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Report on the PhD dissertation *Mathematical analysis of a new model of bone pattern formation* **by Paramita Chatterjee**

The work concerns some mathematical aspects of a model introduced by T. Glimm, R. Bhat and S.A Newman in 2014 (Journal of Theoretical Biology 34, 86-108) describing the morphogenesis and patterning of the avian limb skeleton. Ms Chatterjee is a co-author of two papers, one mathematical research paper, joint with her PhD supervisor, on some other subject and one survey paper on the topic of the thesis written jointly with the supervisor and T.Glimm. It seems that none part of the thesis was ever published. Most of the investigations concern model (1.11) -(1.16) (c.f. dissertation) which is a modification of model (1.1) -(1.6) (c.f. dissertation). To simplify the reading of this report the main system of equations studied in the thesis is formulated below with use of a more convenient notation then the original one. The problem is to prove that there exist functions $R = R(t,x,u,v)$, $w_i = w_i(t,x)$, $i = 1,2$ such that

$$\frac{\partial R}{\partial t} = d_R \Delta_x R - \nabla \cdot R(K(R) - \frac{\partial}{\partial u} g_1(w_1, w_2, u) R - \frac{\partial}{\partial v} g_1(w_1, w_2, v) R, \qquad (0.1)$$

$$\frac{\partial w_1}{\partial t} = d_1 \Delta w_1 + a_1 \int_0^{+\infty} \int_0^{+\infty} vRdudv - w_1 , \qquad (0.2)$$

$$\frac{\partial R}{\partial t} = d_2 \Delta w_2 + a_2 \int_0^{+\infty} \int_0^{+\infty} uRdudv - w_2 , \qquad (0.3)$$

where (t,x,u,v) belongs to some domain $(0,T)\times\Omega\times(0\,,+\infty)\times(0\,,+\infty)$ and $d_R\,, d_1\,, d_2\,, a_1\,, a_2$ are positive constants. The functions g_1 and g_2 are smooth bounded functions while $K = K(R)$ is an integral non-local operator modeling adhesion of cells with density R and w_i are densities of some ligands playing the role in the process of morphogenesis of limb skeleton. The system is supplemented by suitably regular initial conditions and boundary condition of homogeneous Neumman type on the boundary of Ω and Dirichlet homogeneous boundary conditions for $u = v = 0$. The main difficulty from the mathematical view point stems from the fact that the main operator in the first equations is degenerate as the terms $\frac{\partial^2 R}{\partial u^2} + \frac{\partial^2 R}{\partial v^2}$ are not present in (0.1) and the first equation is neither parabolic nor hyperbolic. It is worth to underline that the case when $K = 0$ in (0.1) i.e. the adhesive transport of cells is precluded the problem is significantly easier to study. The well-posedness of the system i.e. the existence of solutions and their uniqueness are not *a priori* clear and this was the subject of investigation for Ms Chatterjee.

General remarks about the thesis

- The work does not concern modeling issues, simulations, correspondence to real life data- features which would be expected in the thesis related to applied mathematics or mechanical engineering.
- Most of analysis concern some simplified versions of model (0.1)-(0.3) e.g. all Part II being nearly one half of the work deals with application of the theory of potential to some linear equation being a simplification of the first equation (0.1). Very similar problems have been studied in the literature using other methods which was not mentioned in the bibliography .

- The notational convention in all body of the text is really weird and non-intuitive, for instance c_8^1, c_8^8 denote some independent variables because the notation corresponds to the names of some chemical compounds in the original model. What for is this strange notation from the original paper taking into account that the work is purely mathematical without any detailed reference to the modeling issues.
- Many papers related to the degenerate parabolic problems, studied in Part II, are lacking in the bibliography.
- The methods used in the paper are old fashioned. Moreover the analysis of linear problems presented in Part II is not used in Part III which is devoted to the study of the original nonlinear model (0.1)-(0.3)During last half of the century the concepts of weak solutions proved to be more suitable for studying global-in-time solutions to the class of degenerate problems - the class to which (0.1)-(0.3) belongs. It seems that the semigroup theory and fixed point methods could be more beneficial for studying solutions to this class of problems.

Detailed remarks

1. Paradoxically the original model (1.1) -(1.6) (c.f. dissertation) seems to be easier to analyze then the modified one ((0.1)-(0.3) since it is decoupled as the first equation (1.1) (c.f. dissertation) is independent from the remaining equations and at least in the case of simplified adhesion operator the existence of solutions can be proved by means of fixed point method.
2. Part II concerns only various linear problems related to the first equation (0.1). The results are not surprising in view of the existing literature. Problem (3.1) (c.f. dissertation) belongs to the class of linear degenerate parabolic problems. The related Cauchy problem was extensively studied using regularization techniques or semigroup approach:

   (a) Oleinik, O.A., On the smoothness of the solutions of degenerate elliptic and parabolic equations, Sov. M. DokL, (1965), 972-976.

   (b) Igari, K., Degenerate Parabolic Differential Equations, Publ. RIMS, Kyoto Univ. 9 (1974), 493-504.

   (c) Wong-Dzung B., L^p-Theory of degenerate-elliptic and parabolic operators of second order, Proc. Royal Society of Edinburgh. Sec A, 95 (1983), 95-113.

   The authoress used classical Green function approach, probably being unaware of earlier works and methods which could be used to solve the problem. It is also worth to mention at least a few papers from the long list of works devoted to structured population models in which the method of characteristic was linked with the semigroup theory to represent the solution of quiet similar problem of solution to the structured population with diffusion in space.

   (a) Webb, G.F., Population Models Structured by Age, Size, and Spatial Position, in Megal, P., Ruan, S. eds. Structured Population Models in Biology and Epidemiology, Springer, (2008).

(b) Kato, N. Linear Size-structured Population Models with Spacial Diffusion and Optimal Harvesting Problems, Math. Model. Nat. Phenom. Vol. 9, No. 4, (2014) , pp. 122130

3. The argumentation and the role of results in section 5 and 6 are not clear to me. The way of reasoning is hard to grasp since often there appear some parameters which are not defined e.g. r and s on page 24. line 4. and statements and results are not well separated. It makes reading difficult, see Sec. 5.1..The style of reasoning in which a final statement e.g. lemma is preceded by consecutive assumptions made ad hoc is not used in contemporary mathematics. The correct schema is in the inverse order- first assumptions and assertions and then proofs. Yet another reading obstacle of the text is due to making references to definitions which are in forthcoming lines somewhere in next sections (see e.g. Lemma 9.1.). Why in lemma 9.1 is there the condition $T_k \geq \mathcal{T}_1$?

4. In Part II the method of Rothe is used to prove the existence of local in time solutions to a simplified version of the model (0.1)-(0.3) in which the nonlocal adhesion operator (the term with K) is replaced by some linear advection operator. The method demands very high regularity of initial data of class C^4 which is certainly related to the method itself rather then the nature of the problem. Such result is not satisfactory for farther numerical studies of the model. I would expect that global in time solutions to the model defined in some suitable weak sense do exist since all nonlinearities which appear in the model are bounded.

5. Language editing of the text is fairly good but the style of mathematical content is far from being perfect. There are undefined parameters e.g. what are $d\tilde{P}$, D_{ϱ_0}, $\tilde{c}_1$ on page 2? I detected few misprints or typographical errors e.g the lack of "$\int$" in (1.3) (c.f. dissertation) or $\frac{1}{\Delta t}$ in the line between (15.4) and (15.5) (c.f. dissertation).

Concluding remarks

The problem posed in the thesis in its full generality turned out to be difficult, so that only existence-uniqueness problems ware investigated without apparent references to qualitative properties of solutions and the modeling issues. The authoress revealed her determination in studying a difficult scientific problem and in some restricted sense showed its solution. The dissertation satisfies minimal requirements to receive a doctor degree in Poland.

Prof. Dariusz Wrzosek

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