Letters

PSO/ACO Algorithm-based Risk Assessment of Human Neural Tube Defects in Heshun County, China*

LIAO Yi Lan[1,2], WANG Jin Feng[1,#], WU Ji Lei[2], WANG Jiao Jiao[1,3], and ZHENG XiaoYing[2,#]

1. The State Key Laboratory of Resources and Environmental Information System, Institute of Geographical Sciences and Nature Resources Research, Chinese academy of Sciences, Beijing 100101, China; 2. Institute of Population Research, Peking University, Beijing 100871, China; 3. College of Geoscience and Surveying Engineering, China University of Mining & Technology, Beijing 100083, China

Abstract

Objective To develop a new technique for assessing the risk of birth defects, which are a major cause of infant mortality and disability in many parts of the world.

Methods The region of interest in this study was Heshun County, the county in China with the highest rate of neural tube defects (NTDs). A hybrid particle swarm optimization/ant colony optimization (PSO/ACO) algorithm was used to quantify the probability of NTDs occurring at villages with no births. The hybrid PSO/ACO algorithm is a form of artificial intelligence adapted for hierarchical classification. It is a powerful technique for modeling complex problems involving impacts of causes.

Results The algorithm was easy to apply, with the accuracy of the results being 69.5%±7.02% at the 95% confidence level.

Conclusion The proposed method is simple to apply, has acceptable fault tolerance, and greatly enhances the accuracy of calculations.

Key words: Neural tube birth defects; GIS; PSO/ACO algorithm; Hierarchical classification; Risk map

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INTRODUCTION

According to the March of Dimes Birth Defects Foundation, birth defects refer to "any anomaly, functional or structural, that presents in infancy or later in life and is induced by events preceding birth, whether inherited, or acquired"[1]. Varying from minor cosmetic irregularities to life-threatening disorders, birth defects are a major cause of infant mortality and a leading cause of disability[2]. Neural tube defects (NTDs) are one of the most common forms of birth defects, often occurring between the third and fourth weeks of gestational age. They result in structural defects that occur anywhere along the neuroaxis from the developing brain to the sacrum, and often result in the exposure of neural tissue[3]. China has a high occurrence of NTDs, which account for up to one third of stillbirths and one quarter to one third of neonatal deaths[4]. Data collected from a

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#Correspondence should be addressed to ZHENG Xiao Ying, Tel: 86-10-62756331. Fax: 86-10-62751976. E-mail: xzheng@pku.edu.cn; and to WANG Jin Feng, Tel: 86-10-64888965. Fax: 86-10-64889630. E-mail: wangjf@igsnrr.ac.cn

Biographical note of the first author: LIAO Yi Lan, female, born in 1980, Ph.D, assistant researcher, majoring in spatial analysis and its application in epidemiology.

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hospital-based surveillance system revealed a prevalence of NTDs of approximately 27.4 per 10 000 births in 1987. As birth defects can often be prevented, early intervention is important in minimizing their consequences. However, the etiology of the vast majority of birth defects is still unknown.

Recently, geographical information system (GIS) technology has emerged as an innovative and important component of many public health and epidemiology projects. One of the most useful functions of GIS in terms of epidemiology is in risk assessment[5]. It can be used to describe the spatial variation in disease incidence for explorative and descriptive purposes. It can also be used to identify areas of unusually high risk where preventive action should be taken. More significantly, GIS can provide a reliable map of disease risk in a region and thus also important clues about the etiology of a disease[6-7].

Disease rate, and in particular the standardized morbidity ratio, is often used as a measure of relative risk. However, disease rates cannot be calculated when birth data are missing or no births have occurred in a geographical area. Researchers have proposed numerous methods of using GIS to assess the risk of birth defects. Some methods of mapping relative risk are based on regression models of relative risk and use information about geographical locations and established risk factors. However, spatial epidemiological investigations of NTDs are mostly exploratory and are based on limited knowledge of putative risk factors. Approaches such as empirical Bayesian estimation[1,8-9] and spatial filtering[10-11] have exploited the spatial correlation of cases to overcome this problem. However, birth defect cases actually have little effect on one another, especially in rural areas where they are low-probability events. Use of statistical or geo-statistical techniques that do not account for relevant physical laws and that are not based on deductively valid principles often leads to nonsensical inferences and uninformative maps[12]. There is therefore a need to develop suitable techniques for assessing the risk of birth defects among different human groups.

In some sense, assessing the NTD risk based on relationships between spatial attributes and the incidence of NTDs is a classification problem. The hybrid particle swarm optimization/ant colony optimization (PSO/ACO) algorithm is a form of artificial intelligence adapted for hierarchical classification. This hybrid algorithm follows the top-down approach for hierarchical classification, using the predictions of higher-level classes to guide the search for rules predicting lower level classes[13]. Since it was first developed in 2005, the hybrid PSO/ACO algorithm has gained a reputation as a powerful technique for modeling complex problems involving impacts of causes[14-15]. In the present study, we used the hybrid PSO/ACO algorithm to assess the risk of birth defects. We first used training data to determine relationships between spatial attributes and the incidence of NTDs based on the PSO/ACO algorithm. We then used these decision rules to determine the risk of birth defects in other areas. Because different birth defects may be caused by different risk factors, we limited our research to NTDs. The results indicate that this method is simple to apply, has acceptable fault tolerance, and greatly enhances the accuracy of calculations.

MATERIALS AND METHODS

Description of the Study Site

Shanxi province in the north has the highest rate of NTDs in China: 105.5 per 10 000 births in 1987 and 60.88 per 10 000 births in 1996-2002[16]. Thus, we selected Heshun, a county in Shanxi province, as the study area. Heshun is also one of the pilot regions for the National Birth Defect Intervention Project launched by the State Family Planning Commission.

Heshun lies in the Tai Hang Mountain Region (Figure 1). It consists of 326 administrative villages and has a total area of 2 250 km^2. Most resident are farmers whose living environments seldom change, and there has been no large-scale movement of inhabitants in the history of the region. Most types of birth defects designated by the World Health Organization can be found in Heshun, but NTDs predominate[1]. From 1998 to 2005, there were 7 880 births in Heshun and 187 NTDs. The inherited and congenital causes are similar among the NTDs in this region, but these factors explain only a small fraction of all NTDs.

Data Sources

The present analysis included all live births and stillbirths occurring in Heshun from January 1, 1998, to December 31, 2005. Births occurred at the hospital or at home, and mothers were residents of the county during that time period. Also included were

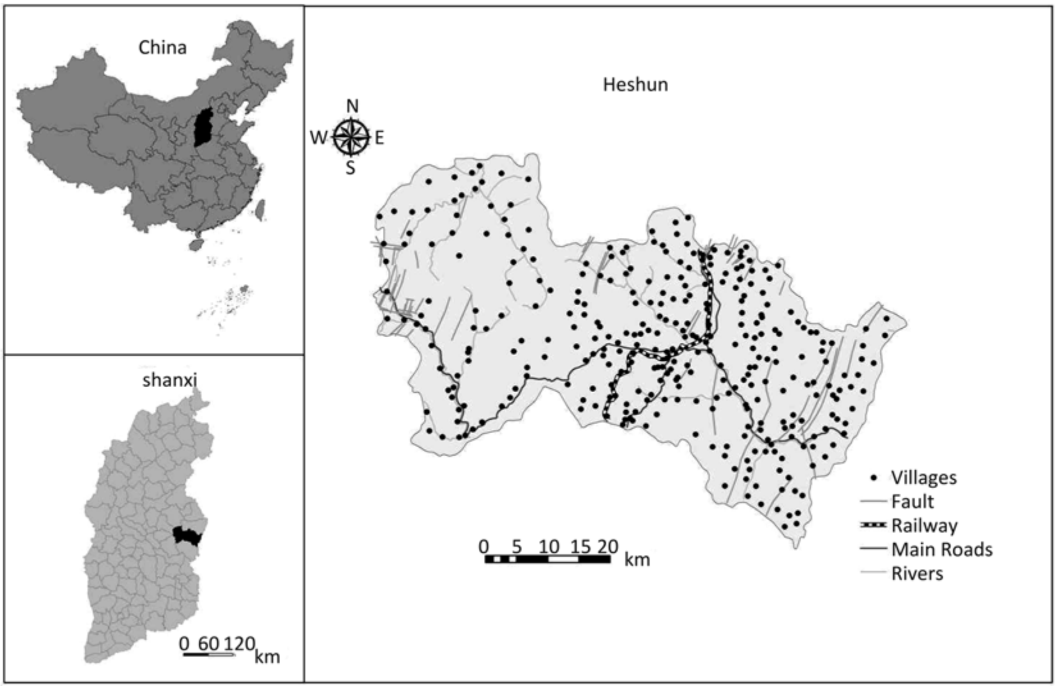

Figure 1. Heshun County.

all therapeutic abortions performed on residents of the area whose estimated delivery date fell within the time period of interest. All NTD cases, regardless of pregnancy outcome, were verified by doctors in the hospital. Records of NTD cases were collected from the local family planning department. NTDs included anencephaly, spina bifida, encephalocele, holoprosencephaly, and hydrocephalus, among others.

The local planning department declined to provide identifiers to link substantiated NTD cases to births, so we were unable to conduct the study at the individual level. Instead, we aggregated the NTD cases by village of mother's residence. The 326 villages were mapped using ArcGIS 9.2i. Because the main objective of this study was to estimate the disease risk based on the relationships between environmental risk factors and NTDs, towns were not included as the environmental factors are somewhat complex. In addition, birth defect registers in towns were not included.

The environmental factors of various villages were classified into socioeconomic and physical factors. The socioeconomic factors reported useful information on medical conditions (number of doctors), the per-capita income (per-capita net income), exposure to agricultural chemicals (use of fertilizers and pesticides), and crop yields (vegetable and fruit production) for every village from 1998 to 2005. Taking spatial interactions into account, we also collected these socioeconomic factors for neighboring villages within a specified distance. All socioeconomic data were provided by the Heshun statistical bureau. The physical factors included elevation, soil type, watershed, gradient, vegetation coverage (normalized difference vegetation index), access conditions (distance to main roads), pollution risk (influence of coal mines and distance to factories), and geological background (distance to faults) of the villages. The normalized difference vegetation index (NDVI) provides a standardized method of comparing vegetation greenness between satellite images and can be used as an indicator of relative biomass and greenness. The source of the NDVI dataset used in this study was the VITO (Flemish Inst. Technological Research, Belgium, http://www.vgt.vito.be). Furthermore, LI et al.[17] found that the occurrence ratio of NTDs in Heshun has a significant negative correlation with increasing distance from faults, so we considered the distance between villages and faults to be an important factor.

First, the hybrid PSO/ACO algorithm was used to find the relationship between risk factors and NTD risk. Then the acquired relationship was used to estimate NTD risk in the villages with no births. In this study, the NTD rate for each village in which babies had been born was regarded as its NTD risk (see Table 1). The selected risk factors were divided into numerical and categorical data. The numerical data were the number of doctors, the use of fertilizers and pesticides, per capita net income, vegetable and fruit production, NDVI, elevation, and the influence of coal mines. The categorical data were soil type, watershed, gradient, river buffer, road buffer, and fault buffer. All of the numerical data were discretized before being input PSO/ACO algorithm.

Table 1. Some Input Variables for the Hybrid PSO/ACO Algorithm

Variables Name	Initial Values	Corresponding Categorical Values
NTDs risk (unit: 1/1 000)	0	1
	0.1 ~ 50	2
	50.1 ~ 100	3
	More than 100	4
Soil type	leaching cinnamon soil	3
	cinnamon soil	4
	calcareous cinnamon soil	5
	infant cinnamon soil	7
	neural lithosols	20
	neural skeletisols	22
	calcareous skeletisols	23
	fluvo-aquic soil	27
River buffer (unit: m)	0-2 000	2
	2 001-4 000	4
	4 001-6 000	6
	6 001-8 000	8
	8 001-10 000	10
	10 001-12 000	12
Road buffer (unit: m)	0-2 000	1
	2 001-4 000	2
	4 001-6 000	3
	6 001-8 000	4
	8 001-10 000	5
	10 001-12 000	6
Gradient (unit: degree)	0-8	1
	8-15	2
	16-25	3
	>25	4
Fault buffer (unit: m)	0-2 000	2
	2 001-4 000	4
	4 001-6 000	6
	6 001-8 000	8
	8 001-10 000	10
	10 001-12 000	12
	12 001-14 000	14
	14 001-16 000	16

The Hybrid PSO/ACO Algorithm

We now explain more about why finding relationships between spatial attributes and the incidence of NTD is, in essence, a classification problem. Classification is the problem of assigning an individual or observation having k characteristics to one of two populations. The solution to the classification problem is a decision rule that enables one to assign a new individual or observation to the population most likely to be correct based upon historical sets of samples from the two populations[18]. In this article, we focus on extracting decision rules for epidemiology research using the hybrid PSO/ACO algorithm. The decision rules found in the sample data were used to classify the reference data.

The hybrid PSO/ACO algorithm is useful for hierarchical classification. An advantage of hierarchical classification is that it is easier to recognize problems and to find suitable and efficient approaches for solving them. In the hybrid PSO/ACO algorithm, classes are arranged in a tree structure in which each node (class) has only one parent. The algorithm discovers a set of rules for each internal node of the class hierarchy. The rules are of the form IF (conditions) THEN ($class_i$), where $class_i$ is one of the child classes of that internal node. Each rule predicts a single class, but the set of rules as a whole predicts all classes, because the algorithm guarantees that one or more rules will be discovered in the process of predicting each of the child classes[13]. This hybrid algorithm achieves a native support of nominal data by combining ideas from ant colony optimization and particle swarm optimization to create a classification meta-heuristic that supports both nominal and continuous attributes. The design of this hybrid algorithm was motivated by the fact that nominal attributes are common in data mining, but the algorithm can in principle be applied to other kinds of problems involving nominal variables[19].

The algorithm is applied in four stages (Figure 2). First is the use of the sequential covering approach to discover one classification rule at a time. The algorithm starts by initializing the rule set with the empty set. Then, for each hierarchical class level and for each of the classes to be predicted, the algorithm performs a WHILE loop. Every iteration of this loop performs one run of the PSO/ACO algorithm, returning the best rule discovered for predicting examples of the current class. Each rule is added to the rule set, and the examples correctly covered by that rule are removed from the sub-training set.

```
Initialize population
REPEAT for MaxInterations
  FOR every particle P
    /* Rule Creation */
    Set Rule R = "IF ∅ THEN C"
    FOR ever dimension d in P
      Use roulette selection to choose whether the state should be set
      to off or on. If it is on then the corresponding attribute-value pair
      set in the initialisation will be added to R otherwise, if off is
      selected nothing will be added.
    LOOP
    Calculate Quality Q of R
    /* Set the past best position */
    IF Q > P's Best past rule's (Rp) Quality Qp
      Qp= Q
      Rp = R
    END IF
  LOOP
  FOR every particle P
    Find best Neighbour Particle N according to N's Qp
    FOR every dimension d in P
      /* Pheromone updating procedure */
      IF best state selected for Pd = best state selected for Nd THEN
        pheromone_entry for the best state selected for Pd is
        increased by Qp
      ELSE
        pheromone_entry for the best state selected for Pd is
        decreased by Q
      END IF
      Normalize pheromone_entries
    LOOP
  LOOP
LOOP
```

Figure 2. Pseudo code for the hybrid PSO/ACO algorithm[20].

Second is moving the particle with respect to categorical (nominal, non-numeric) attributes. At each iteration, the value of each categorical attribute in the rule antecedent represented by each particle is chosen to give the particle a fixed position and thus quality.

The third stage is particle fitness (rule quality).The fitness of a given particle is based on the rule it represents and is given by the following measure of predictive accuracy:

Rule Quality = Sensitivity×Specificity = TP / (TP + FN) ×[1+ TP (1+k+TN + FP)], (1)

where TP is the number of cases that match both the rule antecedent (attribute values) and the rule consequent (class). These are desirable correct predictions. FP is the number of cases that match the rule antecedent but do not match the rule consequent. These are undesirable incorrect predictions. FN is the number of cases that do not match the rule antecedent but do match the rule consequent. These are undesirable uncovered cases and are caused by an overly specific rule. TN is the number of cases that do not match either the rule antecedent or the rule consequent. These are desirable and are caused by a rule's antecedent being specific to its consequent class. Finally, k is the number of classes.

The fourth stage is rule pruning. Rule pruning generalizes and simplifies the rule. It generalizes the rule by removing the most irrelevant terms and thus increasing the number of examples covered by the rule. It simplifies the rule by removing terms that make the rule overly specific, or that do not affect its quality.

Once the quality of each term in the rule was computed, one of two alternative rule pruning procedures was tried: (1) Selecting a fixed number N of relevant terms, where N is a parameter. To achieve a greater diversity of selected terms across different rules (i.e., to avoid selecting the same top-quality terms in all the rules in which they appear), we recomputed the quality of each term by multiplying the original quality value by a random number in the range [0,1]. Terms were then sorted by their updated quality values using merge sort, and only the top N terms were kept "turned on" in the pruned rule. We "turned off" the other terms by setting the corresponding attribute value to the off state in the particle representation. (2) Selecting a variable number of terms in proportion to the quality of the terms. For instance, if the quality of a rule term (i.e., its normalized value in the range [0,1]) was 0.6, then that term was preserved in the rule with a probability of 0.6 and therefore removed from the rule with the complementary probability of 0.4[19-20]. In the end, we used 10-fold cross-validation to calculate the accuracy of the PSO/ACO algorithm.

The algorithm software tool used in this study, PSO/ACO2 (http://www.mirrorservice.org/sites/dl.sourceforge.net/pub/sourceforge/p/project/ps/psoaco2/), was developed by Nicholas Holden. PSO/ACO2 is a GUI, Java implementation of the PSO/ACO rule induction algorithm. This software is inspired by Ant-Miner, but handles continuous attributes using PSO or Differential Evolution.

RESULTS AND DISCUSSION

Rule Extraction and Identification of Unseen Objects

A total of 123 decision rules were generated by the hybrid PSO/ACO algorithm. We can use these rules to identify unseen objects and build a knowledge base to discover the real causes of the disease. They can also be used to develop strategies to prevent or even control the disease by changing the local environment or improving living conditions[21].

Based on the quality of the rules, we selected four rules synthesized by the hybrid PSO/ACO algorithm and used them to analyze the influences of the risk factors. These rules are summarized in Table 2. As can be seen from these rules, various factors were associated with different levels of NTD risk. No one factor by itself explained the risk of NTDs. For example, Rule 3 found that the NTD risk increased suddenly when the use of pesticide was within a certain range. Although this conclusion is similar to that of Heeren et al.'s study[22], the use of pesticide alone did not guarantee an NTD risk of 3.

Table 2. Four Rules Extracted from the Hybrid PSO/ACO Algorithm

No.	Rules
1	IF fertilizer<=174.95 and NDVI<= 936.17 THEN risk=1;
2	IF doctor>=5 and fruit<=21.74 and pesticide<=4.93 and vegetable between 413.21 and 1 567.49 and elevation<=1 343.25 THEN risk=2;
3	IF road buffer =2 and pesticide between 0.99 and 2.94 and vegetable<=424.35 THEN risk=3;
4	IF fertilizer<=208.47 and net income <=5943.31 THEN risk=4.

These rules revealed that villages with vegetable production between 413.21 and 1567.49 ton/year would have a high risk of NTDs. In Heshun, most farmers consume their own vegetables, and in poor areas the locals often eat old sprouted potatoes. Sprouting blighted potato tuber is low in zinc, which is important for the development of the fetus. Long-term consumption of such tubers by pregnant woman could potentially lead to teratogenic complications in the baby, such as NTDs[23]. In a geographical-based health risk assessment, Wang et al.[24] also found that basic nutrition was more important than man-made pollution in terms of the spatial pattern of NTDs in Heshun. The increasing risk of NTDs with increasing distance to roads and decreasing net income reflects the poor health status of people who live in remote areas. These inequities in quality of life and accessibility to services must be improved. Furthermore, the rules showed that excessive use of fertilizers may increase the NTD risk. Although no data point to any particular fertilizer as causing birth defects, medical and public health departments should work to increase the public's knowledge about the importance of minimizing exposure to chemicals.

NTDs Risk Mapping

Figures 3(a) and 3(b) illustrate, respectively, the spatial distribution of NTD occurrences and the estimated NTD risk based on the hybrid PSO/ACO algorithm. The maps show two clusters with a high NTD risk in the central and southeast regions. The central region contains the majority of coal mines and high-pollution factories in the county. The government should work to reduce the effects of environmental pollution there. The southeastern region of Heshun County is mountainous and has a relatively complex geological background. In 2006, Li et al. verified that people residing near a geological fault have an increased risk of having a baby with an NTD. To reduce NTD risk in these areas, questions that must be answered are which microelements released from faults affect NTDs, and how they affect NTDs. The results of the risk estimation suggest that the government needs to adapt intervention measures to local conditions. However, Figure 3(b) shows that the algorithm obviously underestimated the NTD risk of the villages in the northwest region. The risk factors of NTDs in this region need to be identified by further study.

Accuracy Analysis

315 villages into which babies had been born in the study period were randomly partitioned into 10 parts. Of these 10 parts, one was retained as validation data for testing the model, and the remaining 9 were used as training data. The cross-validation process was then repeated 10 times (the folds), with each of the 10 parts being used as the validation data. The 10 results from the 10 folds were then averaged (or otherwise combined) to produce a single estimation. We repeated the 10-fold cross-validation 20 times. The best estimate for prediction accuracy was 69.5%±7.02% at the 95% confidence level.

CONCLUSION

Many disease risk estimation methods have been used to analyze the size, behavior and spatial distribution of NTDs. However, none has been very good at discovering which factors actually affect NTD

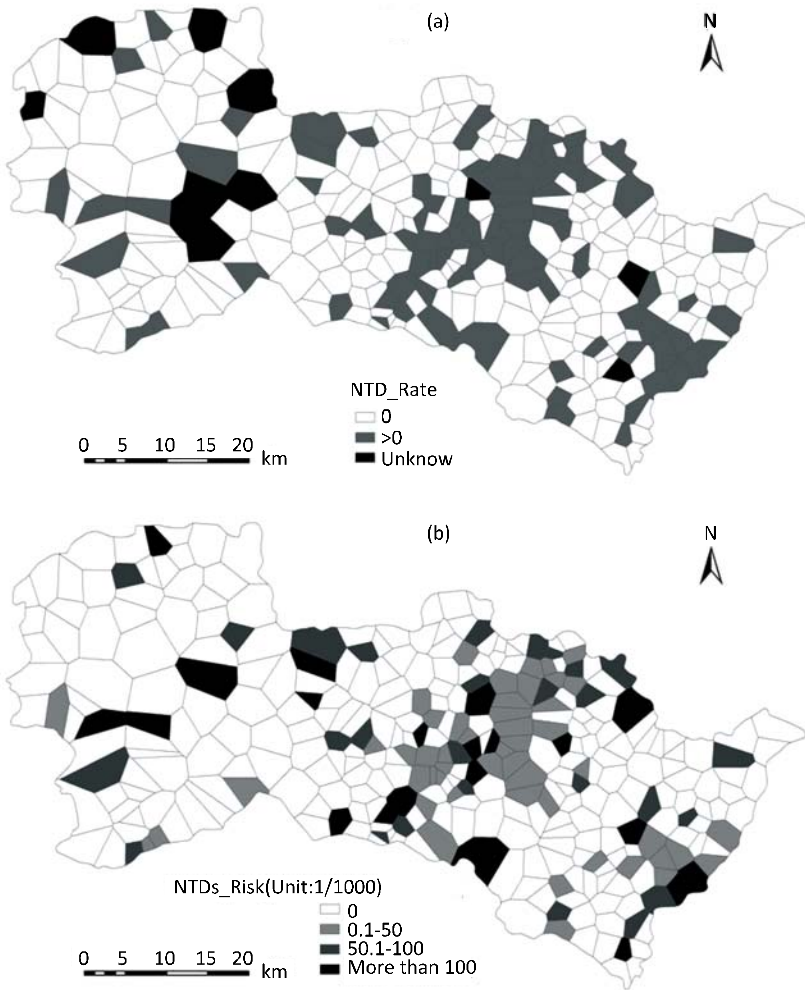

Figure 3. Heshun County: (a) real NTD rate, and (b) estimated NTD risk based on the hybrid PSO/ACO algorithm.

risk in a specific region and how. We reviewed the existing disease risk estimation methods and introduced a creative hybrid PSO/ACO algorithm to estimate NTD risk using variables derived from GIS. The results show that this hybrid PSO/ACO algorithm produces spatial models of NTD risk with a moderate level of accuracy.

There are many advantages to using the hybrid PSO/ACO algorithm to estimate NTD risk: (1) the algorithm is highly flexible in its capacity to accept input and provide output; (2) the rule representation is intuitively comprehensible to the user; (3) all observations can be used for both training and validation, and each observation can be used for validation exactly once; and (4) the algorithm can be used not only to estimate NTD risk but also to discover new relationships between risk factors and NTD risk[12-13,18]. Although the hybrid PSO/ACO algorithm has only been tested in Heshun, a rural region in the north of China, it is general enough to be used to assess the risk of NTDs and other diseases in a variety of areas.

Despite these advantages, there are some limitations to our method and our study. The hybrid PSO/ACO algorithm produces many rules, and it is difficult to integrate all of these rules to determine new relationships between risk factors and disease risk. This may bring about information loss. Moreover, the selection of risk factors is crucial to improving the accuracy of the method. In addition, the present study focused only on environmental factors, which may have decreased our likelihood of identifying other factors that contribute to the risk of NTDs. We placed most of our attention on risk assessment and less on discovering new relationships between risk factors and NTD risk, which is another limitation of this study.

REFERENCES

1. Wu JL, Wang JF, Meng B, et al. Exploratory spatial data analysis for the identification of risk factors to birth defects. BMC Public Health, 2004; 4, 23-33.
2. Carmona RH. The global challenges of birth defects and disabilities. Lancet, 2005; 366, 1142-4.
3. Frey L, Hauser WA. Epidemiology of neural tube defects. Epilepsia, 2003; 44, 4-13.
4. Li ZW, Ren AG, Zhang L, et al. A population-based case-control study of risk factors for neural tube defects in four high-prevalence areas of Shanxi province, China. Paediatr Perinat Ep, 2006; 20, 43-53.
5. RytkÖnen MJP. Not all maps are equal: GIS and spatial analysis in epidemiology. Int J Circumpolar Health, 2004; 63, 9-24.
6. Lawson AB, Biggeri AB, Boehning D, et al. Disease mapping models: an empirical evaluation. Disease Mapping Collaborative Group. Stat Med, 2000; 19, 2217-41.
7. Lawson AB, Biggeri A, BÖhning D, et al. Disease mapping and risk assessment for public health. John Wiley & Sons Ltd, 1999; Chichester, England.
8. Ismaila AS, Canty A, Thabane L. Comparison of Bayesian and frequentist approaches in modeling risk of preterm birth near the Sydney Tar Ponds, Nova Scotia, Canada. BMC Med Res Meth, 2007; 7, 39-52.
9. Hemmi I. Bayesian estimation of the incidence rate in birth defects monitoring. Congenital Anomalies, 2008; 28(2), 103-9.
10. Rushton G, Lolonis P. Exploratory spatial analysis of birth defect rates in an urban population. Stat Med, 1996; 15, 717-26.
11. Chi WX, Wang JF, Li XH, et al. Application of GIS-based spatial filtering method for neural tube defects disease mapping. J Wuhan Univ (Nat Sci Ed), 2007; 12(6), 1125-30.
12. Christakos G. On the assimilation of uncertain physical knowledge bases: Bayesian and non-Bayesian techniques. Adv Water Resour, 2002; 25, 1257-74.
13. Holden N, Freitas AA. Hierarchical classification of G-Protein-Coupled receptors with a PAO/ACO algorithm. Proc. of the 2006 IEEE swarm intelligence symposium, 2006; Indianapolis, USA.
14. Sordo M, Ochoa G, Murphy SN. A PSO/ACO approach to knowledge discovery in a pharmacovigilance context. GECCO’09, 2009; Montréal, Canada.
15. Mangat V. Increasing performance of rule mining in the medical domain using natural intelligence concepets. WCECS 2010, 2010: San Francisco, USA.
16. Gu X, Lin LM, Zheng XY, et al. High prevalence of NTDs in Shanxi province: a combined epidemiological approach. Birth Defects Res A Clin Mol Teratol, 2007; 79, 702-7.
17. Li XH, Wang JF, Liao YL, et al. A geo-analysis for the environmental cause of human birth defects. Toxicol Environ Chem, 2006; 88(3), 551-9.
19. Liittschwager JM, Wang C. Integer programming solution of a classification problem. Manage Sci, 1978; 24(14), 1515-25.
20. Holden N, Freitas AA. A hybrid particle swarm/ant colony algorithm for the classification of hierarchical biological data. 2005 IEEE Swarm Intelligence Symposium, 2005; Pasadena, USA.
21. Holden N, Freitas AA. A hybrid PSO/ACO Algorithm for classification. GECCO’07, 2007; London, UK.
22. Bai HX, Ge Y, Wang JF, et al. Using rough set theory to identify villages affected by birth defects: the example of Heshun, Shanxi, China. Int J Geogr Inf Sci, 2010; 24(4), 559-76.
23. Heern GA, Tyler J, Mandeya A. Agricultural chemical exposures and birth defects in the Eastern Cape Province, South Africa A case-control study. Environ Health, 2003; 2, 11.
24. UIman C, Taneli F, Oksel F, et al. Zinc-deficient sprouting blight potatoes and their possible relation with neural tube defects. Cell Biochem Funct, 2005; 23, 69-72.
25. Wang JF, Li XH, Christakos G, et al. Geographical Detectors-Based Health Risk Assessment and its Application in the Neural Tube Defects Study of the Heshun Region, China. Int J Geogr Inf Sci, 2008; 24(1), 107-27.