. The co s equation with co ein binding sites. F o that the reaction	lysis. It is due to the omplexity comes from the efficients according to the For example, PIP3 has four on will follow the Hill's
	This is agreed on by authors in the conclusions section.	equation with a polynomial equ we couldn't find the positivity analysis can be the interaction coefficient or equation.	coefficient four. nation when trying d the solution. Furt and stability of obtained if we re- terms, for examp if the model do	We obtained a 26 <sup>th</sup> degree g to analyze the model, so thermore, we can't analyze the model. Mathematical educe or simplify some of ble by reducing the Hill's es not follow the Hill's
		In this paper, w with a model w Hill's equation. to providing r analysis. We added a sta Discussions in p "The model equ to allow us to co in this paper. w	we want to show the which the biocher Therefore, in this numerical simula tement at the beging page 5 as follows nations $(1) - (5)$ is conduct the mathem e only provide numerical shows the statement of the st	ne dynamics of the protein nical reaction follows the paper, we are only limited tions and no theoretical ning of section Result and not sufficiently accessible natical analysis. Therefore, merical simulations."

### **REVIEW #2**

No.	The reviewer's comments	Our responses
1	In page 2, third paragraph, line 10,	In page 2, third paragraph, line 10, We have changed
	change "Adi et al in [1] has been	"Adi et al in [1] has been studied" to "Adi et al in
	studied" to "Adi et al in [1]	[1] studied"
	studied"	
	In page 2, third paragraph, line 11,	In page 2, third paragraph, line 11, We have changed
	change "The model has not	"The model has not included" to "The model did not
	included" to "The model did not	include"
	include"	
	In page 3, line 5, change "Our	In page 3, line 5,We have changed "Our model is
	model is focused to discuss" to	focused to discuss" to "Our model is focused on
	"Our model is focused on	discussing"
	discussing"	

### **REVIEW #3**

No.	The reviewer's comments	Our responses
1	Introduction and model formulation	Thank you
	parts are satisfactory	
2	parts are satisfactory Section of the analytical solution of the model is missing; the following should be included i) Boundedness of the model ii) Positivity iii) Stability analysis of the model Note: however in the conclusion part, the authors recommended these aspects will be captured in future work.	The model is not sufficiently accessible to allow us to conduct the mathematical analysis. It is due to the complexity of the model. The complexity comes from the use of the Hill's equation with coefficients according to the number of protein binding sites. For example, PIP3 has four binding sites so that the reaction will follow the Hill's equation with a coefficient four. We obtained a $26^{th}$ degree polynomial equation when trying to analyze the model, so we couldn't find the solution. Furthermore, we can't analyze the positivity and stability of the model. Mathematical analysis can be obtained if we reduce or simplify some of the interaction terms, for example by reducing the Hill's coefficient or if the model does not follow the Hill's equation. In this paper, we want to show the dynamics of the protein with a model which the biochemical reaction follows the Hill's equation. Therefore, in this paper, we are only limited to providing numerical simulations. We added statement in the begining of section Result and Discussions in page 5 as follows.
		accessible to allow us to conduct the mathematical analysis. Therefore, in this paper, we only provide
		numerical simulations."
3	In the numerical simulation part,	We have revised the range of some parameter values
	some parameter values used which	The range of parameter value of $K_1$ should be $0.1 -$
	are different from the range of value	1.0 and the parameter value of $K_3$ should be written

	as per Table 2. For example, K1, K3 and K5, the author should explain why?	between $0.08 - 0.4$ . The range of parameter value of $k_5$ should be written $0.000297 - 2.92$ . The value of the $K_5$ parameter is obtained from the assumption as given in the description at the bottom of the table and is appropriate. This range of parameter values is taken from Adi-Kusumo and Wiraya [2], Karabekmez [10] and from Wee and Aguda [21]. We have added Wee and Aguda in the references [21].
4	The author refers to the wrong figure that Figure 3a instead of Figure 2a in page 6 "It can be seen that FOXO3ap reaches a peak in 100 minutes then decreases and oscillates to a certain level (see Figure 3a)."	We have reffered to the right figure.
5	The caption of figure two is placed in the wrong place. The caption should be below the figure	We have placed the caption in the right place.
6	In page 7, the figure which justifies "We note that if the constant rate of FOXO3a phosphorylation set to be zero, the concentration of FOXO3ap will be zero (not shown in the figure)." Should be included	We have added Figure 2c to justify the statement
7	There are no explanations for the figure 3, the explanation should be given	We have rewritten this part to provide explanation in first paragraph, page 8.

5. Permintaan revisi minor pada 29 Oktober 2018 dan hasil revisi dikirim pada 2 November 2018

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	Dear Dr. Adi.			
	Following the review of your Research Article titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia," by Yudi Adi, Fajar Adi-Kusume Mardiah Hardianti, I recommend that it should be revised taking into account the changes requested by the reviewer(s). Please login to the Manuscript Tra read the submitted review report(s) and submit the revised version of your manuscript not later than Monday, November 12, 2018.	Lina A cking S	ryəti ə İystem	200
	To submit your revised manuscript, please access "Current Manuscripts" in your account and upload the PDF file of your revised manuscript. You are also your replies to the reviewer(s) comments as an additional PDF file	insked	to sub	N
	Best regards,			
	Professer Okwole D. Makinde			
	makinded@pmail.com			
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9	makinded@gmail.com         2983138: Revised Version Received > Intext #         Journal of Applied Mathematics +maryam.hazem@inidawi.com+         to me, maryam hazem, 1_addhusumo, line, diantudiyanto +         Dear Dr. Adl.         The revised version of Research Article 2983138 bited "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia" by Yudi Adi, Fajar Adi-Koss         Mardiah Hardianti has been received. The editor assigned to handle the review process of your manuscript will inform you as soon as a decision is reach         Thank you for submitting your work to Journal of Applied Mathematics.         Best regards.         -	☆ mo, Li ad	<b>و</b> دم ۱۹ Ary	

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	Dear Dr. Adi,	
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	Thank you for your cooperation.	
	Best regards.	
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7. Artikel dinyatakan diterima pada **5 November 2018** dan permintaan biaya untuk open akses jurnal

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)	Oluwole D. Makinde -jamghindawi.com+ folme, makinded, f_adikusuma, lina, diahbudiyanto +	¢	fi,	1
	Dear Dr. Adl.			
	The review process of Research Article 2983138 titled "A Dynamic Model of PI3K/AKT Pathways in Acute Myeloid Leukemia " by Yudi Adi, Fajar Adi-Kusun Mardiah Hardianti submitted to Journal of Applied Mathematics has been completed. I am pleased to inform you that your manuscript has now been accept in the journal.	no, Lin ted for	a Arya public	ti an atio
	The publication process of your manuscript will be initiated upon the receipt of electronic files. Please log in to the Manuscript Tracking System at the link b username and password, and upload the electronic files of your final accepted version within the next 2-3 days.	elow u	sing yı	JUC
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	If you have deposited your manuscript on a preprint server (e.g. arXiv, bioRxiv, chemRxiv), now would be a good time to update it with the accepted version deposited your manuscript on a preprint server, you are free to do so.	n. If yo	u have	no
	Thank you again for submitting your manuscript to Journal of Applied Mathematics.			
	Best regards,			
	Professor Oluviole D. Makinde			
	makinded@gmail.com			

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	If I can be of any assistance with the payment process, please let me know			
	Kind regards.			
	Nouthayla Megdy Accounts Receivable Specialist Hindewi			

8. Galleyproofs

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	Dear Dr. Adi.				
	This is to confirm the receipt of the first galley proof corrections of Research Article 2963138 titled "A Dynamic N	Model of PI3K/AKT Pathways in Acute Myel	old Lei	ikəmi	а,"
	Thank you for your cooperation.				
	Best regards.				
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to me, dishbudiyanto, lina, f.,adikusumo +

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J

I am pleased to lat you know that the first set of galley proofs of your Research Article 2983138 titled "A Dynamic Model of PGK/AKT Pathways in Acute Myeloid Leukemia ?" is ready. You can apply your corrections directly to the manuscript with the Online Proofing System (OPS).

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#### 9. Pemberitahuan artikel dipublikasikan pada 14 November 2018



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