Institution: University of Leicester

Unit of Assessment: Unit of Assessment 10 - Mathematics

Title of case study: Efficient planning of healthcare for people living in Russia's Far North

1. Summary of the impact

Russia's Far North region, located mainly north of the Arctic Circle, is home to around seven million people. Living conditions are harsh and a combination of extreme climate, genetics, diet and behaviour mean delivering healthcare has multiple challenges [**3**.7]. Mathematical methods developed within the Unit have been used to monitor the health of the population of Russia's Far North, and thereby enabled Government bodies to improve the planning and provision of healthcare, resulting in increased well-being within the population, and efficiency gains for the administration.

2. Underpinning research

The Department of Mathematics at the University of Leicester has a strong research group in analysis of dynamical models of adaptation [**3**.1, **3**.2]. The group is led by Professor Alexander N Gorban and Dr Ivan Tyukin, both of whom have been in Leicester throughout the REF period, and includes research assistants (Tyukina, Mirkes, and Penkova) and PhD students.

The group has created a system of dynamic models of physiological adaptation based on the quantitative formalisation of endocrinologist Hans Selye's ideas about the general adaptation syndrome and adaptation resources. Studying how systems facing stress react in terms of becoming more interdependent and volatile reveals patterns that help to predict when a crisis may occur and the likelihood of death or recovery. A key finding is that, as the crisis approaches, systems become more dependent on each other but at the same time more likely to react differently.

Research in this area began in 1987 and explored critical conditions for development of babies in the first week of life, and the work of the Unit in Leicester has built on this early work. Criteria for early evaluation of the risk of such crises are developed on the base of these dynamic models [**3**.1, **3**.3, **3**.4]. These criteria are based on the analysis of the dynamics of correlations between physiological attributes in ensembles of similar systems.

In 2009, Gorban and Tyukina, working with Professor Elena Smirnova from the Siberian Federal University, Russia, published [**3**.3] which studied ensembles of similar systems under load of environmental factors. It showed that, typically, when the load increases above some threshold, then the adapting systems become more different (variance increases), but the correlation increases too. If the stress continues to increase then the second threshold appears: the correlation achieves maximal value, and start to decrease, but the variance continue to increase. It proposed that, in many applications, this second threshold is a signal of the approach of a fatal outcome. This effect was supported by experiments and observation of groups of humans, mice, trees, grassy plants, and on financial time series.

In 2010 the same academic team published [**3**.1], in which a general approach to the explanation of the effect through dynamics of individual adaptation of similar non-interactive individuals to a similar system of external factors was developed. Qualitatively, this approach followed Selye's idea concerning adaptation energy.

In 2011, the same researchers, joined by L.I. Pokidysheva, Professor of Computer Science, Siberian Federal University, Russia, published [**3**.4] which exploits, criticizes and develops further the concept of the "Law of the Minimum". This concept, originally applied to plant or crop growth (Justus von Liebig, 1840) states that growth is controlled by the scarcest resource (limiting factor).

Violations of this law in natural and experimental ecosystems were also reported.

Leicester's research studied models of adaptation in ensembles of similar organisms under the load of environmental factors and proved that violation of Liebig's law follows from adaptation effects. If the fitness of an organism in a fixed environment satisfies the Law of the Minimum then adaptation equalizes the pressure of essential factors and, therefore, acts against Liebig's law. This is the Law of the Minimum paradox: if for a randomly chosen pair "organism-environment" the Law of the Minimum typically holds, then in a well-adapted system, we have to expect violations of this law.

For the opposite interaction of factors (a synergistic system of factors which amplify each other), adaptation leads from factor equivalence to limitations by a smaller number of factors. Some other typical forms of organization of the system of factors are studied. The most important of them is synergetic interaction of factors and combinations of synergetic and Liebig's systems.

For analysis of adaptation, the research developed a system of mean-field multi-agent models of adaptation based on Selye's idea of the universal adaptation resource (adaptation energy). These models predict that under the load of an environmental factor a population separates into two groups (phases): a less correlated, well adapted group and a highly correlated group with a larger variance of attributes, which experiences problems with adaptation. Some empirical data were presented and evidences of interdisciplinary applications to econometrics were discussed. These models and criteria are intensively used in medical applications [**3**.5, **3**.6] and in financial econometric studies of crises [**3**.3].

3. References to the research

Grant

"Development of Systems of Optimal Control of Adaptation by Controllable Crises", the Russian Federal Ministry of Education and Science, Russian Federal Program "Scientific and scientific-pedagogical personnel of innovative Russia", State Contract # 02.740.11.5086, Oct 2009 – Sept 2011. This grant was awarded for research and development under the supervision of foreign scientists. The foreign supervisor and PI of this project was Prof. Gorban. Duration of the project: 2009-2010. The value was 2,000,000 RUR.

Publications

1. A.N. Gorban, E.V. Smirnova, T.A. Tyukina, Correlations, risk and crisis: From physiology to finance, Physica A, Vol. 389, Issue 16, 2010, 3193-3217. DOI: 10.1016/j.physa.2010.03.035

2. I. Tyukin. Adaptation in Dynamical Systems, Cambridge University Press, 2011. ISBN:9780521198196

3. A.N. Gorban, E.V. Smirnova, T.A. Tyukina, General Laws of Adaptation to Environmental Factors: from Ecological Stress to Financial Crisis. Math. Model. Nat. Phenom. Vol. 4, No. 6, 2009, 1-53. DOI: 10.1051/mmnp/20094601

4. A.N. Gorban, L.I. Pokidysheva, E,V. Smirnova, T.A. Tyukina. Law of the Minimum Paradoxes, Bull Math Biol, 73(9) (2011), 2013-2044. DOI: 10.1007/s11538-010-9597-1

5. V. N. Razzhevaikin, M. I. Shpitonkov, The model of correlation adaptometry and its use for estimation of obesity treatment efficiency, Russian Journal of Numerical Analysis and Mathematical Modelling 26 (6), 565-574 (2011), DOI: 10.1515/rjnamm.2011.033

6. L. Pokidysheva, I. Ignatova, Principal Component Analysis Used in Estimation of Human's Immune System, Suffered from Allergic Rhinosinusopathy Complicated with Clamidiosis or without

it, Advances in Intelligent Analysis of Medical Data and Decision Support Systems, Studies in Computational Intelligence, Vol. 473, Springer 2013, pp. 147-156.

7. Is Arctic medicine a distinct science? A Russian perspective, Dimitrii G. Tikhonov, Int J Circumpolar Health 2013, 72: 21248 - http://dx.doi.org/10.3402/ijch.v72i0.21248

4. Details of the impact

The research has impacted on the provision of healthcare in the Far North of Russia, involving thousands of patients. This is the main source of impact. However, the research has also received media attention [**5**.4] and [**5**.5] in explaining how economic stress leads to financial crisis **[3**.3].

Healthcare

The provision of healthcare to the people of the Far North is complex. The health of the population is influenced by many factors, including the physical environment, climate, genetics, health-related behaviours, and living conditions. Healthcare provision in the Far North faces serious and unique challenges, and has led to calls within Russia to recognise a distinct branch of science called Arctic Medicine, in the same way that Tropical Medicine is globally recognised. Identification of this need for specialist healthcare provision, further fuelled by plans for intensive industrial development in the Far North, has led to the establishment of the Scientific Research Institute of Medical Problems of the North.

The official mission of the Institute is the "preservation and development of the health, longevity and active life of the human population of the Far North and Siberia''. This institute not only has a research function but also a huge clinical mission, It has been directly involved in a number of activities, based on the work of the Leicester team, discussed below, which have improved the health and well-being of inhabitants of the Far North. To fulfil its mission, the Institute carries out research, provides medical treatment and organises expeditions to the region to monitor the health of the population, consult with practitioners and prepare recommendations for local authorities and medical service providers.

The Unit's analysis of dynamical models of adaptation research has been used by the Institute to reveal the mechanisms of human adaptation to the harsh living conditions in the Far North.

The director of the Institute, VT Manchuk, one of the most prominent Russian experts in polar medicine, has testified to the value of the research findings in guiding the organisation's expeditions and monitoring work. In a letter, he stated that: "the developed methods of adaptation monitoring and control are now widely used in the practice of health monitoring in the Russian Far North. Many groups and regions and thousands of people have been monitored with the help of this technique.'' [**5**.1]

Professor Manchuk has also provided several specific examples of the ways in which the research had been applied. These include:

- A study of 4,770 inhabitants of Evenkia (a district of Krasnoyarsk) including 1,248 natives and 3,522 migrants showed the difference in response to various allergic disorders. The results have been used in recommendations to the local authorities concerning treatment of the different groups of people [**5**.2].

- A study of 305 Eastern Siberians between the ages of 15 and 79 of the interaction between intracellular pathogens with allergic diseases. Adaptometric methodology developed in Leicester allowed for estimation of the strength of the immune system to such diseases, and diagnosis of the adaptation of the system at the cellular level [**5**.3].

- The monitoring of gastric secretory function in children living in northern conditions (500 patients) which led to treatment and recommendations for differentiated treatment according to ethnicity and diet [**5**.1].

- Development of differentiated interventions for different ethnic groups of the Far North, who demonstrate different adaptation response to environmental change (pollution, global warming, translocation). A study of 388 patients using adaptometry identified the different factors which are most harmful to each group.

Not only has the research from Leicester allowed for specific intervention such as detailed above, but it has also led to a systematic approach to the monitoring of patients: (i) identification of groups who need treatment; (ii) identification of high risk groups; (iii) evaluation of new treatments and interventions. This more systematic approach has been applied across many thousands of patients in addition to the cases mentioned above.

Manchuk states in his letter to the University that: "there are many other examples of applications involving in total thousands of patients for monitoring, consultation and treatment. The methods for adaptation modelling, monitoring and control developed by Professor Gorban and his team already have valuable impact on the health monitoring and management in Russian Far North and Siberia". [**5**.1]

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. Factual statement from Member of Russian Academy of Medical Sciences, Director of the State Research Institute for Medical Problems of Northern Regions, Krasnoyarsk, Russia.

2.I.A. Ignatova, S.V. Smirnova, L.I. Pokidysheva. *Allergic Rhinosinusopathy in Inhabitants of Siberia. System Analysis*, Germany: Lambert Academic Publishing, 2012, 168 pp. ISBN: 978 -3-659-17861-0.

3.L. Pokidysheva, I. Ignatova, Principal Component Analysis Used in Estimation of Human's Immune System, Suffered from Allergic Rhinosinusopathy Complicated with Clamidiosis or without it, Advances in Intelligent Analysis of Medical Data and Decision Support Systems, Studies in Computational Intelligence, Vol. 473, Springer 2013, pp. 147-156.

4. ScienceDaily: Plants and Animals Under Stress May Provide the Key to Better Stock Market Predications (Nov. 3, 2010), http://www.sciencedaily.com/releases/2010/11/101103082312.htm.

5. NewsRoom America: Stressed Plants And Animals May Help Predict Stock Market http://www.newsroomamerica.com/story/71963/stressed_plants_and_animals_may_help_predict_stock_market.html.