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Research

Modeling the Ecological Niche: A Case Study on Bioclimatic Factors Related to the Distribution of *Phlebotomus tobbi* Adler & Theodor (Diptera: Psychodidae) in Two Endemic Foci of Adana

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Abstract

Cutaneous leishmaniasis (CL) is a zoonotic infectious disease caused mainly by *Leishmania infantum* Nicolle, 1908 (Kinetoplastida: Trypanosomatida) transmitted by dominant species *Phlebotomus tobbi* Adler & Theodor (Diptera: Psychodidae) in Adana, Turkey. CL has been reported to be detected commonly in low-socioeconomic status population scattered in rural areas. The environmental determinants are relatively poorly understood, especially in Adana despite the fact that Adana is endemic foci of CL. The subject of this study was the current and future probability model of *P. tobbi* in the study areas, and to determine the underlying factors affecting its distribution. Sticky papers and CDC light traps were used for capturing the sand fly specimens. The current and future presence of *P. tobbi* was modeled using maximum entropy (MaxEnt) techniques. The predictive model indicated the presence of *P. tobbi* in the southeast and south part of the selected study area with 0.816 area under the curve (AUC) value. The model also implied that its survival could tend to expand with suitable climatic conditions in future (2070) with 0.798 AUC value. In addition, aspect, digital elevation model, BIO3, BIO 10, BIO12, and BIO14 were determined as the most influential variables for current and projected future. ArcGIS and MaxEnt software were used for the ecological niche model analysis to explore the ecological conditions of the disease. I suggest that produced models contribute to better understanding of epidemiology and controlling of vector-borne diseases.

Key words: *Phlebotomus tobbi*, ArcGIS, MaxEnt, *Leishmania*, ecological niche model

Leishmaniases are types of vector-borne diseases, and are a worldwide major public health problem (Desjeux 1996). Two observed clinical forms of the disease, cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL), are presented in Turkey, and CL was reported especially in the southeastern and eastern Mediterranean regions of Turkey (Ok et al. 2002). Every year, 200 CL cases had been reported in Adana before Syrian refugees started to migrate to Turkey (Ozkeklikci et al. 2017). In addition, *L. infantum* transmitted by *P. tobbi* is a parasitic agent of CL in two endemic areas of Adana (Svobodova et al. 2009, Kavur et al. 2015).

Intracellular *Leishmania* Ross, 1903 (Kinetoplastida: Trypanosomatida) parasites, on the other hand, are transmitted by infected female sand flies, blood feeding to vertebrates (Ok et al. 2002, World Health Organization [WHO] 2010). Among more than 800 recognized sand fly species, only 50 are known as the vector of the *Leishmania* protozoon. There are 29 sand fly species belonging to five subgenera, and 18 of them have been identified as probable or proven vector of leishmaniasis in Turkey, 7 of which have been identified in Adana (Houin et al. 1971, Ozcel and Daldal 1997, Yaman and Ozbel 2004, Svobodova et al. 2009, Atakan et al. 2010, WHO 2010, Kasap et al. 2015, Kavur et al. 2015).

Phlebotomus tobbi, a proven vector of the *L. infantum*, has been identified to be dominant in Karaisali and Imamoglu, known as endemic districts of CL in Adana (Kavur et al. 2015). In total, 147 and 483 CL cases were reported between 2008 and 2016 in Karaisali and Imamoglu, respectively (Turkish Ministry of Health [TMoH] 2017).

The distribution of sand flies is associated with various geographical factors such as altitude, vegetation, and temperature. Geographical information system (GIS), consisting of several

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computer-based tools, can be safely used to determine this association examining the maps produced (Ostfeld et al. 2005, Garni et al. 2014). On the other hand, ecological niche modeling (ENM), including maximum entropy (MaxEnt) present-only data, is widely used in ecology and biodiversity conservation in modeling species distribution. It is a novel technique for the determination of sand fly and vector-borne disease distribution with qualified predictive function. MaxEnt, including a general-purpose computer learning method with a simple and precise mathematical formulation, is used to construct an ENM (Elith et al. 2006, Abdullah et al. 2017).

The present study aimed to investigate the probability of the presence of proven CL vector *P. tobbi* distribution under current and projected future (2070) bioclimatic conditions in Imamoglu and Karaisali districts of Adana and to determine the role of environmental factors affecting its distribution by using MaxEnt novel modeling techniques.

Materials and Methods

Study Area

Our initial study area was Imamoglu, basin is 424 km^2. It is located in the southeastern mountain range of Taurus, and it is 50 km away from the Adana province (altitude: 78 m, latitude: 37°15′33.94″00N, longitude: 35°39′41.34″00E; Fig. 1). The second study area was Karaisali and it spans in an area of 1.526 km^2. The mountain range of Taurus is located in the northern part of the study area and lies between Karaisali and the inner Anatolian region of Turkey. Karaisali and Imamoglu consist of 62 and 19 villages, respectively, and they have viable ecological and climatic conditions. The geographical structure of Imamoglu has lowland characteristics, but Karaisali is generally forested in higher altitude (Fig. 1).

Sand Fly Collection

Our sand fly fauna data included three entomological survey (five field works) results between 2013 and 2017. The first was carried out in July 2013 and September 2014 in Imamoglu, the second was performed in August 2015 and July 2016 in Karaisali, and the last one was in September 2017 in Imamoglu. Bioclimatic variables represent annual trends, seasonality, and extreme or limiting environmental factors. Therefore, in the created model, the data of sand flies collected in the summer months are used (Bojd et al. 2014). Sand fly specimens were caught by CDC light traps and sticky papers. Two hundred eighty-one indoor and outdoor (146 in Imamoglu and 135 in Karaisali) CDC light traps were set up in these field work areas. Also, 98 of them (52 in Karaisali and 46 in Imamoglu) consisted of *P. tobbi* (Fig. 2). Sand flies were preserved in 70% ethanol and identified by using several systematic keys (Theodor 1958, Lewis 1982, Killick-Kendrick et al. 1990).

Environmental Data

The environmental data (Table 1) included 19 bioclimatic (bioclim) variables and 3 variables derived from remotely sensed data. The current and 2070 bioclim variables were downloaded from the WorldClim website, v1.4 (WorldClim 2016). They both had a nominal resolution of approximately 1 km^2. The current bioclimatic data were developed from monthly average climate data observed between 1950 and 2000. Downscaled and calibrated general circulation model (GCM) data, such as HadGEM2-ES and rcp60, were used for 2070. The current and projected future (2070) bioclimatic variables describe the climatic conditions such as temperature, relative humidity, evaporation, total rainfall, and number of freezing and rainy days.

Ecological Niche Modeling

Maximum entropy models were utilized using the MaxEnt v3.3.3 software, which is freely downloadable at https://biodiversityinformatics.amnh.org/open_source/maxent/. For the ENM, a file was prepared for proven vector sand fly species *P. tobbi* with several environmental variables in ASCII format and was entered into MaxEnt software. Similar to the work of Sofizade, for the produced model, 75% of the *P. tobbi* presence points in 98 location were used for the modeling construct, and the remaining 25% of data were used in testing the model (Sofizadeh et al. 2017). The software was used with its default parameters with 10,000 as the maximum



Fig. 1. Study areas and sand flies collected points.

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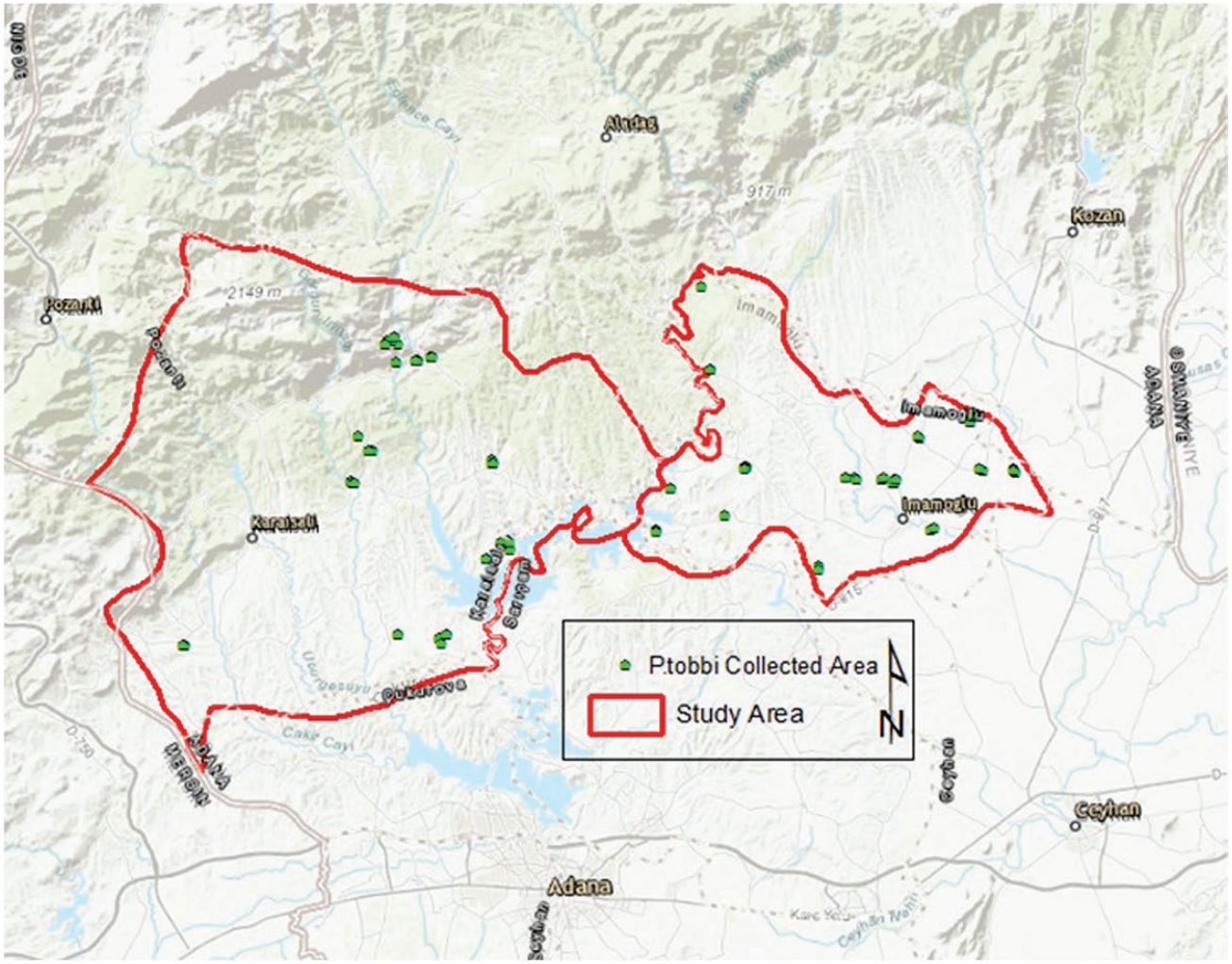


Fig. 2. *Phlebotomus tobbi* collected areas.

number of background absences, 0.00001 convergent thresholds, 15 replicates and 5,000 as the maximum numbers of iterations, and a logistic output presenting a continuous presence probability ranging from 0 to 1. A Jackknife procedure was administered to calculate the contribution of each variable in the modeling process. The area under the curve (AUC) and receiver operating characteristic curve (ROC) were recorded for the model (Phillips et al. 2006). Furthermore, a probability threshold representing the 10th percentile training presence points was selected as a cutoff probability used to convert continuous probability maps for today and 2070 into binary maps.

The produced maps for today and 2070 showed the probability of the presence of *P. tobbi* in both endemic areas in the current time and projected future.

Results

In total, 1,415 sand flies were caught in previous and present studies between 2013 and 2017 in two CL endemic areas in Adana. Collected sand flies were identified as *P. tobbi*, *P. papatasi* Scopoli, *P. perfiliewi* Perfil'ev, *P. neglectus/syriacus* Tonnoir, Adler & Theodor, *P. sergenti* Parrot, *P. simici* Theodor, *Sergentomyia dentata* Sinton, and *S. theodori* Parrot. *Phlebotomus tobbi* known as a proven vector of *L. infantum* in Turkey, especially in southeast part of Turkey, was detected as the most abundant species in all field work areas. The current and projected future (2070) ENM, based on MaxEnt software with details for *P. tobbi* distribution, are presented in Fig. 3A and B. The produced model displays the current probability of *P. tobbi* presence in southeastern part of Imamoglu and southern part of Karaisali, though future prediction of *P. tobbi* presence seems to be more extensive in both districts. The present-day AUC values of the training and test points verifying the validity of the model were calculated as 0.816 and 0.689, respectively. In the future projection (2070), the AUC of the training points was 0.798 and test points was 0.710 (Fig. 4A and B).

Jackknife test was administered in 19 climatological and three geographical parameters in order to investigate the most effective factors for determining the current and future (2070) distribution of *P. tobbi*. Jackknife test revealed that aspect, digital elevation model (DEM), BIO3, and BIO14 contributed the most individually contributed the current model, for the 2070 model, aspect, DEM, BIO10, BIO12 were determined as the most influential variables. The total accuracy (training gain) of both models in the presence of all variables was ~0.34 (Fig. 5A and B).

Eight environmental factors found in the response of *P. tobbi* in current and future (2070) are shown in Fig. 6A and H. In present days, two environmental variables (aspect and DEM) showed an inverse relationship, whereas two other variables (isothermality and

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precipitation of driest month) showed a direct relationship with occurrence of *P. tobbi*. In addition, 'aspect' and 'DEM' are inversely proportional in the future as they are today. An increase in the mean temperature of warmest quarter and annual precipitation leads to an increase in the probability of presence for this particular sand fly (Fig. 6A and H).

Table 1. Environmental data

Name of data	Description
DEM	Digital elevation model (m)
Slope	Slope in degrees obtained from altitude (%)
Aspect	Aspect in degrees obtained from altitude (direction)
BIO1	Annual mean temperature (°C)
BIO2	Mean diurnal range (mean of monthly [max temp – min temp]) (°C)
BIO3	Isothermality (BIO2/BIO7) (×100)
BIO4	Temperature seasonality (standard deviation × 100)
BIO5	Max temperature of warmest month (°C)
BIO6	Min temperature of coldest month (°C)
BIO7	Temperature annual range (BIO5–BIO6) (°C)
BIO8	Mean temperature of wettest quarter (°C)
BIO9	Mean temperature of driest quarter (°C)
BIO10	Mean temperature of warmest quarter (°C)
BIO11	Mean temperature of coldest quarter (°C)
BIO12	Annual precipitation (mm)
BIO13	Precipitation of wettest month (mm)
BIO14	Precipitation of driest month (mm)
BIO15	Precipitation seasonality (coefficient of variation)
BIO16	Precipitation of wettest quarter (mm)
BIO17	Precipitation of driest quarter (mm)
BIO18	Precipitation of warmest quarter (mm)
BIO19	Precipitation of coldest quarter (mm)

Discussion

The findings of the present study shed more lights on usage of ENM. To the best of our knowledge, this is the first study describing how to use MaxEnt model for this purpose in Turkey. Several entomological surveys were carried out in Adana due to many CL endemic areas. The most important data obtained have been sand fly fauna, distribution, and their vectorial capacity. Almost all fauna data were associated with *P. tobbi*, the most abundant species which are known to be a proven vector of *L. infantum* (Svobodova et al. 2009). In previous studies conducted in Adana, *P. tobbi* was always found to be the dominant species: 32.5% in 2007, 65.6% in 2009, 67.03% in 2010, 67.48% in 2011, 50.3% in 2015, and 41.54% in 2017 (Simsek et al. 2007, Erisoz Kasap et al. 2009, Atakan et al. 2010, Belen and Alten 2011, Kavur et al. 2015). Rural areas in Karaisali and Imamoglu districts of Adana are favorable for *P. tobbi* for outdoor breeding because of viable environmental and geographical factors (Kavur and Artun 2017). The increase in sand fly bites and CL infection are seen in 80% of the land composed of rural areas and forests. In Karaisali and Imamoglu, 173 and 223 CL cases were reported between 2008 and 2016, respectively (TMoH 2017).

Various computer software, such as ArcGIS, GARP, and MaxEnt, are used for geographical interpretation of the obtained data conducting field works for different purposes (Phillips et al. 2006). The distribution of the vector arthropods is of great importance for understanding vector-borne disease epidemiology (Ostfeld et al. 2005).

ROC analysis characterizes the performance of a model at all possible thresholds by a single number, the AUC, which may be then compared between algorithms. AUC value, which a good fit of the model to the testing data, could imply high predictive power calculated by MaxEnt software. Reliability of prediction depends on increasing or decreasing values of AUC: 1) higher predictive power (AUC > 0.5),

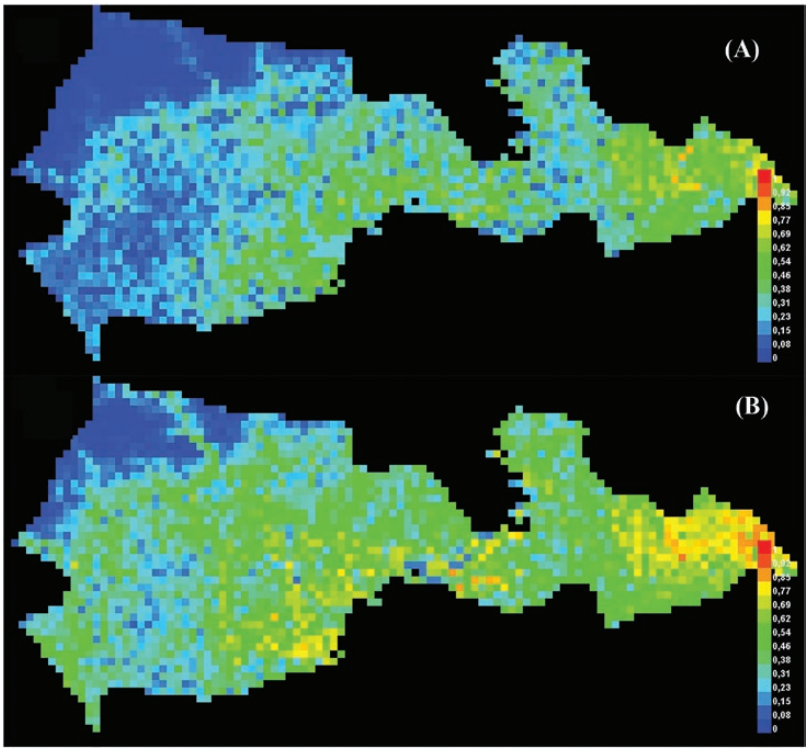


Fig. 3. Distribution of *P. tobbi* in (A) present day and (B) 2070 when the ENM was used. Relatively higher suitable areas are shown with warmer colors.

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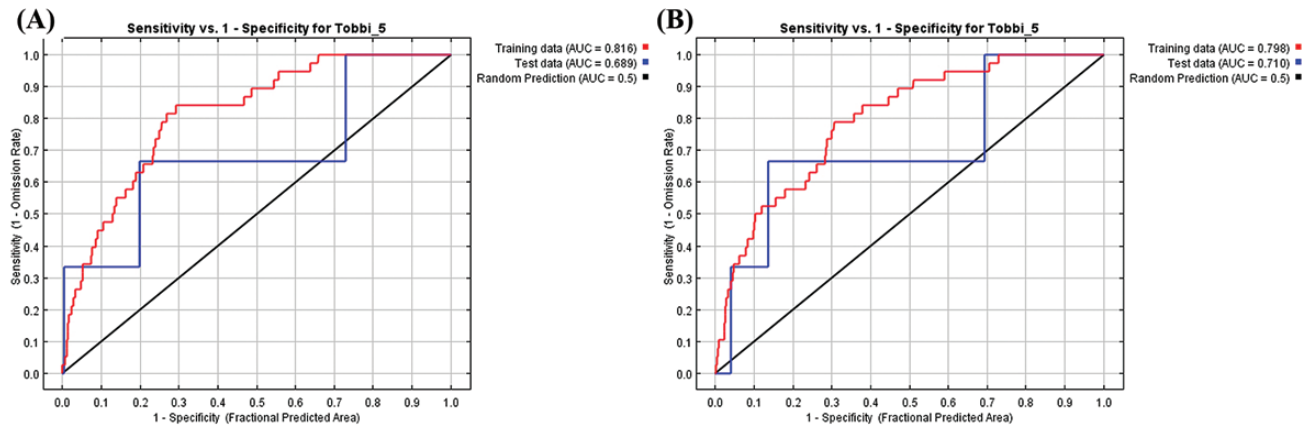


Fig. 4. AUC of MaxEnt model for *P. tobbi*, in Karaisali and Imamoglu, Turkey: (A) the current and (B) the future (2070).

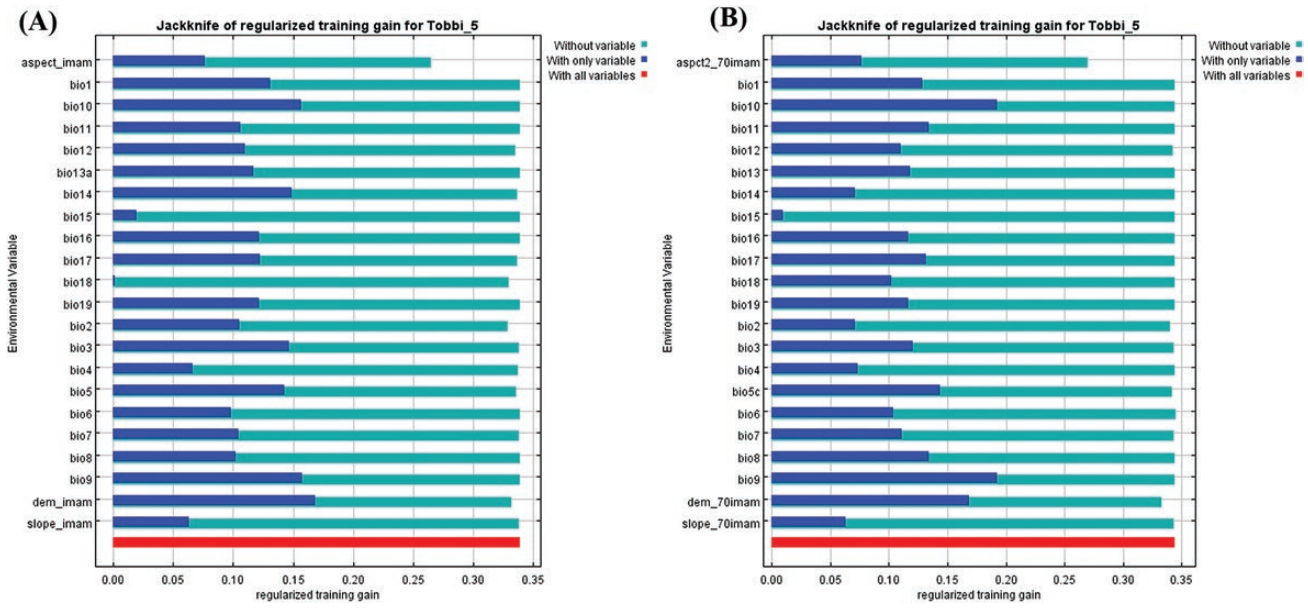


Fig. 5. Jackknife test in MaxEnt model for *P. tobbi*: (A) the current and (B) the future (2070).

2) random chance (AUC = 0.5), and 3) worse than random (AUC < 0.5). Both AUC values (present and future) of this study were found to be above 0.5 (Phillips et al. 2006, Abdullah et al. 2017).

Some of the extensive sand fly fauna research projects funded by European Union have been conducted in Turkey though several ENM studies have been carried out. The findings of these studies shed light into understanding the distribution of sand flies in the present and future time (Ready 2010). Determined *P. tobbi*'s distribution, with 0.986 of current AUC and 0.86 of forecasting AUC (2070) values, could help us predict the expansion in current time, and the climatic conditions are projected to remain suitable over the considered time period in Turkey (current to 2070). Similar to our findings, Koch et al. (2017) reported that BIO10 was the most important variable and BIO15, BIO18, and BIO19 were generally less important for the distribution of *P. tobbi*.

In addition to predicted potential distribution of *P. tobbi*, the potential predicted distribution of *P. papatasi*, *P. major* Yakimoff and Schokhor, *P. kandelakii* Shchurenkova, *P. alexandri* Sinton, and only leishmaniasis cases was investigated. *Phlebotomus papatasi*, the proven vector of *L. major* Yakimoff and Schokhor, 1914 was found to be dominant sand fly species in the Golestan district of Iran. Its predictive distribution map was produced in 0.90 of AUC values, and BIO1, vegetation, slope, and altitude were found to be important variables. Other studies also emphasized the probable distribution of *P. major*, *P. kandelakii*, *P. alexandri* in Iran (Sofizadeh et al. 2017).

According to the predicted responses to climate changes by 2050, in South America, *Lutzomyia intermedia* Lutz & Neiva and *L. neivai* Pinto will mostly shift its range southwards in Brazil and Argentina. Similarly, the distribution of *P. tobbi* in 2070 could be more extensive in central and northwards of both Karaisali and Imamoglu (McIntyre et al. 2017).

Previous studies have reported the effects of geographical variables on sand fly distribution using statistical methods (univariate and multivariate regression analysis) and ArcMAP 10.0 software. DEM has shown an inverse relationship between *P. tobbi*, *P. neglectus*, and *P. similis* Perfiliew, 1963 distribution in Adana and Aydin, similar to the findings of the present study (Ozbel et al. 2011, Olgen et al. 2012, Artun and Kavur 2017).

It is my opinion that bioclimatic data are likely to be compatible with each other in the ecological models of the vector sand fly and the disease it infects. In parallel with the results of the study, *P. tobbi* is known as the CL vector in Adana's western neighbor Mersin, and

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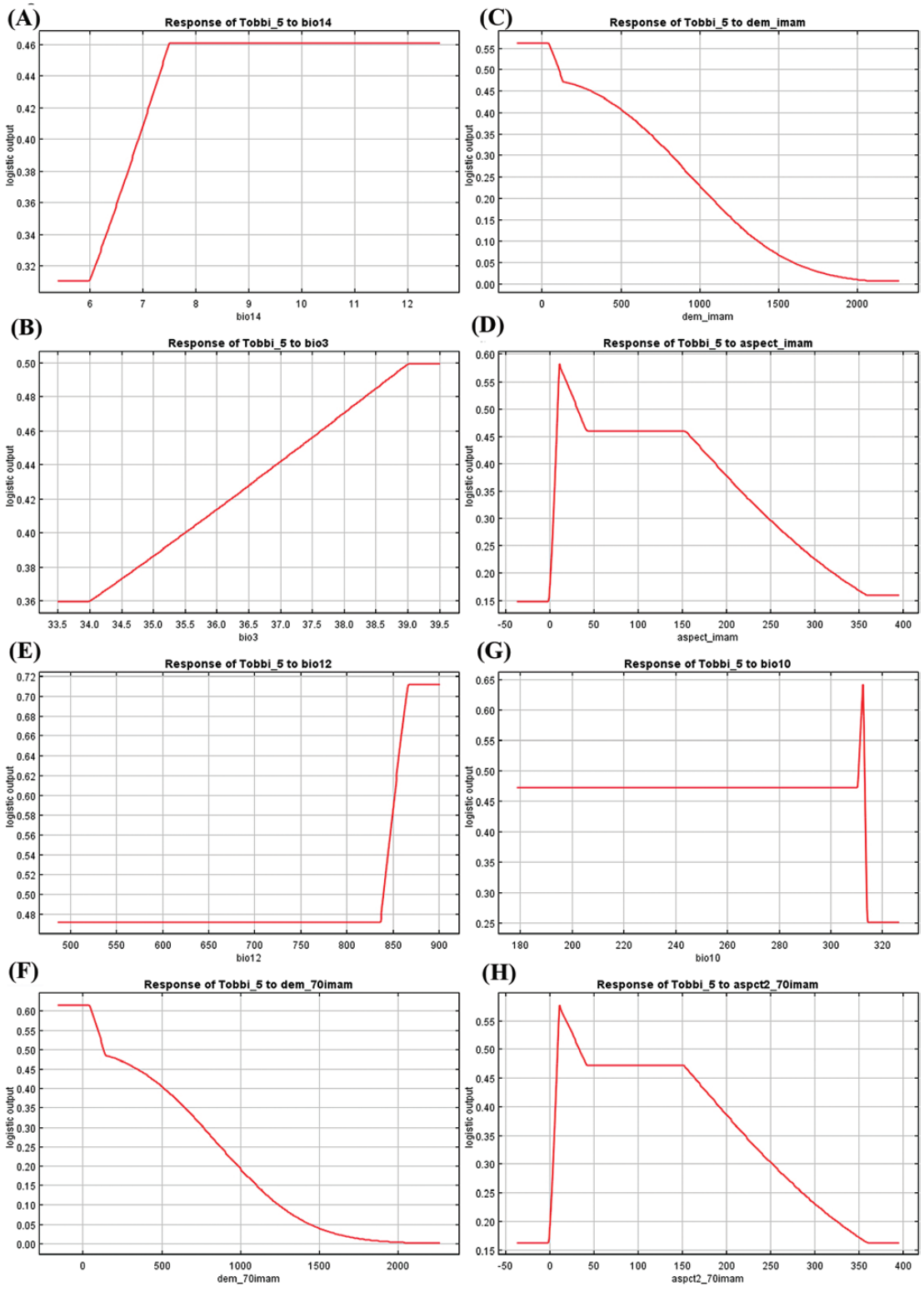


Fig. 6. Response of *P. tobbi* to the most influencing factors: (A) precipitation of driest month in current times, (B) isothermality in current times, (C) DEM in current times, (D) aspect in degrees obtained from altitude in current times, (E) annual precipitation in 2070, (F) DEM in 2070, (G) mean temperature of the warmest quarter in 2070, and (H) aspect in degrees obtained from altitude in 2070.

BIO10 was found to be an influential bioclimatic variable for the current distribution of CL (Artun and Kavur 2018).

In countries such as Nepal, India and Bangladesh where there are more people at risk for leishmaniasis, health expenditure is approximately 350 million dollars annually. Estimation of the ecological distribution of diseases is important for the prevention of these economic losses (Bern et al. 2005, Abdullah et al. 2017).

The possibility of increment in the endemic border of CL and the level of risk in CL transmission in Karaisali and Imamoglu districts are higher than in the mountainous and urban areas since the rural areas of

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two endemic areas provide more viable conditions for *P. tobbi*. Current and future prediction of *P. tobbi*'s occurrences are of great importance for the determination of CL disease situations for the ministry of health and the local managers in the above-mentioned areas in terms of taking precaution of the economic and socioeconomic problems.

Apart from the studies conducted for the species of CL vector in Iran, there is no other study with the same method in our region. The study focusing on sand fly vectors in Turkey is thought to contribute to the literature as a new study by ENM.

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