IMPACT OF VARYING THE INITIAL DATA ON THE TYPE OF STABILITY IN GLUCOSE- INSULIN REGULATORY SYSTEM USING NUMERICAL METHOD

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Abstract
In this study a robust MATLAB ODE45 is designed for the stabilization of glucose-insulin regulatory system utilizing the variations of the initial data. We have ascertained that as the initial data increases in its multiples, the bifurcation interval occurs beforehand and stability sets in earlier. The results of this novel contribution have not been seen elsewhere. These are presented and discussed in this paper.

***Keywords**: stability, impact, glucose-insulin, numerical method, initial data, regulatory system.*

Introduction
Since nineteen sixties (1960's), the homeostasis of glucose concentration associated with the release of the insulin hormone has been the subject of many mathematical models: [13], [2], [5], [7], [10] and [9]. Insulin secretion oscillation models have been reviewed by [11], [8], [3], 12], and [4]. Other related models include [15], [14]. Six models for the subcutaneous insulin kinetics were reviewed by [14] of which four are ordinary differential equations (ODE) models, the other two being partial differential equation (PDE) and delay differential equation (DDE) respectively. Notwithstanding, it is uncommon to see how the variations of the initial data can affect the type of stability in a glucose-insulin regulatory system. It is against this background that we have proposed for the first time to design a supportive and cutting-edge mathematical model in a developing country like Nigeria where the control of diabetes is a major health challenge.

Mathematical Formulations
Following [8], [13], and [1], we have considered the following mathematical formulations:

$$\frac{dG(t)}{dt} = -[b_1 G(t) - [(G(t),]X(t) + b_1 G_b, \qquad G(0) = G_0 > 0 \qquad (1)$$

$$\frac{dX(t)}{dt} = -b_2 X(t) + b_3[(I(t) - I_b], \qquad X(0) = X_0 > 0 \qquad (2)$$

$$\frac{dI(t)}{dt} = b_4\left[G(t) - b_5\right]t - b_6\left[I(t) - I_b\right] \qquad I(0) = I(0) > 0 \qquad (3)$$

Where,
$G(t)$ [mg/dl] represents the blood glucose concentration at time t [min];
$X(t)$ [min^{-1}] represents the insulin-excitable tissue glucose uptake activity;
$I(t)\ [\mu\upsilon I / ml]$ represents the blood insulin concentration;
$G_b\ [mg / dl]$ is the subject's baseline glycemia;
$I_b\ [\mu\upsilon I / ml]$ is the subject's baseline insulinemia;
b_0 [mg/dl] is the theoretical glycemia at time zero;
$b_1\ [\min^{-1}]$ is the insulin-independent rate constant of tissue glucose uptake;
$b_2\ [\min^{-1}]$ is the rate constant of the spontaneous decrease of tissue glucose uptake activity;
$b_3\ [\min^{-2}(\mu\upsilon I / ml)^{-1}]$ is the insulin-dependent increase in tissue glucose uptake activity per unit of insulin concentration excess over baseline insulin;
$b_4[(\mu\upsilon I / ml)\,(mg / dl)^{-1} \min^{-1}]$ is the rate of pancreatic release of insulin after the bolus, per minute and per mg/dl of glucose concentration above the "target" glycemia;
$b_5[mg / dl]$ is the pancreatic ''target glycemia'';
$b_6[\min^{-1}]$ is the first order decay rate constant for insulin in plasma.

Method of Analysis

We have used a computational efficient numerical scheme called MATLABODE45 to calculate the effect of varying the initial data on the type of stability under the simplifying assumption of increasing the initial condition in terms of its multiples. The key contribution of using this method are presented and discussed in the next section of this paper.

The following parameter values given by [8] are used in the simulation for the dynamical system: (1) - (3) in order to facilitate the interpretation of the mathematical analysis: b_0=1, b_1=0.233, b =0.044, b_3=0.213, b_4=0.594, b_5 = 0.062, b_6 = 0.062, G_b= 0.072, I_b = 0.074.

Results and Discussion

The results of this present simulation in terms of the impact of varying the initial data on type of stability in glucose-insulin regulatory system using numerical method are presented and discussed in this section of the paper.

Table 1: Predicting the type of stability for every week using the initial condition: [0.4, 0.2, 0.24]

Example	Time (weeks)	Ge	Xe	Ie				TOS
1	1	0.400000000000000	0.200000000000000	0.240000000000000	-0.601353417412925	0.031176708706463	0.031176708706463	Unstable
2	2	0.378493059639128	0.202847522700707	0.258345470150606	-0.597445013149086	0.027798745224189	0.027798745224189	Unstable
3	3	0.358196027880417	0.206057935342453	0.275340242653750	-0.593964428158639	0.024453246408093	0.024453246408093	Unstable
4	4	0.339034574139769	0.209601767419003	0.291062095289119	-0.590898365217915	0.021148298899456	0.021148298899456	Unstable
5	5	0.320940774658030	0.213451282919731	0.305584107296492	-0.588234656310349	0.017891686695309	0.017891686695309	Unstable
6	6	0.303852402122098	0.217580383524467	0.318975023043025	-0.585962082499356	0.014690849487444	0.014690849487444	Unstable
7	7	0.287712418315884	0.287712418315884	0.331299179335641	-0.584070323601772	0.011552837850571	0.011552837850571	Unstable
8	8	0.302973700277284	0.226960485381734	0.349801618954837	-0.591961366099448	0.013000440358858	0.013000440358858	Unstable
9	9	0.290919595397723	0.231956369650437	0.362008762573167	-0.591787368029105	0.010415499189334	0.010415499189334	Unstable
10	10	0.279271679055554	0.237182639097029	0.373435431278916	-0.591889421256987	0.007853391079979	0.007853391079979	Unstable
11	11	0.268000543278210	0.242616642606206	0.384124398559975	-0.592253679290805	0.005318518342300	0.005318518342300	Unstable
12	12	0.257110946723738	0.248246960904851	0.394089211625636	-0.592883654284337	0.002818346689743	0.002818346689743	Unstable
13	13	0.246586949492075	0.254055791154047	0.403361434967449	-0.593771588567336	0.000357898706644	0.000357898706644	Unstable
14	14	0.236419375826200	0.260027742684112	0.411967064637614	-0.594912732850177	-0.002057504916968	-0.002057504916968	Stable
15	15	0.226600428331220	0.266148072042664	0.419931261900770	-0.596302493500948	-0.004422789270858	-0.004422789270858	Stable

16	16	0.217125099698100	0.272403107762732	0.427277285365412	-0.597937180281509	-0.006732963740612	-0.006732963740612	Stable

Table 2: Predicting the type of stability for every week using the initial condition: [0.8, 0.4, 0.48]

Example	Time (weeks)	G_e	X_e	I_e				TOS
1	1	0.800000000000000	0.400000000000000	0.480000000000000	-0.809764753541325	0.035382376770663	0.035382376770663	Unstable
2	2	0.752285706104052	0.407301010299407	0.519765789795159	-0.807515610794223	0.030607300247408	0.030607300247408	Unstable
3	3	0.706970384589640	0.415382928798969	0.556532153936523	-0.806111594449001	0.025864332825016	0.025864332825016	Unstable
4	4	0.663922274384325	0.424180244952399	0.590455750423433	-0.805532680459627	0.021176217753614	0.021176217753614	Unstable
5	5	0.623025997957407	0.433630982067434	0.621684936222801	-0.805760822408830	0.016564920170697	0.016564920170697	Unstable
6	6	0.584180060817753	0.443676533904212	0.650360636066794	-0.806779244653719	0.012051355374753	0.012051355374753	Unstable
7	7	0.547294236333702	0.454261832180392	0.676616020023985	-0.808571922257905	0.007655045038757	0.007655045038757	Unstable
8	8	0.512278350077657	0.465332917513809	0.700585200223425	-0.811119597748431	0.003393340117310	0.003393340117310	Unstable
9	9	0.479050010145386	0.476839126823651	0.722395728679375	-0.814402387389949	-0.000718369716851	-0.000718369716851	Stable
10	10	0.447534224944820	0.488732793707428	0.742169486476209	-0.818399337160470	-0.004666728273479	-0.004666728273479	Stable
11	11	0.417660941582118	0.500968875085089	0.760023821767062	-0.823087601518981	-0.008440636783054	-0.008440636783054	Stable
12	12	0.389366001697371	0.513504923626010	0.776071379709506	-0.828442541770537	-0.012031190927737	-0.012031190927737	Stable
13	13	0.362725107183182	0.526320251511589	0.790347344362095	-0.834477128834473	-0.015421561338558	-0.015421561338558	Stable
14	14	0.337667768874249	0.337667768874249	0.802957786198429	-0.841160059071814	-0.018608315462937	-0.018608315462937	Stable
15	15	0.314087123326678	0.552632794190040	0.814026267919815	-0.848445927153366	-0.021593433518337	-0.021593433518337	Stable

16	16	0.291906996992112	0.566053653040123	0.823656647731287	-0.856295588356201	-0.024379032341961	-0.024379032341961	Stable

Table.3: Predicting the type of stability for every week using the initial condition: [1.2, 0.6, 0.72]

Example	Time (weeks)	G_e	X_e	I_e				TOS
1	1	1.200000000000000	0.600000000000000	0.720000000000000	-1.001703867543761	0.031351933771880	0.031351933771880	Unstable
2	2	1.105062037083315	0.611749924218240	0.780548820228530	-1.000501400743296	0.024875738262528	0.024875738262528	Unstable
3	3	1.016507368049658	0.624672635261934	0.835292998148179	-1.000840415487497	0.018583890112782	0.018583890112782	Unstable
4	4	0.933920972615048	0.638643882729240	0.884634070979294	-1.002672807675544	0.012514462473152	0.012514462473152	Unstable
5	5	0.856937068252734	0.653548245084810	0.928947884620158	-1.005950610733996	0.006701182824592	0.006701182824592	Unstable
6	6	0.785231162058524	0.669278653373865	0.968586983747926	-1.010624331499578	0.001172839062856	0.001172839062856	Unstable
7	7	0.718510197917503	0.685736852584137	1.003878565462341	-1.003878565462341	-0.004047435404255	-0.004047435404255	Stable
8	8	0.656454808962631	0.702825556507175	1.035160397962922	-1.023935932068366	-0.008944812219405	-0.008944812219405	Stable
9	9	0.598765206591781	0.720455504395515	1.062749094859015	-1.032434010620752	-0.013510746887382	-0.013510746887382	Stable
10	10	0.545216633341913	0.738549401419323	1.086918711078839	-1.042070150329657	-0.017739625544833	-0.017739625544833	Stable
11	11	0.495816983722548	0.757054921427260	1.107832434056307	-1.052814982657844	-0.021619969384708	-0.021619969384708	Stable
12	12	0.450295518784011	0.775900399393554	1.125762054446000	-1.064580169989594	-0.025160114701980	-0.025160114701980	Stable
13	13	0.408428469441461	0.795023102674692	1.140948332138210	-1.077281153512670	-0.028370974581012	-0.028370974581012	Stable
14	14	0.369964587729003	0.814362761094054	1.153632909539592	-1.090824862899424	-0.031268949097315	-0.031268949097315	Stable
15	15	0.334625146799681	0.833861566941913	1.164058311573166	-1.105111679725466	-0.033874943608224	-0.033874943608224	Stable

16	16	0.302110128480969	0.853464564449406	1.172465607879133	-1.120038485458414	-0.036213039495496	-0.036213039495496	Stable

Table 4: Predicting the type of stability for every week using the initial condition: [1.6, 0.8, 0.96]

Example	Time (weeks)	G_e	X_e	I_e				TOS
1	1	1.600000000000000	0.800000000000000	0.960000000000000	-1.189686577623494	0.025343288811746	0.025343288811746	Unstable
2	2	1.443415047245611	1.040889124020987	1.040889124020987	-1.190376539548654	0.017590448861291	0.017590448861291	Unstable
3	3	1.300100853468161	0.833938106246877	1.112404975615241	-1.193422891637493	0.010242392695308	0.010242392695308	Unstable
4	4	1.169017110900751	0.853030024685988	1.175360571823227	-1.198713808417493	0.003341891865752	0.003341891865752	Unstable
5	5	1.049243542928413	0.873291572265621	1.230505473370170	-1.206132848168523	-0.003079362048548	-0.003079362048548	Stable
6	6	0.939963292993000	0.894559360908568	1.278531052602857	-1.215557605334053	-0.009000877787257	-0.009000877787257	Stable
7	7	0.840433902936340	0.916687323361620	1.320064198703322	-1.226859838284000	-0.014413742538810	-0.014413742538810	Stable
8	8	0.749777406382300	0.939527330300970	1.355776513982821	-1.239873723400826	-0.019326803450072	-0.019326803450072	Stable
9	9	0.667408211326566	0.962961525676744	1.386195513369527	-1.254462306641234	-0.023749609517755	-0.023749609517755	Stable
10	10	0.592909229642944	0.986891752236169	1.411758528312535	-1.270502017400843	-0.027694867417662	-0.027694867417662	Stable
11	11	0.525774913923535	1.011222524546920	1.432911712108063	-1.287850045472669	-0.031186239537126	-0.031186239537126	Stable
12	12	0.465447455697186	1.035863257087345	1.450096501288647	-1.306352986247735	-0.034255135419806	-0.034255135419806	Stable
13	13	0.411309545785799	1.060727818628416	1.463752323345303	-1.325849793476946	-0.036939012575735	-0.036939012575735	Stable
14	14	0.362684374304332	1.085734532233732	1.474316596727524	-1.346175595152188	-0.039279468540772	-0.039279468540772	Stable
15	15	0.318998312980353	1.110814036089623	1.482168737166756	-1.367184229213073	-0.041314903438275	-0.041314903438275	Stable

16	16	0.280002047796621	1.135920330741634	1.487549152755504	-1.388775785518645	-0.043072272611495	-0.043072272611495	Stable

Table 5: Predicting the type of stability for every week using the initial condition: [2.0, 1.0, 1.2]

Example	Time (weeks)	G_e	X_e	I_e				TOS
1	1	2.000000000000000	1.000000000000000	1.200000000000000	-1.377293729281919	0.019146864640960	0.019146864640960	Unstable
2	2	1.767780874636571	1.020638210845884	1.300795533979488	-1.380552624798044	0.010457206976080	0.010457206976080	Unstable
3	3	1.559333843812441	1.043180052387605	1.387933837575616	-1.387042746571093	0.002431347091743	0.002431347091743	Unstable
4	4	1.372436611090665	1.067342054054937	1.462841568615416	-1.396542098619937	-0.004899977717500	-0.004899977717500	Stable
5	5	1.205130029748394	1.092871077673791	1.526811518639845	-1.408820727306014	-0.011525175183888	-0.011525175183888	Stable
6	6	1.055692658170668	1.119542135447115	1.581012933871651	-1.423642805480482	-0.017449664983316	-0.017449664983316	Stable
7	7	0.922561958598416	1.147159695861423	1.626478044071552	-1.440769795155247	-0.022694950353089	-0.022694950353089	Stable
8	8	0.803895482105056	1.175524846655160	1.664318182946639	-1.459911446549874	-0.027306700052643	-0.027306700052643	Stable
9	9	0.698582044742822	1.204491202919447	1.695334865587145	-1.480846077747005	-0.031322562586221	-0.031322562586221	Stable
10	10	0.605623198535929	1.233931201796222	1.720241260153006	-1.503359105733071	-0.034786048031576	-0.034786048031576	Stable
11	11	0.523919980182181	1.263724270142790	1.739740827783576	-1.527225635328980	-05.03774931740690	-0.037749317406905	Stable
12	12	0.452272911052978	1.293756824531821	1.754527322597618	-1.552216540027720	-0.040270142252050	-0.040270142252050	Stable
13	13	0.389382297598027	1.323922282017439	1.765284702033439	-1.578103870662483	-0.042409205677478	-0.042409205677478	Stable
14	14	0.334205573643360	1.354134385946017	1.772576846310075	-1.604696657895285	-0.044218864025367	-0.044218864025367	Stable
15	15	0.286165211301376	1.384334194997889	1.776781771739833	-1.631858999729205	-0.045737597634342	-0.045737597634342	Stable

16	16	0.244592262207210	1.414465570761683	1.778278067055740	-1.659457360036542	-0.047004105362571	-0.047004105362571	Stable

Table 6: Predicting the type of stability for every week using the initial condition: [2.4, 1.2, 1.44]

Example	Time (weeks)	G_e	X_e	I_e				TOS
1	1	2.400000000000000	1.200000000000000	1.440000000000000	-1.565704192165468	0.013352096082734	0.013352096082734	Unstable
2	2	2.078583973113695	1.225077678256114	1.560276706168449	-1.572051217265885	0.003986769504886	0.003986769504886	Unstable
3	3	1.795703710806424	1.252399159173191	1.661942761807868	-1.582518613324498	-0.004440272924347	-0.004440272924347	Stable
4	4	1.547141030364899	1.281583178299657	1.747271323572237	-1.596726112674335	-0.011928532812661	-0.011928532812661	Stable
5	5	1.329211771054882	1.312296216153492	1.818284139698725	-1.614289640718100	-0.018503287717696	-0.018503287717696	Stable
6	6	1.138739378036141	.1344248708862007	1.876770032993366	1.634830424156084	-0.024209142352962	-0.024209142352962	Stable
7	7	0.972851789809172	1.377196461351128	1.924262999800430	-1.657980916786032	-0.029107772282549	-0.029107772282549	Stable
8	8	0.828114993565527	1.410887038809187	1.962445174272257	-1.683324536157762	-0.033631251325713	-0.033631251325713	Stable
9	9	0.702664962681337	1.445149786108554	1.992424399576042	-1.710523477657405	-0.037163154225574	-0.037163154225574	Stable
10	10	0.594623758145508	1.479831547814686	2.015230509849712	-1.739300220792509	-0.040115663511088	-0.040115663511088	Stable
11	11	0.501971410319925	1.514789181533379	2.031869184774878	-1.769357658609170	-0.042565761462104	-0.042565761462104	Stable
12	12	0.422545918939456	0.422545918939456	2.043321949576836	-1.800405717276422	-0.044591920317173	-0.044591920317173	Stable
13	13	0.354380595605924	1.585019551437594	2.050452356182456	-1.832189698414714	-0.046264926511440	-0.046264926511440	Stable
14	14	0.296363804244523	1.620104401963670	2.053823702306295	-1.864535213268967	-0.047634594347351	-0.047634594347351	Stable
15	15	0.247339733793971	1.655076284115501	2.053969528489152	-1.897280399524664	-0.048747942295419	-0.048747942295419	Stable

16	16	0.206090435930227	1.689872294026915	2.051407008546883	-1.930274159958892	-0.049649067034012	-0.049649067034012	Stable

Table 7: Predicting the type of stability for every week using the initial condition: [2.8, 1.4, 1.68]

Example	Time (weeks)	G_e	X_e	I_e				TOS
1	1	2.800000000000000	1.400000000000000	1.680000000000000	-1.755260009887254	0.008130004943627	0.008130004943627	Unstable
2	2	2.376237406443352	1.429514090307338	1.819341123332345	-1.765083529130931	-0.001715280588203	-0.001715280588203	Stable
3	3	2.010626376970472	1.461596087633043	1.934492469921810	-1.779901053109476	-0.010347517261784	-0.010347517261784	Stable
4	4	1.695846934155151	1.495756437076063	2.028832853499341	-1.799130232358099	-0.017813102358982	-0.017813102358982	Stable
5	5	1.425592607482672	1.531575833414649	2.105308680570491	-1.822201769315749	-0.024187032049451	-0.024187032049451	Stable
6	6	1.194610646152120	1.568701479865507	2.166444990175466	-1.848582044366231	-0.029559717749638	-0.029559717749638	Stable
7	7	0.997878057135960	1.606834514364914	2.214435110721615	-1.877752574922659	-0.034040969721127	-0.034040969721127	Stable
8	8	0.829833264982193	1.645675008498450	2.251594264276433	-1.909149821079766	-0.037762593709343	-0.037762593709343	Stable
9	9	0.687655639875041	1.685033772549146	2.279343576472432	-1.942406060677113	-0.040813855936017	-0.040813855936017	Stable
10	10	0.568193205681339	1.724733860784115	2.299077292273774	-1.977151352366075	-0.043291254209019	-0.043291254209019	Stable
11	11	0.468119165980902	1.764611936624864	2.312142399079776	-2.013029173911249	-0.045291381356808	-0.045291381356808	Stable
12	12	0.384110146635775	1.804522578946719	2.319793585679588	-2.049712463538351	-0.046905057704184	-0.046905057704184	Stable
13	13	0.314056876830470	1.844366650230297	2.322888603366728	-2.086971556002602	-0.048197547113847	-0.048197547113847	Stable
14	14	0.256163126282499	1.884063884738573	2.322141704759139	-2.124616064521928	-0.049223910108322	-0.049223910108322	Stable
15	15	0.208542598212895	1.923540179024467	2.318242927959780	2.318242927959780	-0.050035222263072	-0.050035222263072	Stable

16	16	0.169293826564768	1.962729232726343	2.311839993364677	-2.200374377618227	-0.050677427554058	-0.050677427554058	Stable

What can we learn from Table 1? As the independent variable time (t) in the unit of weeks ranges from week one (1) to week thirteen (13), we have found thirteen (13) valid steady states solutions which are dominantly unstable because of the existence of two positive eigenvalues and one negative eigenvalue. Therefore, on the basis of the sign method of stability the thirteen steady state solutions are considered unstable. The two (2) positive eigenvalues contribute to the unbounded growth of the solution trajectories whereas the negative eigenvalue contribute to the decaying behaviour of the solution trajectories overtime. We have also observed that the earlier observed instability changes to a dominant stability ranging from the fourteenth (14^{th}) week to sixteenth (16^{th}) week. In this context the bifurcation interval has occurred between the thirteenth (13^{th}) week and fourteenth (14^{th}) week. These observations are specific to the initial condition: [0.4, 0.2.0.24]

From Table 2, we have made the following observations: As the independent variable time (t) in the unit of weeks ranges from week one (1) to week eight (8), we have found eight (8) valid steady states solutions which are dominantly unstable because of the existence of two positive eigenvalues and one negative eigenvalue. Therefore, on the basis of the sign method of stability the eight (8) steady state solutions are considered unstable. The two (2) positive eigenvalues contributes to the unbounded growth of the solution trajectories whereas the negative eigenvalues contributes to the decaying behaviour of the solution trajectories overtime. We have also observed that the earlier observed instability changes to a dominant stability ranging from the ninth (9^{th}) week to sixteenth (16^{th}) week. In this context the bifurcation intervals have occurred between the eighth (8^{th}) and ninth (9^{th}) week. These observations are specific to the initial condition: [0.8, 0.4, 0.48]

Our present observations are similar to our predicted results in Table 3 through to Table 7. Therefore, on the basis of this analysis, we are proposing an appropriate health policy should be put into place to monitor the changes in the initial conditions in order to mitigate against the health implication of an increase in the glucose concentration level.

Conclusion

The impact of varying the initial condition has been considered on the type of stability using MATLABODE45 numerical scheme. We have discovered that as the initial data increases in its multiples, the bifurcation intervals occur beforehand and stability sets in earlier than previous times when lower initial data were utilized.

Recommendations

In view of this novel contribution, we hereby make the following useful recommendations:

(1) The effect of varying G_b and I_b model parameters on the type of stability.
(2) Modeling the type of stability in terms of comparing numerical methods.

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