**Model the current and future risk of locally acquiring Chagas with Habitat Suitability Distribution of Chagas Disease vectors triatomine in North America with presence-only data**

**Introduction**

* Chagas Disease, traditionally considered as a disease prevalent in Latin America, is estimated to infect approximately 6-7 million people worldwide.1 In the United States, with no large-scale screening of Chagas Disease,7 currently, the best estimation of 288,000 - 347,000 infected patients and 10,000 autochthonous Chagas infection cases7,8 was calculated from outdated survey data. Alternative measures of the current and future risks of locally acquiring the Chagas Disease are required for us to better evaluate the risk.
* The Chagas Disease has two phases, acute and chronic, with symptoms ranging from asymptomatic in the acute phase to cardiac or gastrointestinal disease during the chronic phase.2 The infection persists for a lifetime without effective treatment.2
* Regarding treatment, the decades-old effective drugs benznidazole and nifurtimox produce side effects which causes one in five patients to abandon treatment,3 while vaccines are still under development4.5
* Early diagnosis during asymptomatic period is essential for effective treatments and potentially prevent congenital transmission and entering chronic phase. However, no large-scale screening exists in the United States for detecting infections during this critical period.7 As of December 2017, Chagas Disease has only been reported in six states: Texas, Arizona, Arkansas, Tennessee, Mississippi, Louisiana, with most cases identified by blood centers.3,7,31
* The Chagas disease is caused by the pathogen *Trypanosoma cruzi*, containing at least 6 genetic linages48, and which is majorly transmitted by the infectious faeces of triatomines contacting with human’s membrane or wound, or food contaminated by the infectious waste been consumed by human.1 Chagas can also be transmitted through contaminated blood transfusion and organ transplantations, ingestion of contaminated food, congenital, and postnatal infections. Other than humans, animals can also be infected. For example, canines (check refs, add chicken, wolves), raccoons, woodrats, opossums, non-human primates, red pandas and red-necked wallabies have all been found infected with *T. cruzi* in United States.6, 40, 41
* The study conducted in 2024 revealed that the pathogen T. cruzi has been found to appear in 18 US states, mostly in Texas, Louisiana and New Mexico34.
* Under climate change, the habitat of the triatomines might extend into traditionally unoccupied regions in North America, increasing the risk of naive populations locally acquiring Chagas, while only a few studies have been done in this area.3,39
* The lack of large-scale and systematic serological screening and monitoring of other Chagas transmission paths hinders us from getting more accurate estimation of current burden. Efforts has been put into research, including the newly formed RAISE project, The buRden of ChAgas dISEase in the contemporary world’37.
* This study seeks to provide an alternative measure by studying the Habitat Suitability Distribution (HSD) of the Chagas Disease vector triatomines. In all the triatomine species observed in North America, we selected and modeled 14 species from our database. All these species except *P. hirsuta* have been reported to carry *T. cruzi* and transmitted Chagas (see details in Appendix 1)10,11,12,13,14,15,33, and P. hirsute has been found to be easily infected experimentally42.
* We created a most complete database for triatomines in North America (referring to United States, Mexico and Canada in this study) and conduct HSD modeling for both historical (1991-2020) and CMIP6 future projected (2071-2100) scenarios with two machine learning models: MaxEnt and down-sample regression Random Forest (RF), which have good performance for modeling species distribution with sparse presence-only data. The triatomine database and HDS maps are presented to support healthcare providers and public health researchers in their decision making.

**Material and Method**

Study Design

A North America triatomine database was constructed, which included observation data till July 2023. The environmental predictors include bioclimatic and land cover data for historical period (1991-2020) and 2071-2100 under 4 CMIP6 scenarios: SSP1 RCP2.6, SSP2 RCP4.5, SSP3 RCP7.0 and SSP 5 RCP8.5 (CO2 emission increases as we go along these 4 scenarios). The variation in bioclimatic and land cover is a slow process and the most significant changes for this century happened at the last few years, the 2071-2100 period was picked as the flag period for the future projected HSD. For each species, we used observation data from this dataset combining with pseudo-absence data to sample historical environmental predictors and train MaxEnt and down-sample Random Forest. Then, the two models produce HSD maps for historical and 2071-2100 CMIP6 scenarios with these environmental predictors. We analyzed the model evaluation metrics and the differences of the HSD maps. Figure 1 is a flowchart presenting the modeling process.

Triatomine Database

We compiled the North America Triatominae Database (version 1.0 as due the date of publishing this study) by combing multiple published datasets: ‘New American dataset’ (19,600 records),16  Disease Vector Database from Moffett et al. (567 records),17 Texas triatomine database 2012-2015 (382 records),18 North Mexico Triatominae dataset (388 records),19 and iNaturalist research-standard citizen science observations (2901 records).20,21  Additionally, we incorporated an unpublished dataset from Alejandro Martínez-Ibarra (220 records) and 875 newly gathered records of triatomine observations published in January 2022 to July 2023, which were collected by our team from databases Semantic Scholar, Science Direct and DataTri.

The Raw Americas Triatomine Dataset combined all the data collected from multiple datasets, and the raw dataset was cleaned and filtered before feeding into models. The North America Triatomine Dataset (United States and Mexico) and Americas Triatomine Dataset (all observations in North and South America) are the cleaned version of the raw dataset. The cleaning process removed points which are duplicated, wrongly/incompletely georeferenced, or not having a clear capture time are removed (scripts available in Appendix 1). The filtering process removed points which are closer than 5 km with the R spThin library(ref). The Raw Americas Triatomine Dataset, North America Triatomine Dataset and Americas Triatomine Dataset are included in the North America Triatomine Database, which is available on Texas Data Repository22. The data filtering script is contained in Appendix 1.

Environmental Predictors

The 39 environmental predictors (Table 1) consist of bioclimatic variables are from the AdaptWest bioclimatic dataset,23,2425 and land cover variables are from the Global 7-land-types LULC projection dataset under SSPs- RCPs dataset,26.27 Both datasets are of 1-km resolution and have historical and future projected data under 4 CMIP6 scenarios. For the land cover historical predictor, due to no land cover data corresponds to the exact time frames exist, we use their 2015 land cover data for historical period since the average land cover for 1991-2020 has not been found and most of our triatomine observations were between 2010-2020.

Machine Learning Models

We used MaxEnt and down-sample regression RF to train and predict habitat suitability. Different from traditional RF, down-sample regression RF randomly selects the pseudo-absence points to match the number of observation points at tree level. These two have been found to be the top performing models for presence-only modeling in a previous study.28 The model performance were assessed with 10-fold cross validation by four evaluation metrics: Area Under the Curve (AUC), True Skill Statistics (TSS), Mean Absolute Error (MAE) and Bias.

The model training setups were selected based on MAE and Bias scores of MaxEnt, following the instructions of Konowalik and Nosol29. Models were trained with pseudo-absence data selecting randomly outside a 5-km buffer and no environmental predictor preprocessing (eliminate correlated variables and perform PCA). Details about the pilot study could be find in Appendix 3. For each species, we trained MaxEnt and down-sample RF with real observation points and 10,000 pseudo-absence points, following previous work of Valavi et al. 28. Aligning with Valavi, Roozbeh, et al.,28 we implemented MaxEnt with dismo::maxent (needs maxent.jar) R package, and down-sample RF using the randomForest R package by modifying code from Valavi, Roozbeh, et al.30 Hyperparameter tuning was performed but did not result in a boost in performance.

**Results**

Database

We created the North America Triatomine Database, which contains Raw Americas Triatomine Dataset, Americas Triatomine Dataset, and North America Triatomine Dataset. Raw America Triatomine Dataset contains 24,933 observations (127 species), Americas Triatomine Dataset contains 20,277 observations (122 species) and North America Triatomine Dataset contains 12,578 observations (35 species). From all the species in the North America Triatomine Dataset, we removed observation points that are closer than 5 km with spThin R package (Figure 2).

According to a new taxonomy proposal44, seven species under the *Triatoma* genera shall be moved under *Hospesneotomae n. gen.*, namely *H. protracta, H. barberi, H. incrassata, H. peninsularis, H. sinaloensis, H. neotomae* and *H. nitida*. In our database, we still used their previous known names to avoid confusion before this proposal got widely accepted in the community.

Within the 35 species in the North America Triatomine Dataset, we selected the 14 species with more than 39 records (the number of environmental predictors) to avoid model overfitting. We proceed to HSD modeling with these 14 species: *T. sanguisuga*, *T. dimidiata*, *T. gerstaeckeri*, *T. protracta*, *T. longipennis*, *T. rubida*, *M. pallidipennis*, *T. barberi*, *T. mexicana*, *P. lecticularia*, *T. recurva*, *T. mazzottii*, *P. hirsute* and *T. indictiva*.

Model Performance

The performance of MaxEnt and RF on different species were evaluated with AUC, TSS, MAE and Bias scores. The AUC and TSS scores follow a similar trend as the number of training samples increases, while this trend is not observed in MAE and Bias scores (Figure 3).

It is agreed by 5 variable importance measurements of MaxEnt and RF that, DD18 (Degree-days above 18 °C) is the most important variables for *T. sanguisuga*; for *T. dimidiata* it is TD (Difference between MCMT (Mean temperature of the coldest month) and MWMT (Mean temperature of the warmest month), as a measure of continentality), for *T. gerstaeckeri* it is PAS (Precipitation as snow), and for *T. protracta* it is CMD (Hargreave’s climatic moisture index). The importance measurement detailed description and spider charts for all 14 species can be found in Appendix 1, and the most important variable has the largest area shown on the spider chart formed by five variable importance measurements.

Habitat Suitability Distribution

The HSDs for the four species having the most observation points are shown below, and the HSDs for the other 10 species can be found in Appendix 1. In historical HSD maps, predictions from both models cover regions located by observation points, with RF giving a higher suitability values for those regions. For 2071-2100 predictions, HSDs tend to spread out more in higher emission scenarios for both models (Figure 4, for the four species with the most observation points after filtering), with predictions from RF generally more aggressive, consistently displaying a higher suitability value and broader spatial coverage.

Among all, *T. sanguisuga*, *T. protracta* and *P. hirsuta* have the largeset suitable habitat historically, and *T. sanguisuga, T. protracta, P. lecticularia, P. hirsuta* and *T. indictiva* have the most significant suitable habitat expansion to the north in 2071-2100.

**Discussion**

* We created the most complete open-sourced North America Triatomine Database combining well-established databases, newly published datasets, and citizen science dataset. The cleaned data could be used for conducting further triatomine ecological niches studies on regional scale, and the filtered version could be directly used for model development.
* MaxEnt and down-sample RF both have good agreements on evaluation metric results for most of the nine species with training samples no fewer than 143; therefore, we would regard habitat suitability maps for these nine species as reliable: *T. sanguisuga*, *T. dimidiata*, *T. gerstaeckeri*, *T. protracta*, *T. longipennis*, *T. rubida*, *M. pallidipennis*, *T. barberi*, *T. mexicana.*
* We applied a new way to evaluate differences between prediction maps on regional scale, for which we calculated the percentage difference of pixel-wise summation of two prediction raster maps. This percentage differences converges to a low value at the right end where models have more training samples (Figure 5).
* RF models have a consistent negative Bias score (Figure 3), which indicates they could be used as an upper bound. At the same time, the observation points are well covered by high suitability regions predicted by RF, while the ‘outlier’ points are sometimes missed by those from MaxEnt models (Figure 4 and Appendix 1).
* The expanding suitable habitat for triatomines signals a growing risk of locally acquired Chagas diseases. Given an increasing locally acquiring risk, integrating habitat suitability modeling with screening and public education programs will be essential for preparing at-risk populations for the challenges ahead.
* For blood donation testing, since unfortunately no single serological test has both high sensitivity and high specificity, WHO advices the use of one high sensitivity test plus one high specificity test to identify Chagas disease.
* In United States, Starting from December 2017, FDA requires blood centers to use a licensed screening test for antibodies of *T.cruzi.* (<https://www.fda.gov/media/101270/download>)45.
* Canadian blood services only conduct tests for donors who were born or lived, or whose mother or maternal grandmother was born or lived in countries where Chagas disease occurs, as well as donors with a travel risk46. (<https://www.blood.ca/en/about-us/media/chagas-disease/faqs-chagas-disease#:~:text=Do%20you%20test%20donated%20blood,also%20be%20tested%20for%20Chagas>. ) With habitat of triatomines expanding to Canada at the end of this century, Canada has a potential growing risk of Chagas Disease, which also agreed with experts opinion on ranking Chagas as one of the top three infectious disease to concern under climate change38.
* For Mexico, it is estimated that between 1.1 to 4 million people are infected with *T. cruzi*, and federal regulations (NOM-253-SSA1-2012) requires all blood donors to be tested for T. cruzi47 (<https://www.gob.mx/cms/uploads/attachment/file/219069/NOM-253-SSA1-2012_Para_la_disposicion_de_sangre_humana_y_sus_componentes_con_fines_terapeuticos.pdf>), while due to limited budget, most blood centers can only afford conducting one test on blood donations35.
* suggestion: potentially make Chagas disease notifiable at national level)(<https://ndc.services.cdc.gov/search-results-year/>)
* The presence of triatomines is not associated with poor housing, but you find them in garages, California case in the bedroom36, and under cement slabs of the patio and inside garage in a south Texas household43.
* Suggestions: (clinician training in US)(US, Mexico cooperation along the boarder)

CDC doesn’t consider Chagas to be endemic in United States, for the reason that they believe the risk of locally acquiring Chagas is low3, but our study shows that the locally acquiring risk is high, which leading to Chagas is potentially endemic but under-reported in United States. (emphasis zoonotic in the endemic argument: ask Carolyn; Carolyn: autochthonous cases is sufficient, include [https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1537-2995.2012.03581.x](https://urldefense.com/v3/__https:/onlinelibrary.wiley.com/doi/abs/10.1111/j.1537-2995.2012.03581.x__;!!PfbeBCCAmug!kF5j2SEeNrHoQpObRwQ0zS4tV41PdWzefFI7TMKzHun7oqBNULKiYUIAWtSk8In0NhEQO2YAIO2SXMaVRGc$), <https://www.sciencedirect.com/science/article/pii/S1567134817300163>

<https://www.sciencedirect.com/science/article/pii/S0001706X19313166> - this one is a review of all published autochthonous cases as of 2020

<https://www.ajtmh.org/view/journals/tpmd/103/3/article-p967.xml>

And this is the first report of autochthonous T. cruzi in the US, from 1955: <https://jamanetwork.com/journals/jama/fullarticle/302589>)

**Tables**

Table 1 (edited)

|  |  |
| --- | --- |
| Species | Number of Observations in Cleaned North America Dataset |
| *Triatoma gerstaeckeri* | 4464 |
| *Triatoma sanguisuga* | 2217 |
| *Triatoma dimidiata* | 1679 |
| *Triatoma protracta* | 864 |
| *Triatoma rubida* | 492 |
| *Triatoma longipennis* | 482 |
| *Meccus pallidipennis* | 465 |
| *Triatoma barberi* | 380 |
| *Triatoma mexicana* | 358 |
| *Paratriatoma lecticularia* | 275 |
| *Triatoma indictiva* | 204 |
| *Triatoma mazzottii* | 158 |
| *Triatoma recurva* | 112 |
| *Dipetalogaster maxima* | 96 |
| *Triatoma phyllosoma* | 71 |
| *Paratriatoma hirsuta* | 64 |

**Figures**

Figure 1

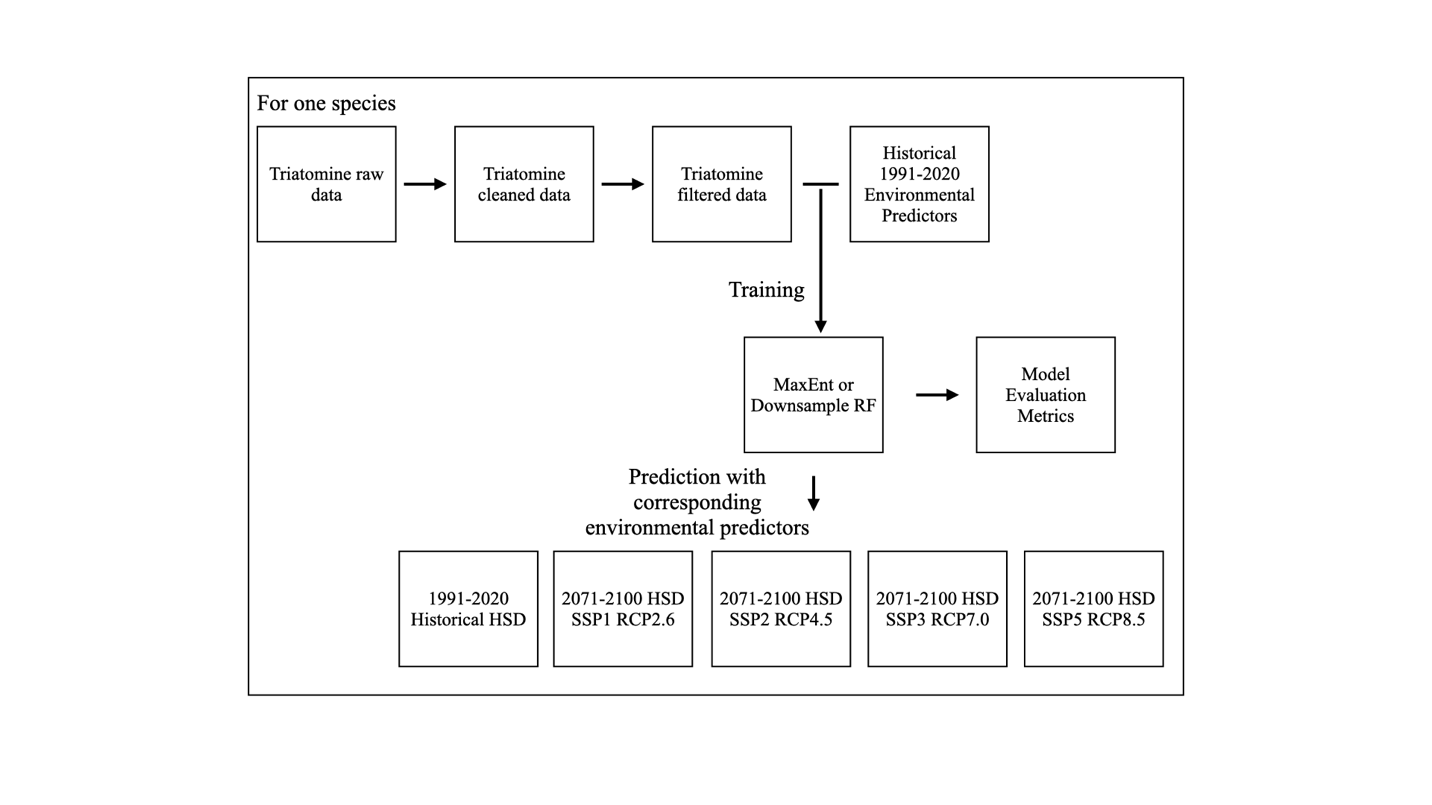


Figure 2: The geospatial distribution of filtered observation points for the 16 species: A) *T. sanguisuga*, B) *T. dimidiata*, C) *T. gerstaeckeri*, D) *T. protracta*, E) *T. longipennis*, F) *T. rubida*, G) *M. pallidipennis*, H) *T. barberi*, I) *T. mexicana*, J) *P. lecticularia*, K) *T. recurva*, L) *T. mazzottii*, M) *P. hirsuta*, N) *T. indictiva*, O), *D. maxima* P) *T. phyllosoma*. The number of filtered observation points (red) and the number of cleaned observation points (black) are noted at the bottom right of each subplot. The subplots are arranged in the ascending order of the number of filtered observation points.

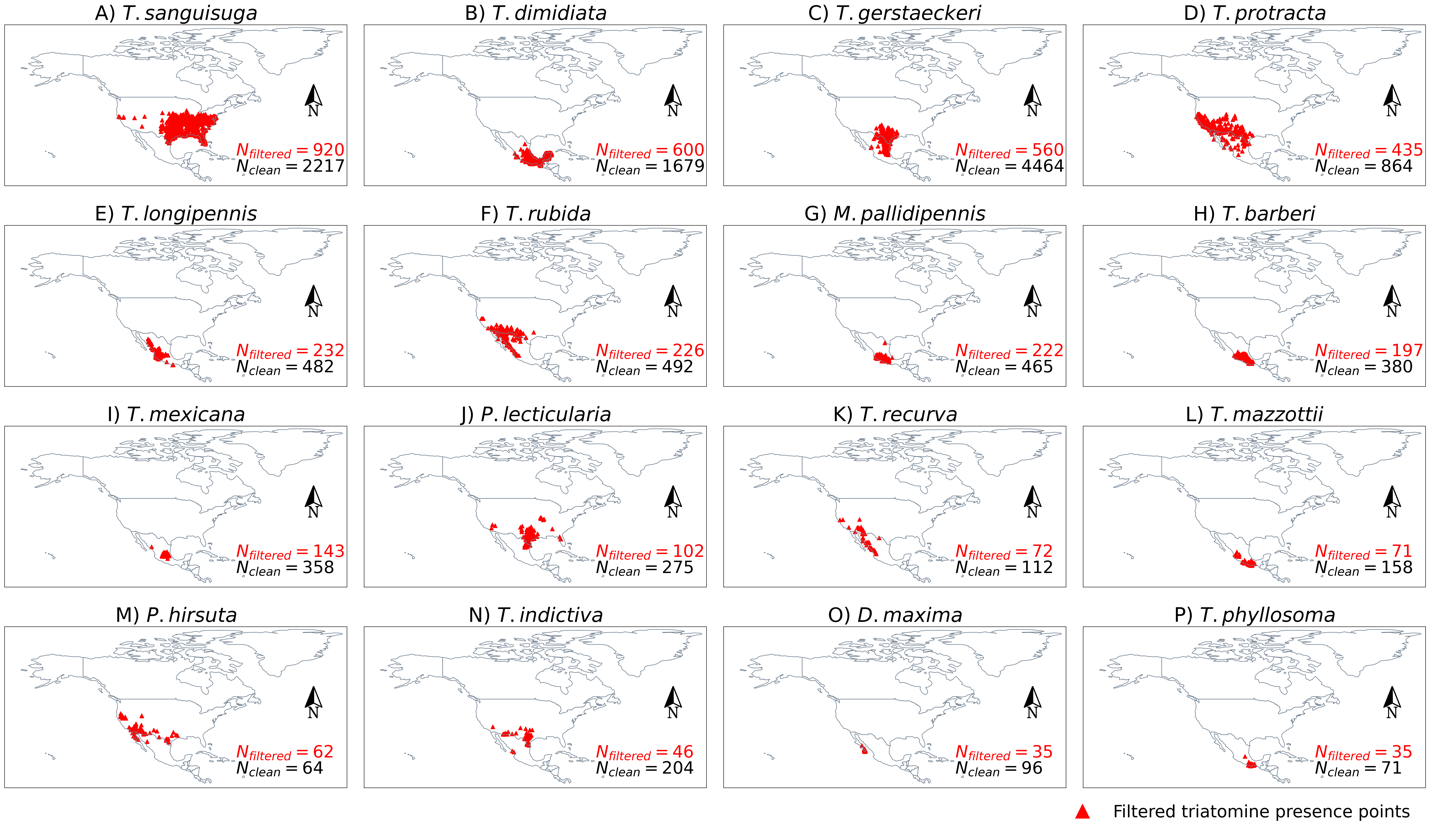


Figure 3

A graph of different sizes and shapes

AI-generated content may be incorrect.

Figure 4a

A screenshot of a map

AI-generated content may be incorrect.

Figure 4b

A screenshot of a computer screen

AI-generated content may be incorrect.

Figure 4c

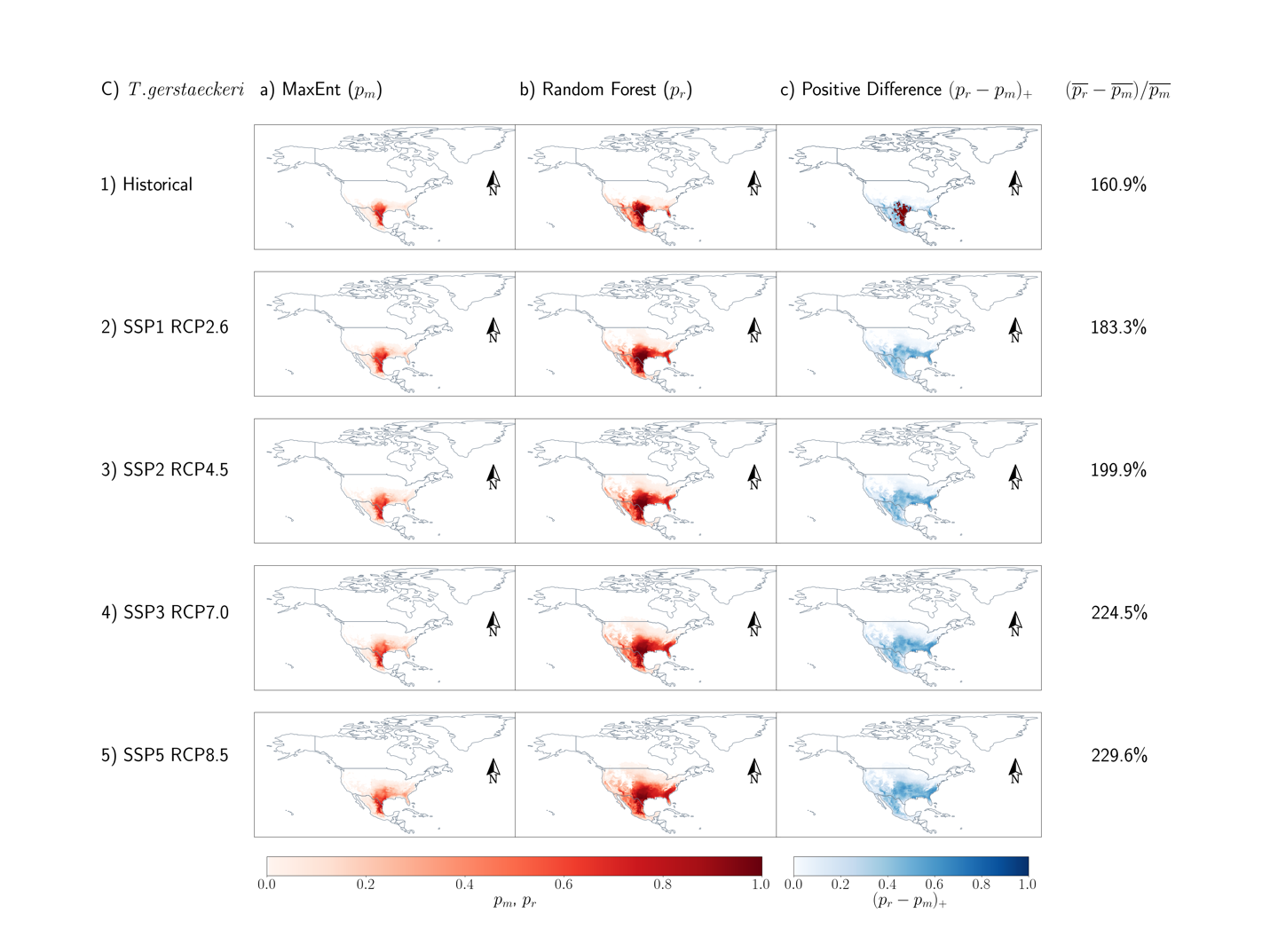


Figure 4d

A screenshot of a map

AI-generated content may be incorrect.

Figure 5

A graph of number of filtereded points

AI-generated content may be incorrect.

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