Climate change influences on the potential geographic distribution of *Ixodes ricinus*, vector of Lyme borreliosis and tick-borne encephalitis virus

By

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Abstract

Background: *Ixodes ricinus* is a hard tick vector species that transmits many diseases in Europe and North Africa, including borreliosis (Lyme disease) and tick borne encephalitis (TBE). Climate change has altered distributions and transmission patterns of many vectors and vector-borne diseases, but such effects on *I. ricinus* have received little attention. In this study, we assessed the potential distribution of *I. ricinus* under both current and future climate conditions to understand possible changes in pathogen transmission patterns in coming decades.

Method: We integrated occurrence datasets and relevant environmental variables to generate ecological niche models to estimate the current distribution of *I. ricinus* with respect to climate, and then assessed its future potential distribution under different climate change scenarios. Future projections were based on 17 general circulation models (GCMs) and 2 representative concentration pathways (RCPs), for 2050 and 2070.

Result: The present potential distribution of the species showed broad agreement with future distributional predictions, including most of western and central Europe, a narrow zone in eastern and northern Europe, and a narrow fringe of North Africa. Potential expansions were observed in northern and Eastern Europe. These results indicate that *I. ricinus* could emerge in presently non-endemic areas, posing increasing risks to human health in these areas.

Keywords: Climate change, ecological niche modeling, Maxent, future projection, Lyme disease, tick-borne encephalitis, Europe, North Africa, Middle East.

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Introduction

Ixodes ricinus is the most common anthropod vector of human disease in Europe and nearby regions [1]. Lyme disease (or Lyme borreliosis, LB) and tick-borne encephalitis (TBE) are the most serious tick-borne diseases in humans [2]. LB is caused by the bacterium *Borrelia burgdorferi*, of the family Spirochaetaceae, and is transmitted by various hard ticks (genus *Ixodes*): *I. ricinus* in Europe and North Africa, *I. persulcatus* in Eurasia, *I. pacificus* in the western United States, and *I. scapularis* in the eastern United States [3]. In fact, many clades exist in the Spirochaetaceae that can cause human disease: *B. burgdorferi*, *B. garinii*, *B. afzelii*, *B. spielmanii*, *B. bissettii*, *B. lusitaniae*, and *B. valaisiana* [4]. These diseases can be transmitted to humans by bites of immature ticks (nymphs), which are small and hard to notice; adult ticks can also transmit the bacteria, but are larger and more easily noticed [5].

LB is the most widespread vector-borne disease in Europe, with 85,000 cases reported annually (probably many more go undiagnosed), and 15,000-20,000 cases annually in the United States; the disease is endemic in 15 states [6]. LB has been recorded in North Africa, with two cases in Morocco, one in Algeria, and 29 in Tunisia [7]. Forests are high-risk areas, so cases are most common among hunters, forest workers, rangers, farmers, and gamekeepers [6]; risk of infection increases when human activities and visits to infested areas overlap with peaks of tick abundance [8].

Some studies have suggested that latitudinal and elevational limits of LB and TBE, and of the ticks themselves, have shifted with increasing global temperatures [9-11]. Over the last century, mean temperature has risen 0.7°C globally; another 1.1°C increase is expected in the 21st century [12]. This additional warming may affect the epidemiology of vector-borne disease in terms of vector development, altering pathogen populations, shifting geographic distributions of vector reservoirs and host populations, and influencing transmission dynamics [12].

The geographic distribution of *I. ricinus* is related to climate factors such as humidity, soil water, and air temperature, and to vegetation type, land use, and disturbance [13]. Climate change can also alter tick abundances [14]. Several recent publications have presented predictions of possible climate change effects on arthropod-borne disease transmission, including ticks, sandflies, and mosquitoes to understand how the various factors driving their distributions might constrain or release future pathogen distribution [15-18].

Modeling ecological requirements of species to anticipate future disease transmission patterns is challenging [12]. Previous studies of the potential distribution of *I. ricinus* have generally covered small geographic extents [2, 19]. For example, some studies included studies in single countries attempting to understand the population dynamic of this species [14, 20]. A recent paper [21] studied effects of global change on *I. ricinus* across its range, but used two old climate scenarios (A2 and B2) from one GCM only for projection. Here, we prepared a data set of *I. ricinus* occurrence that covered its entire geographic range in Europe and North Africa, and removed bias that might affect model predictions. We used a maximum entropy algorithm (Maxent 3.3.3k) to estimate the full ecological requirements of *I. ricinus*, which we transferred onto future conditions for the years 2050 and 2070 under 17 GCMs at two concentration scenarios for greenhouse gases. Ecological niche modeling was used because it is robust, and has been used in many disease applications [22]. We thus present the most comprehensive models developed to date for this important disease vector, and explore their implications under the newest suite of future climate scenarios.

Materials and Methods

Input data

Primary occurrence records for *I. ricinus* were obtained from diverse sources. Data were drawn from the Global Biodiversity Information Facility (GBIF; www.gbif.org; ~2110 occurrence points), VectorMap (www.vectormap.org; ~1801 occurrence points), and the scientific literature (~1195 points; S1 File [15]). Sampling was concentrated particularly in Great Britain and Germany Thanks to continuous surveillance by the European vector map program of the European Center for Disease Prevention and Control (ECDC; http://ecdc.europa.eu/en/healthtopics/vector/vector-maps/). Duplicate records were removed, and occurrence points were filtered by density to reduce bias in calibrating ENMs [23]. As a result, in the end, we had 417 occurrence points (Fig 1), which we separated into five equal subsets. Each subset was then divided into two portions 50% for model calibration and 50% for model evaluation. The five random subgroups provide replicate views of model results and an idea of variation inherent in the system.

We obtained data on 19 climate variables from the WorldClim archive (www.worldclim.org). We removed bioclimatic variables 8-9 and 18-19, in light of known spatial artefacts. We used the data layers at 10ʹ spatial resolution in light of the continental extent of our models. We obtained parallel data layers for 17 general circulation models (GCMs; Table 1) for 2050 and 2070, with two representative concentration pathways (RCPs; RCP 4.5 and RCP 8.5) to estimate future distributional potential of the species and the uncertainty inherent in those predictions.

Ecological niche modeling

Maxent 3.3.3k [24] was used to test and identify the most important environmental variables using its jackknifing function. After that, we used SDMTools in ArcGIS 10.3 to remove variables with high correlations. In the end, we used six variables for analysis: annual mean temperature (bio 1), mean diurnal temperature range (bio 2), isothermality (bio 3), annual temperature range (bio 7), annual precipitation (bio 12), and precipitation seasonality (bio 15). These variables were used to reconstruct the ecological niche of *I. ricinus* and estimate the suitability for the species based on associations between presence points and environmental variables [25]. We hypothesized an accessible area M that included all of Europe, but excluded western Asia for lack of data documenting *I. ricinus* occurrence there; we included North Africa and parts of the Middle East [26]. We used Maxent's bootstrap function to create 10 replicate analyses. We used partial ROC statistics to test model robustness [27] via Niche Toolbox (http://shiny.conabio.gob.mx:3838/nichetoolb2/); the five testing subsets of available occurrence data were used to test model predictions.

To summarize model results, we calculated median values across all median model outputs as an estimate for the species' potential distribution under each corresponding RCP. We calculated the median of the medians across all GCMs for each RCP in each time period. We used the range (maximum - minimum) for present and future (within each RCP) as an index of uncertainty of model predictions [18, 22]. We thresholded models using a fixed allowable omission error rate (E = 5%) [28], given that 5% of the occurrence data may have included errors that misrepresented environmental values. Mobility-oriented parity (MOP) was used to calculate the degree of novelty of climate conditions, compared to the present, for all future-climate scenarios (i.e., 17 GCMs x 2 RCPs x 2 time periods). MOP evaluates general novelty of conditions, and highlights regions where strict extrapolation occurs. MOP is a crucial approach for any model projection, to give a view of certainty and uncertainty across various sectors of the region of interest [29].

Results

Our initial total of 5107 occurrence points for *I. ricinus* from diverse sources was filtered and reduced to 417 spatially unique points at 10ˈ resolution that largely avoided artificial clumping related to biases in sampling and reporting (Figure 1). Calibrating models for *I. ricinus* based on the five subgroups of occurrence points yielded predictions that, when tested using partial ROC analysis, gave AUC ratios above null expectations in all cases ($P < 0.001$).

Models based on present-day conditions revealed high suitability for *I. ricinus* across Central and Western Europe in Great Britain, France, Germany, Belgium, Netherland, Greece, and Italy. In northern Europe, high suitability was concentrated in southern Finland and Sweden, extending to western Norway. Suitable areas were also in western Turkey, the Middle East, and restricted areas in Morocco, Algeria, and Tunisia (Fig 2).

Transferring models to future conditions, current and future distributional patterns largely coincided. However, our model predictions indicated some potential for expansion into areas not identified as suitable under present conditions, particularly in northern Europe (Fig 2). Analysis showed high uncertainty as regards potential distributions in present and future. In future, high certainty was observed in Scandinavian countries and Eastern Europe. Under present-day conditions, low uncertainty was observed across the study area except some areas in Morocco, Ireland, and eastern Norway. Under future predictions, varying levels of uncertainty existed among RCP scenarios and time periods: based on scenario RCP 4.5 for 2050, high uncertainty was concentrated in southern Finland, central Norway and Sweden, and less in Eastern Europe and

North Africa, whereas low uncertainty areas were observed in Eastern Europe and the Middle East. For RCP 8.5 for the 2050s, high uncertainty was restricted parts of southern Finland, eastern Sweden, southern Spain, and northern Morocco; low uncertainty areas were in Eastern Europe and the Middle East.

For RCP 4.5 in 2070, models showed high uncertainty in Finland, Norway, central and northern Sweden, and eastern Belarus. RCP 8.5 for 2070 showed high uncertainty in Finland, eastern Sweden, eastern Belarus and eastern Ukraine, and less in Norway and Central, eastern, and southern Europe. Low uncertainty was in Western Europe, North Africa and the Middle East (Fig 2).

Binary (thresholded) predictions for future conditions showed differences between RCP 4.5 and RCP 8.5 in 2050 and 2070. In terms of present and future agreement, high suitability was in central, southern, and Western Europe, southern Sweden and Finland, and eastern Norway; range expansion was indicated in North Africa in coastal regions of Morocco, Algeria, and Tunisia. Low-confidence predictions of suitability were in Spain and western Turkey. Under RCP 4.5 for 2050, expansions are expected although with low confidence in North Africa, the Middle East, and Eastern and Northern Europe. Expansions in Eastern and Northern Europe, Turkey, and the Middle East were wider for RCP 8.5 for RCP 4.5. Under RCP 8.5, expansions were wider in southern Finland with high confidence. Predictions under RCP 4.5 and RCP 8.5 for 2070s were closely similar in terms of low confidence, with differences in North Africa, Turkey, Iraq, and central Saudi Arabia; suitability increased with high confidence in Norway and much of Sweden and Finland under RCP 8.5 (Fig 3).

MOP results indicated high novelty of and future conditions along the entire Mediterranean rim of southern Europe and North Africa and in northern Scandinavia (Fig 4). MOP detected out-of-range conditions in 10 out of 17 models in both RCPs 4.5 in 2050 and 2070. Some 11 and 13 models were out-of-range in RCP 8.5 in 2050 and 2070, respectively. Hence, strict extrapolation presented commonly in northern extremes of Scandinavian countries.

Discussion

Tick-borne pathogens (TBE and LB) are greatly influenced by tick ecology and other factors such as habitat structure, climate, human activities, and pathogen host community composition and density [30]. Ticks are only intermediate parasites that can spend most of their life cycle in their habitat, and take just one or few large blood meals per life stage (larvae, nymph, and adult) [31]. They often take meals three times during a life cycle that may take 7 years to complete, and they attack birds, reptiles, and mammals including humans [32]. Tick females lay eggs on the ground. After larvae hatch, they climb vegetation and wait for a host; after getting a first meal, they drop to the ground and molt to nymph; nymphs do the same thing, waiting for a host, feeding for second time and dropping off and molting to adult. Adults seek a large mammal host, feed and mate, and females drop off and lay eggs on the ground [5].

Several studies have indicated that increasing temperature could affect the geographic distribution and ecology of *I. ricinus* in Europe [21]. Seasonal activities and feeding behavior of the species can be affected by climate change at different life stages [33, 34]. In fact, temperatures could lead to milder winter conditions, extending spring and fall seasons in northern regions, making them more suitable for *I. ricinus*. Indeed, expansions of northern distributional limits have been reported for this species in Norway and Sweden since the 1980s [6, 10, 35]. Range expansions of *I. ricinus* have been recorded at higher elevations in the Czech Republic and Switzerland [36]. Hypothetical causes of increased TBE in Europe during the last 2 decades include global climatic change, socio-economic changes, and anthropogenic activities [37].

Several factors must be considered before interpreting our model predictions regarding expansions and changes in the potential distribution of *I. ricinus*. First of all, as with all Ixodid ticks, *I. ricinus* spends most of its life cycle in the environment off the host, so climate change may have direct effects on their distribution [38]. Other abiotic factors, such as land use, physical features, and biotic factors such as host abundance and competition, should be considered in tandem with climate effects [39, 40]. Third, newly suitable areas must be accessible to the species via dispersal for actual range expansions to take place [41].

This study differs from that of Porretta et al. [21] in using 6 variables for analysis, more GCMs and the latest scenarios (RCPs 4.5 and 8.5) for 2050 and 2070. Also, we used diverse data sources, and focused on Europe, North Africa, and the Middle East, to develop predictions of the potential distribution of this tick in the future. We did not include Asia for the lack of data from those regions. In addition, we included mobility-oriented parity (MOP) to understand certainty and uncertainty in different areas in the region of interest [29].

Our results were similar to those of Porretta et al., [21] in terms of future predictions where the new expansions predicted in eastern and northern Europe, but we could not predict changes in Asia for reasons mentioned above. *Ixodes ricinus* occurs across most of Europe and parts of North Africa and the Middle East; our future projections anticipated new suitable areas for the species, especially under RCP 8.5 for 2070, where high-confidence expansion is expected in Norway, Sweden, Finland, and western Ukraine. Our results also predicted new suitable areas in eastern Europe, North Africa, and the Middle East, although with low confidence.

Our models anticipated potential range expansion more broadly in northern Europe, with milder winter conditions as temperature increases [21]. In Sweden, for example, the climate has changed to be significantly warmer in the last 3 decades: the 8 warmest Novembers were recorded between 2000 and 2009 [42]. These changes can help more ticks to survive the winter, and the probability of tick bites increases [21]. Given that Lyme disease, TBE, and various tick-borne diseases cause serious health problems, predicting future suitable areas for *I. ricinus* can help to guide plans to manage and mitigate effects of these health threats [43].

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Appendix 1: Figures

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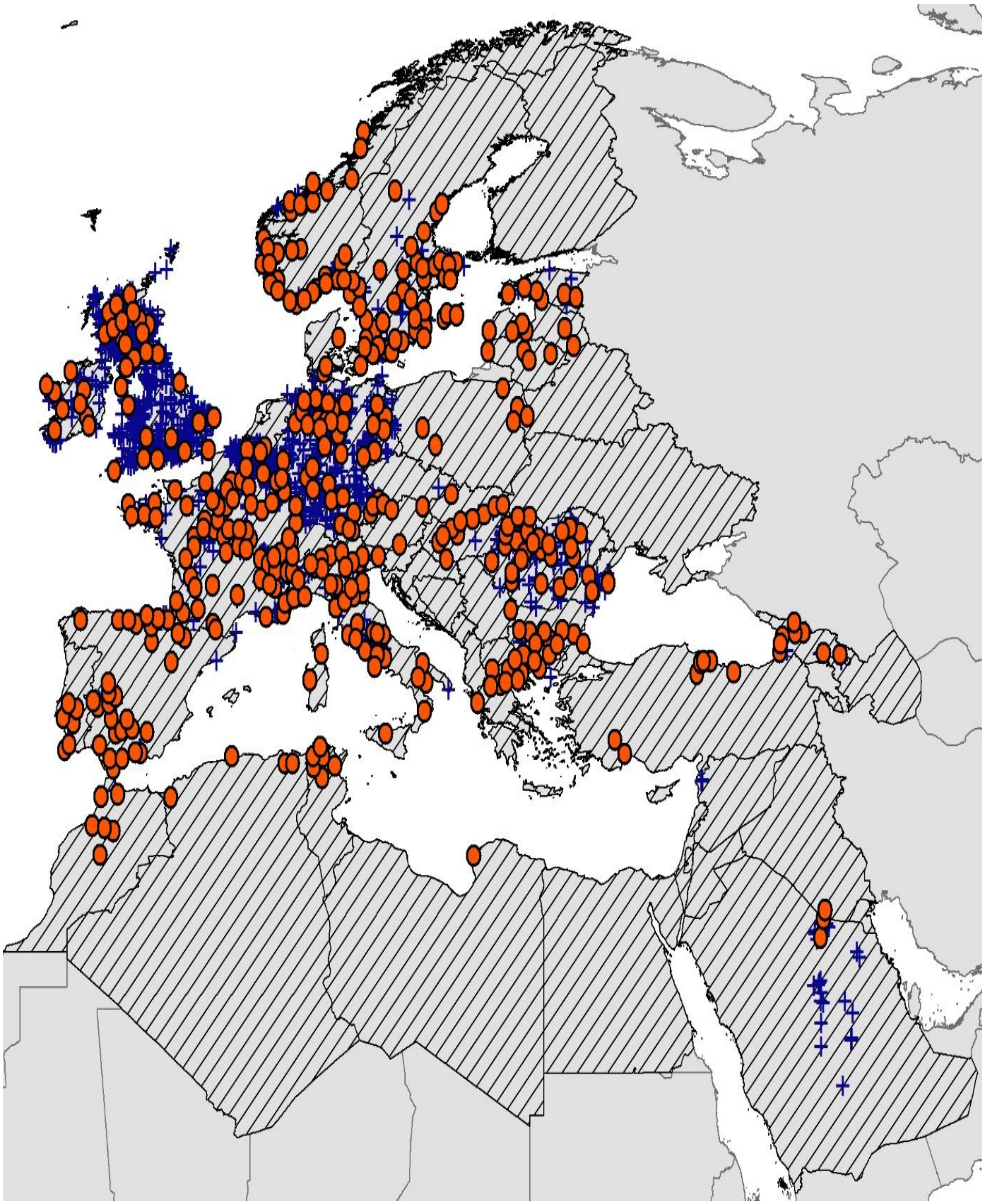


Figure 1.Map showing all occurrence points of *Ixodes ricinus* derived from various sources. Orange circles indicate points retained after distance filtering.

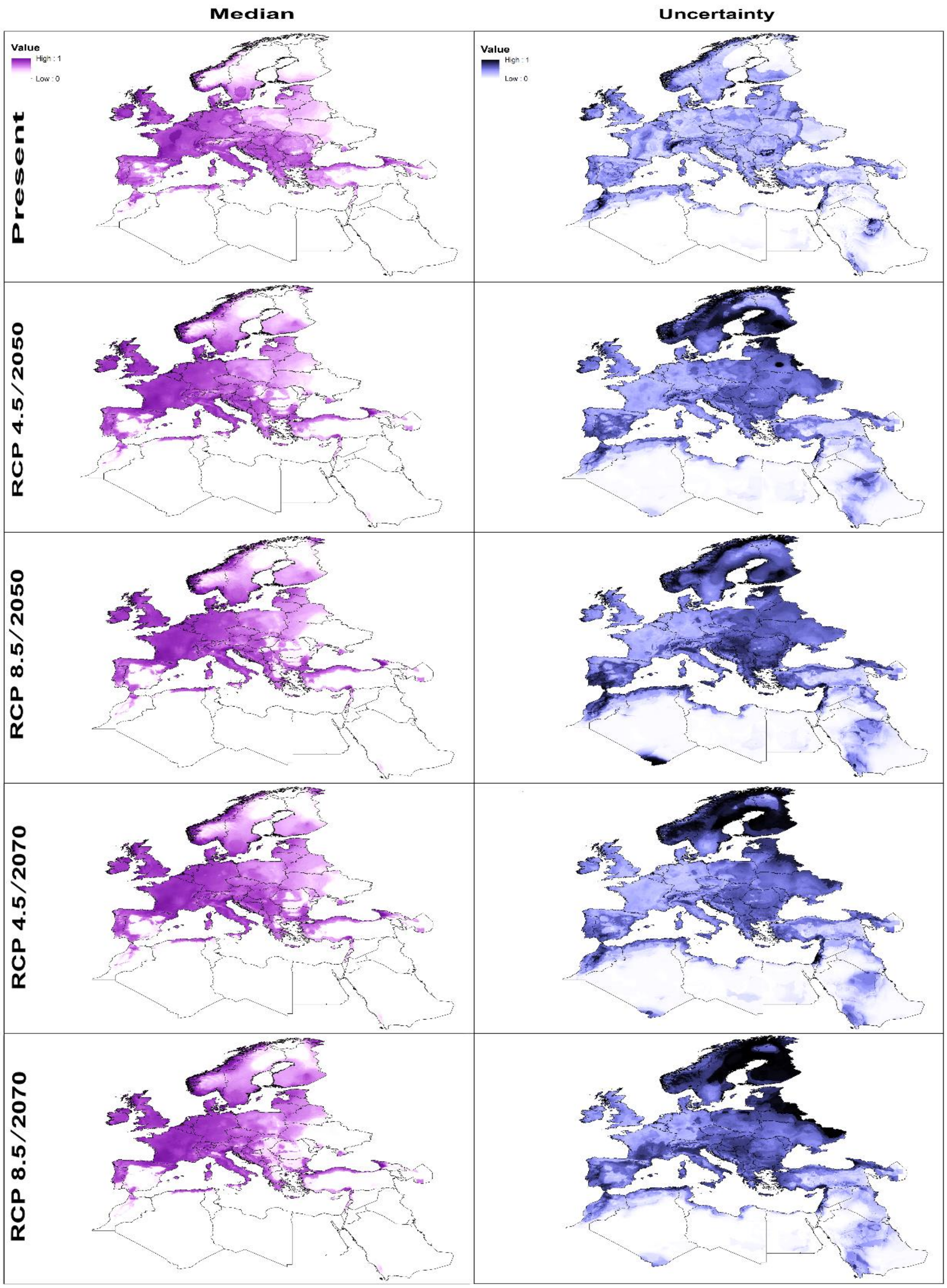


Figure 2. Current and future potential distribution of *Ixodes ricinus* based on present-day and future climatic conditions. Left-hand maps show potential distributions whereas right-hand maps indicate the uncertainty.

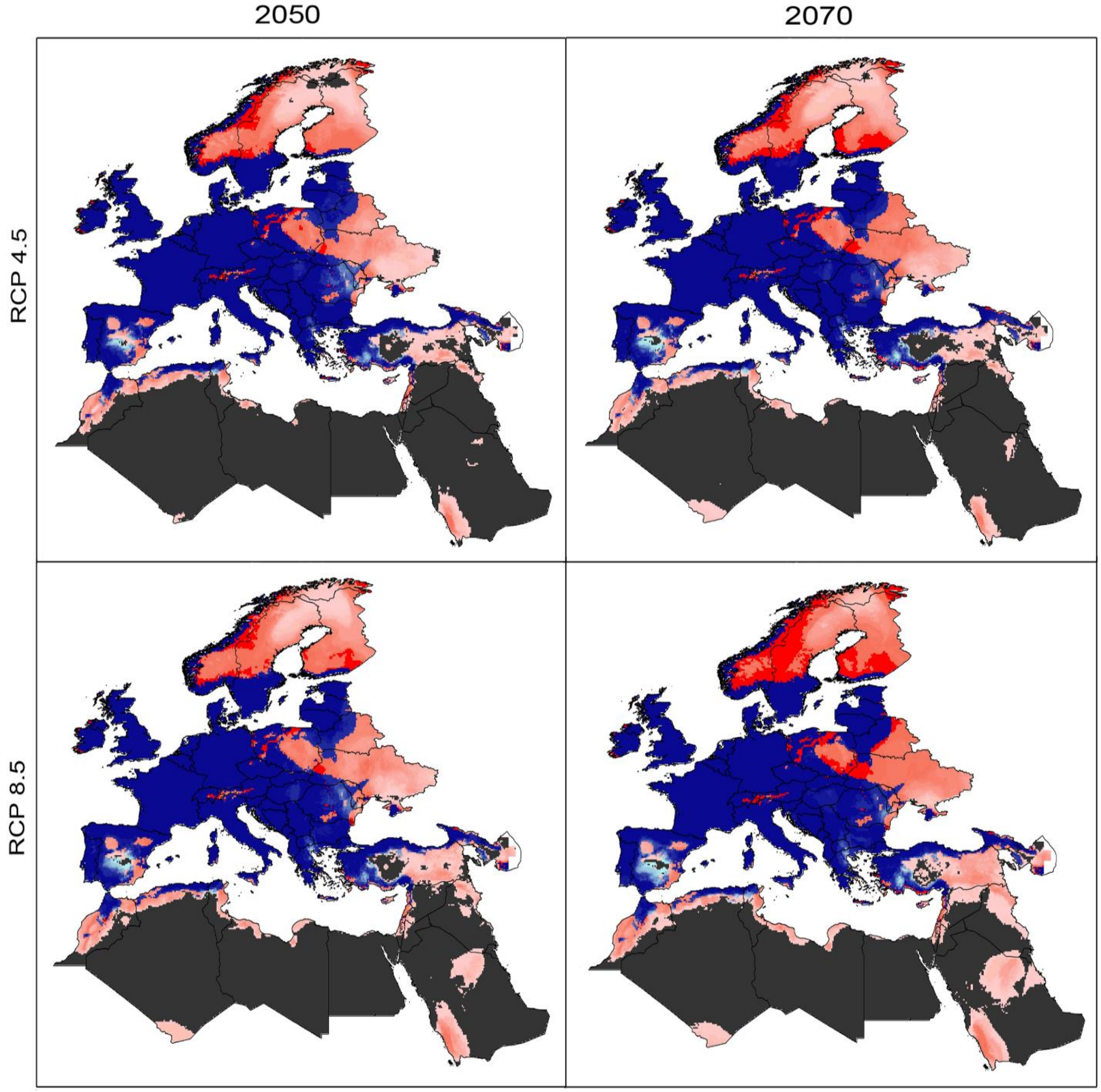


Figure 3. Summary of the binary modeled potential distributions of *Ixodes ricinus* under future conditions to show suitable areas and to illustrate differences between representative concentration pathways (RCPs) and time periods. Blue color indicates model suitability under both present and future suitability (light blue denotes low confidence and dark blue denotes high confidence), red color represents predicted expansion areas in the future suitability (light red denotes low confidence and dark red denotes high confidence); dark gray areas are not suitable.

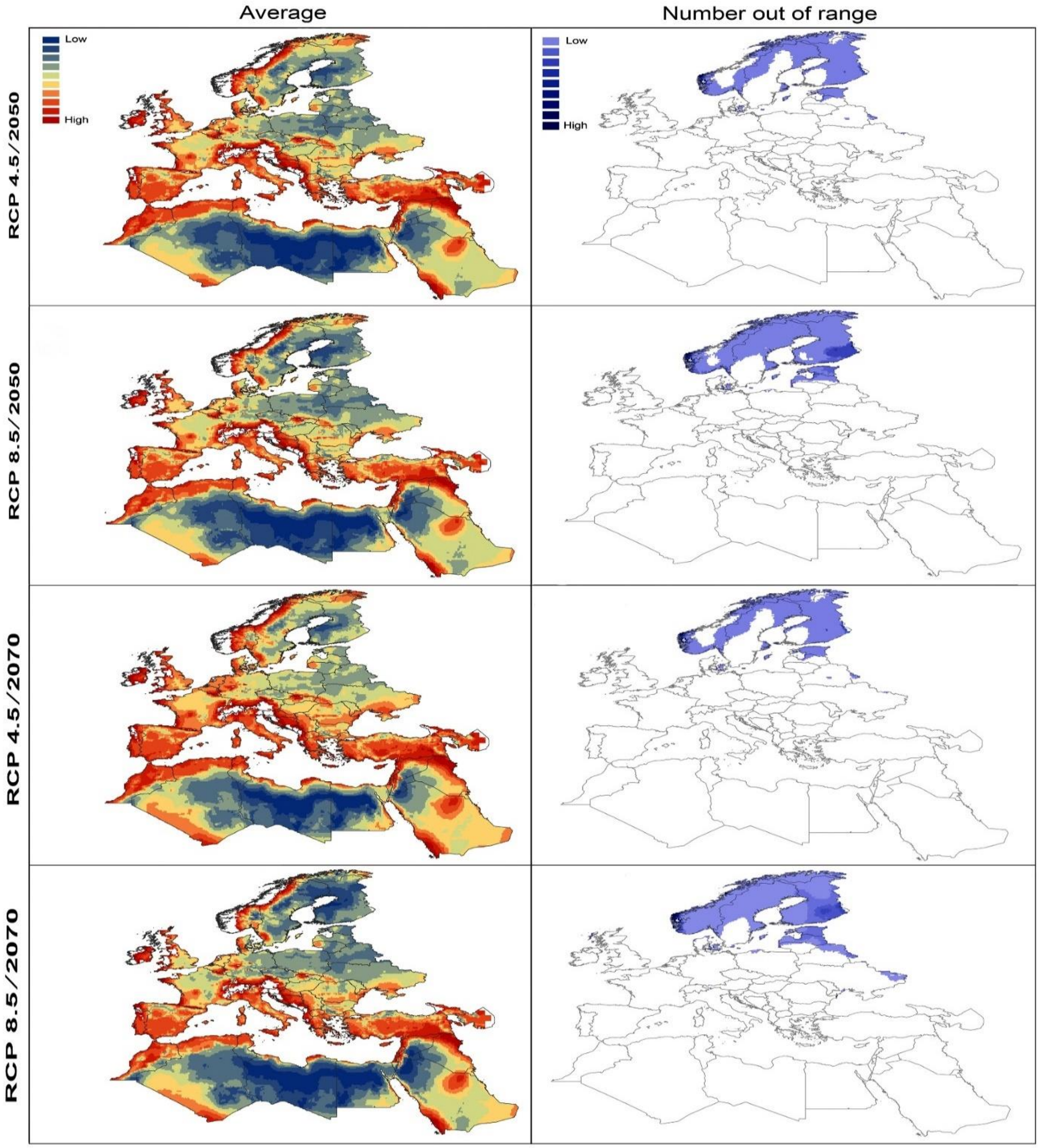


Figure 4. MOP calculations for model transfers from present to future climate scenarios for 17 GCMs (RCP 4.5 and RCP 8.5) in 2050 and 2070. Left panels show the average MOP distance among models (dark red represents high average and dark blue represents low average). The right panels show the number of models out of range (dark blue represents areas with most frequent strict extrapolation).

Appendix 2: Table of GCMs models

Table contains 17 General Circulation Models that used for future projections analysis.

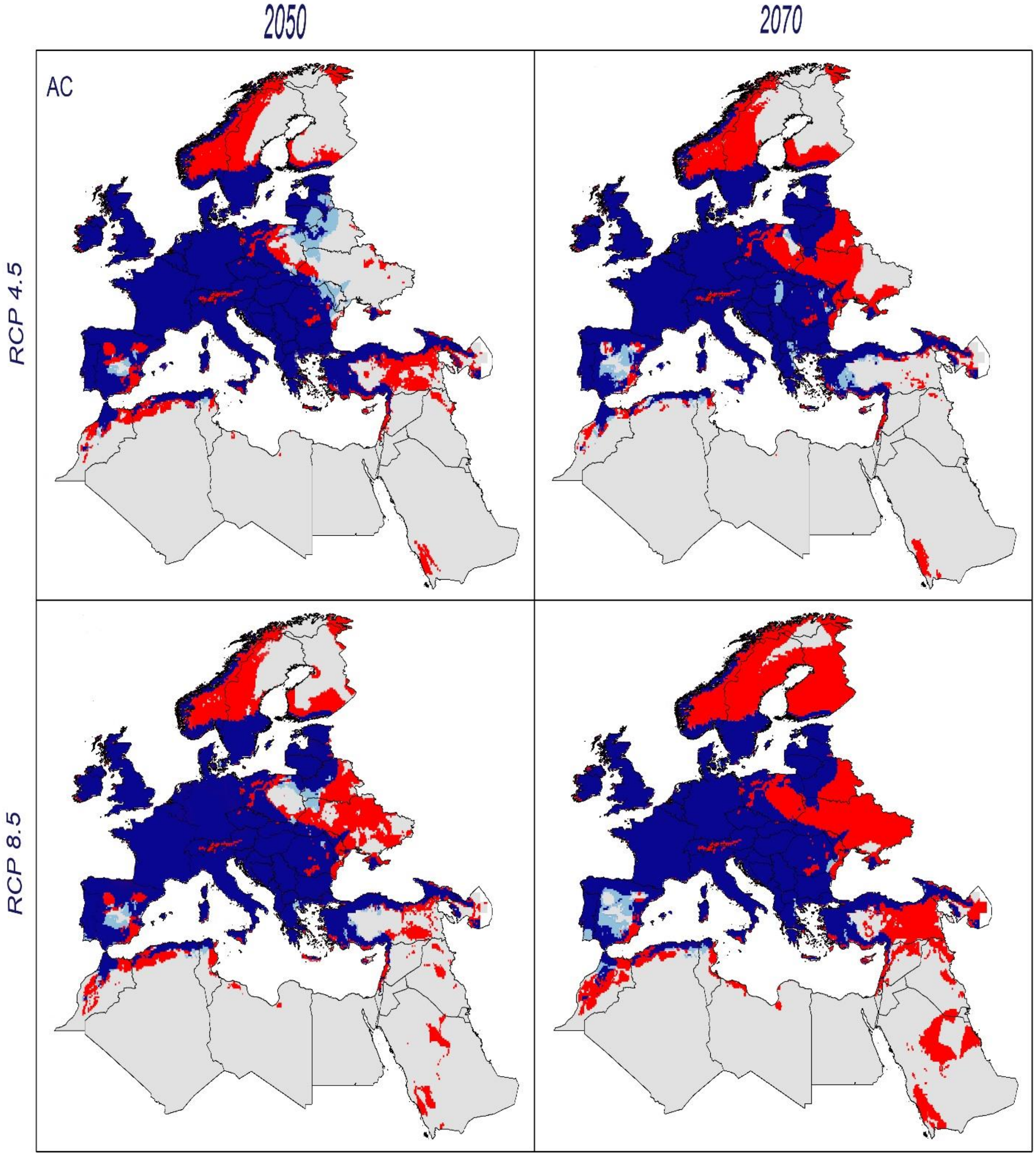
Table 1. . Summary of general circulation models (GCMs) explored in our analysis.

GCM	Code	Model center (or Group)	Institute ID
ACCESS 1 - 0	AC	Commonwealth Scientific and Industrial Research Organization (CSIRO) and Bureau of Meteorology (BOM), Australia.	CSIRO-BOM
BCC – CSM 1 – 1	BC	Beijing Climate Center, China Meteorological Administration.	BCC
CCSM 4	CC	National Center for Atmospheric Research.	NCAR
CNRM – CM 5	CN	Centre National de Recherches Météorologiques	CNRM-CERFACS
GFDL – CM 3	GF	NOAA Geophysical Fluid Dynamics Laboratory.	NOAA GFDL
GISS – E2 - R	GS	NASA Goddard Institute for Space Studies	NASA GISS
HadGEM 2 – AO	HD	National Institute of Meteorological Research / Korea Meteorological Administration.	NIMR/KMA
HadGEM 2-ES	HE	Met Office Hadley Centre (additional HadGEM2-ES realizations contributed by Instituto Nacional de Pesquisas Espaciais).	MOHC (additional realizations by INPE)

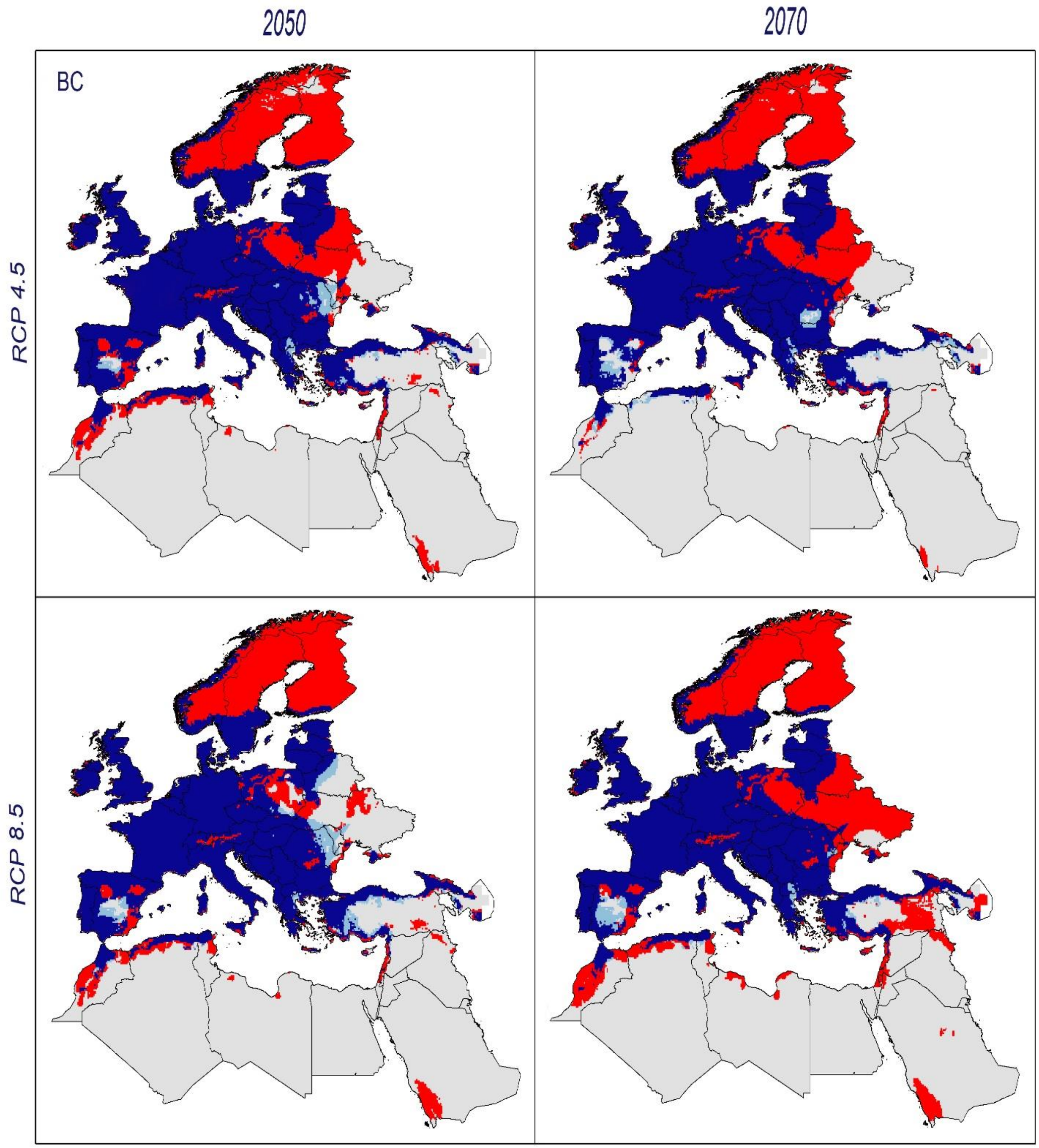
HadGEM 2 – CC	HG	Met Office Hadley Centre (additional HadGEM2-ES realizations contributed by Instituto Nacional de Pesquisas Espaciais).	MOHC (additional realizations by INPE)
INMCM 4	IN	Institute for Numerical Mathematics	INM
IPSL – CM5A – LR	IP	Institute Pierre-Simon Laplace	IPSL
MIROC – ESM – CHEM	MI	Japan Agency for Marine-Earth Science and Technology, Atmosphere and Ocean Research Institute (The University of Tokyo), and National Institute for Environmental Studies.	MROC
MIROC – ESM	MR	Japan Agency for Marine-Earth Science and Technology, Atmosphere and Ocean Research Institute (The University of Tokyo), and National Institute for Environmental Studies.	MROC
MIROC 5	MC	Atmosphere and Ocean Research Institute (The University of Tokyo), National Institute for Environmental Studies, and Japan Agency for Marine-Earth Science and Technology.	MROC
MPI – ESM – LR	MP	Max-Planck-Institut für Meteorolgie (Max Planck Institute for Meteorology).	MPI-M
MRI – CGCM 3	MG	Meteorological Research Institute	MRI
NorESM 1 – M	NO	Norwegian Climate Centre	NCC

Appendix 3: Supplementary figures

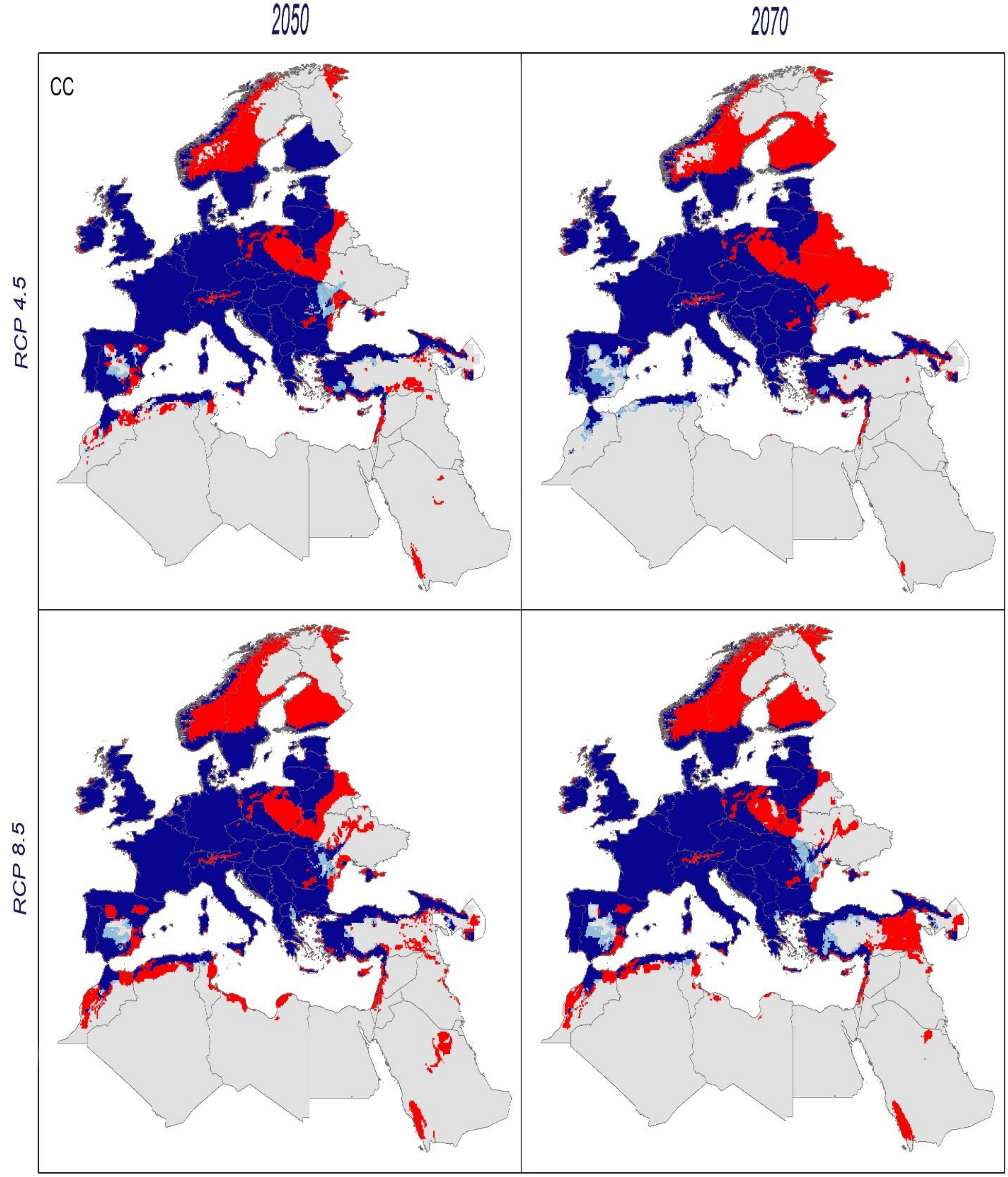
Maps show the differences among models for each GCM in 2 time slides (2050 & 2070) and 2 RCPs (RCP 4.5 & RCP 8.5) emissions.



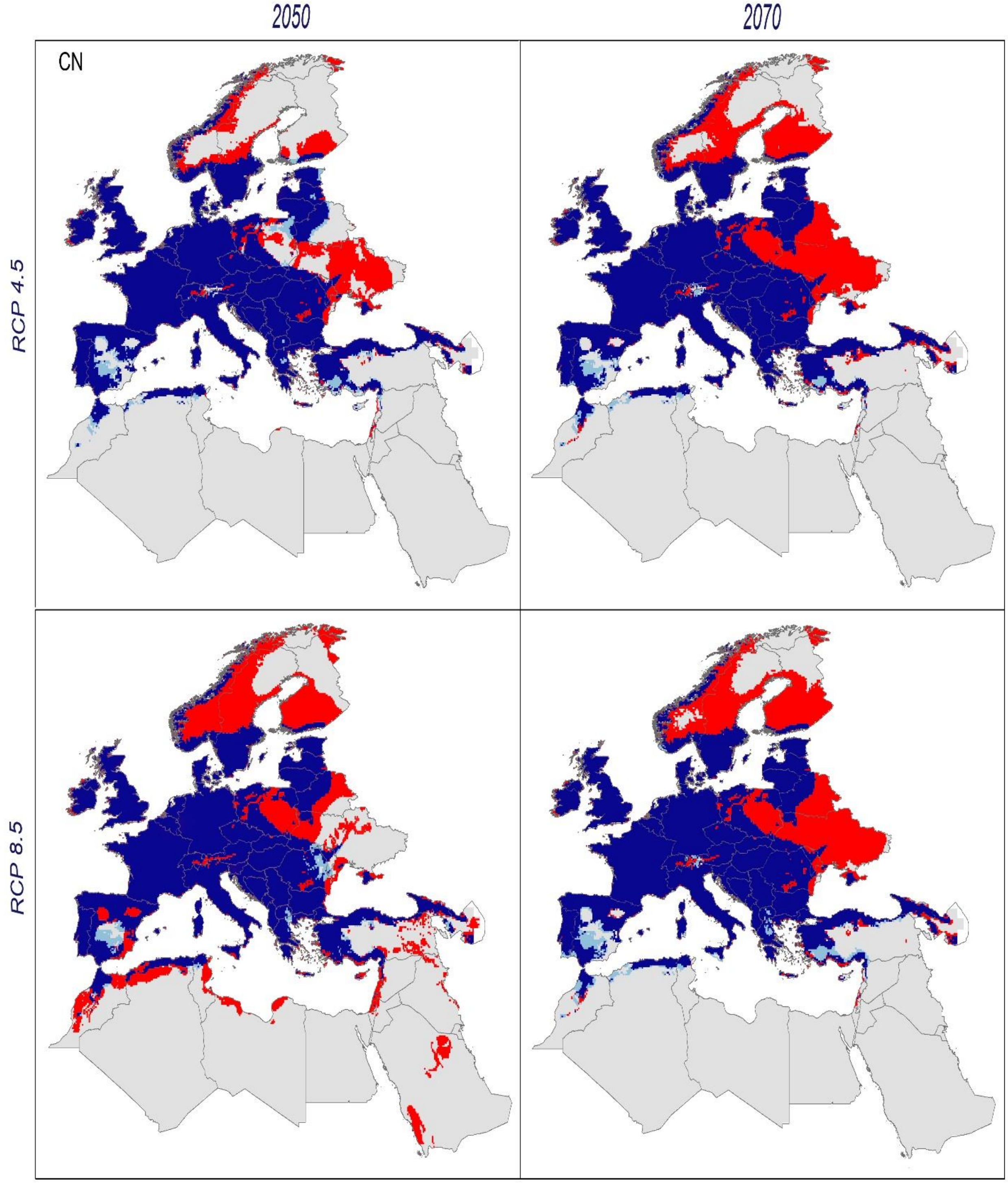
Supplementary fig 1. GCM: Commonwealth Scientific and Industrial Research Organization (CSIRO) and Bureau of Meteorology (BOM), Australia (ACCESS 1 – 0). Red indicates to future suitable prediction, Dark blue indicates to present and future suitable prediction, and light blue indicates to retraction areas.



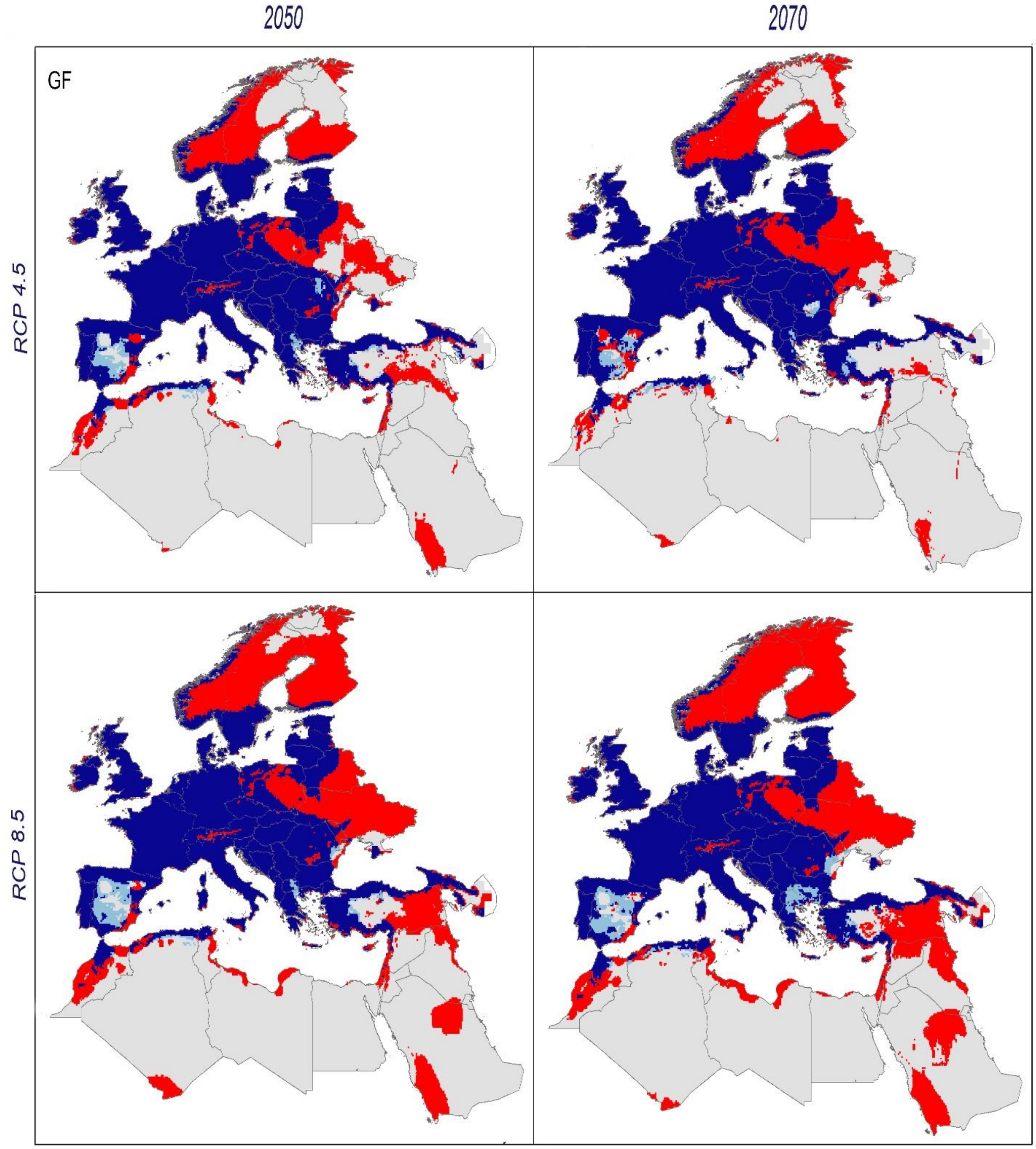
Supplementary fig 2. Beijing Climate Center, China Meteorological Administration (BCC – CSM 1 – 1)



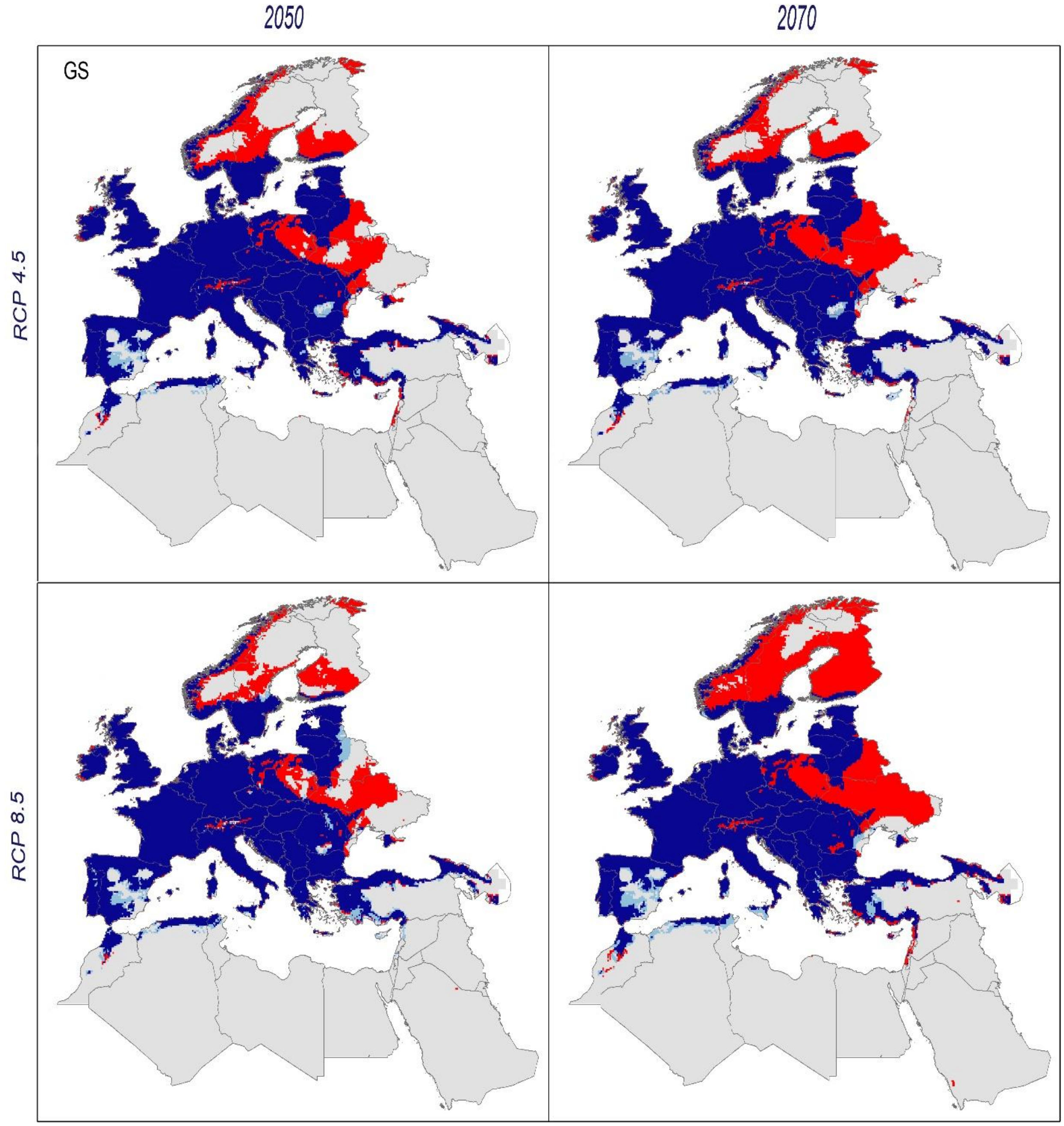
Supplementary fig 3. National Center for Atmospheric Research (CCSM 4).



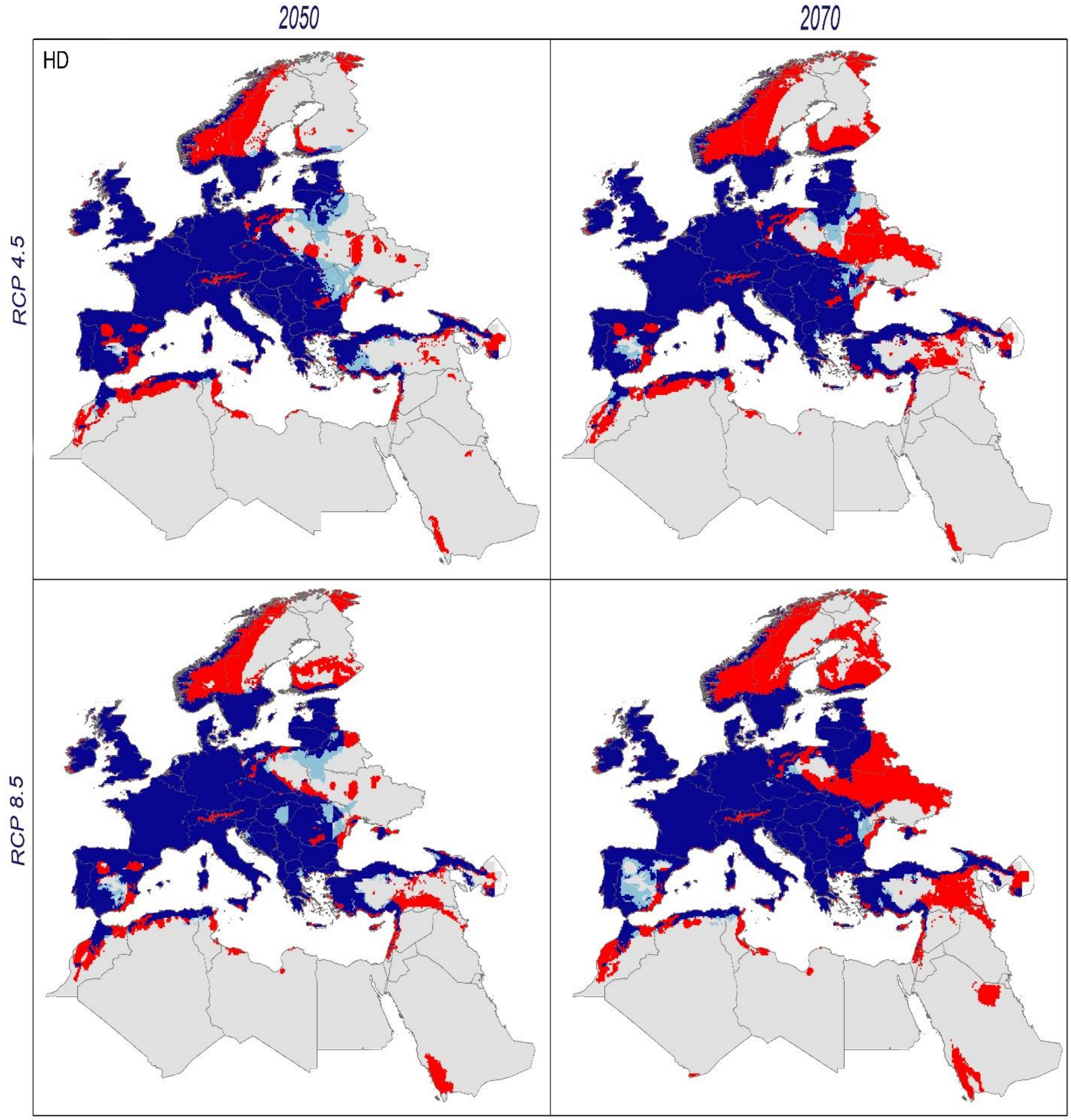
Supplementary fig 4. Centre National de Recherches Météorologiques (CNRM – CM 5).



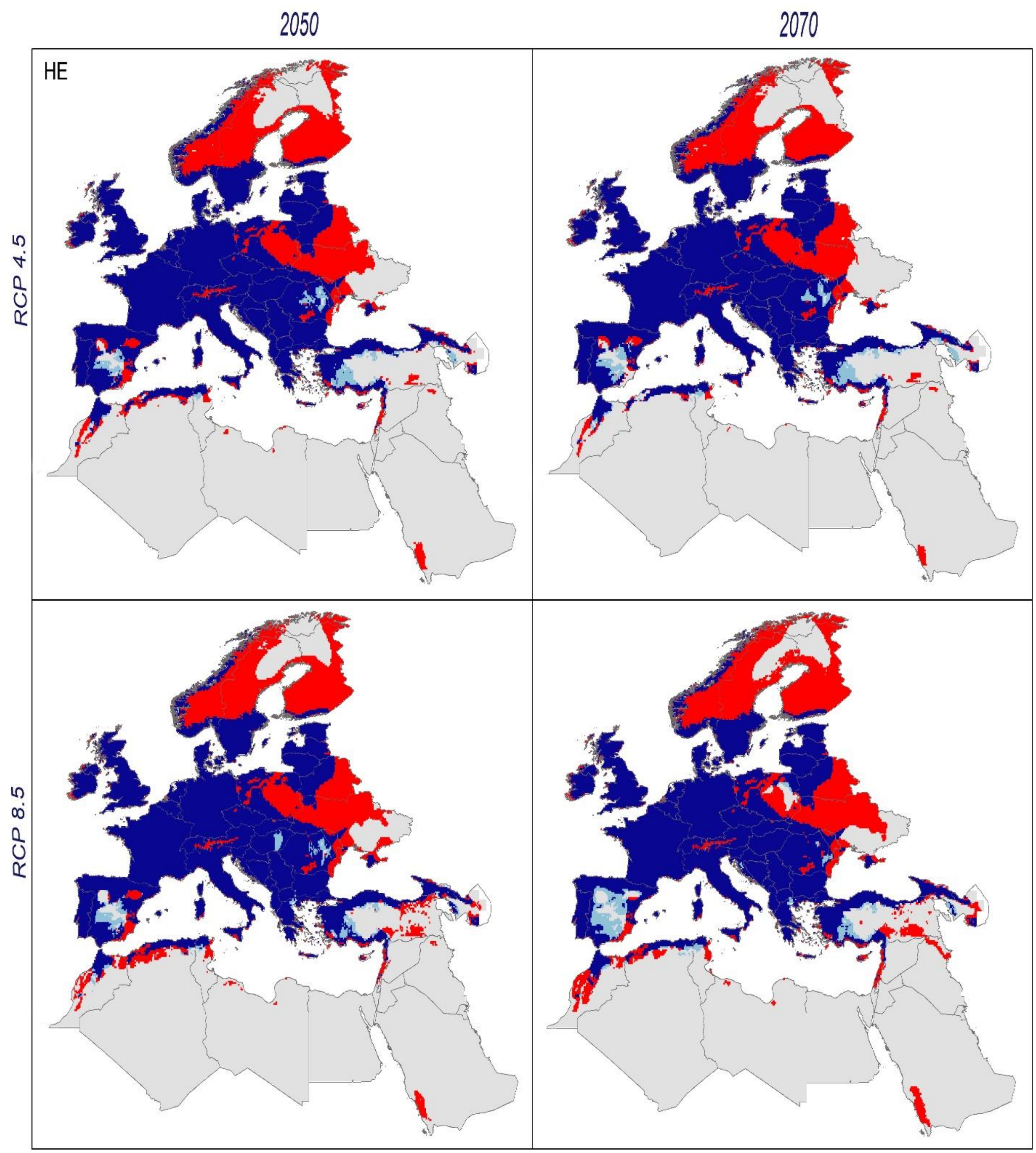
Supplementary fig 5. NOAA Geophysical Fluid Dynamics Laboratory (GFDL – CM 3).



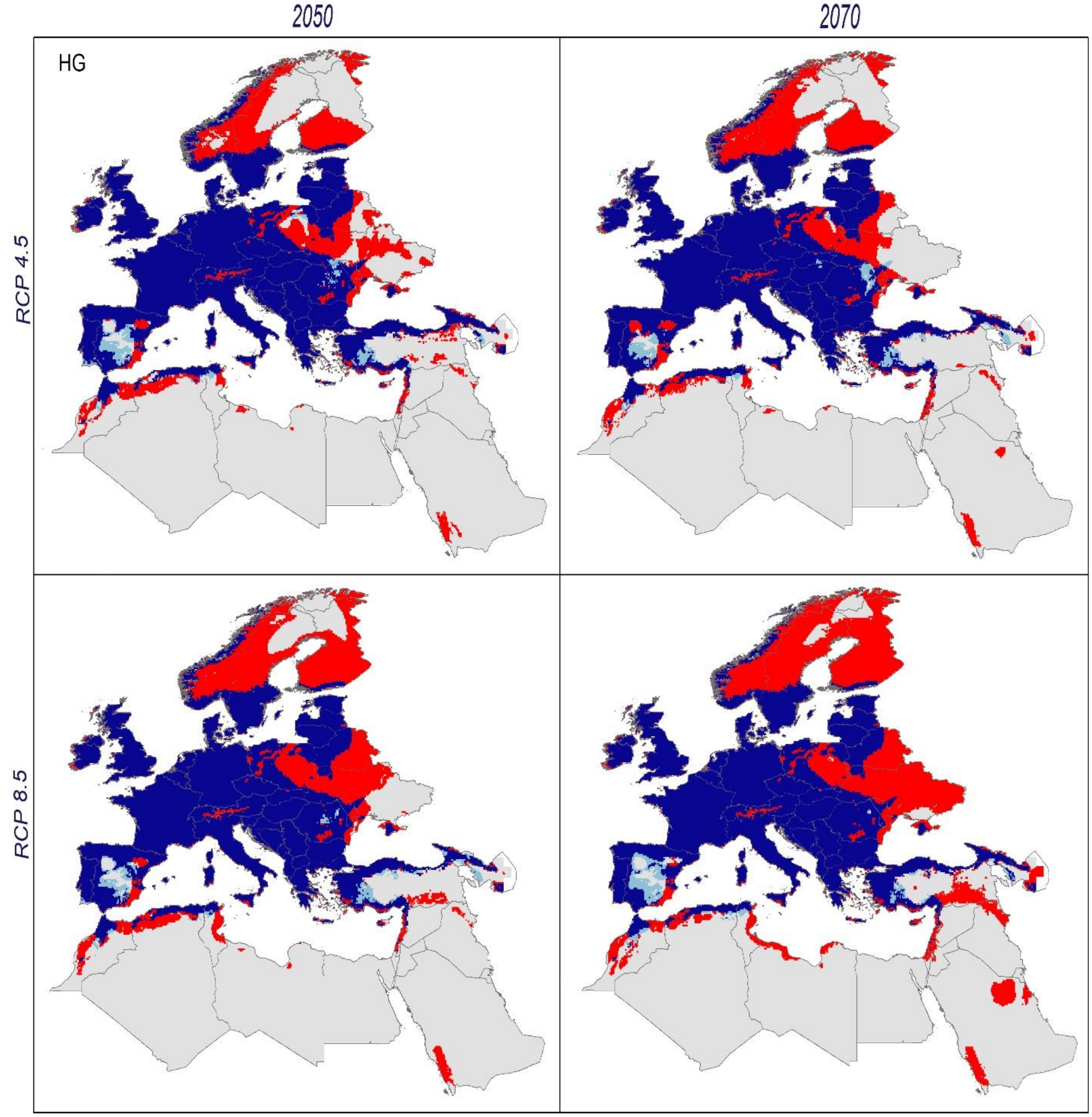
Supplementary fig 6. NASA Goddard Institute for Space Studies (GISS – E2 - R).



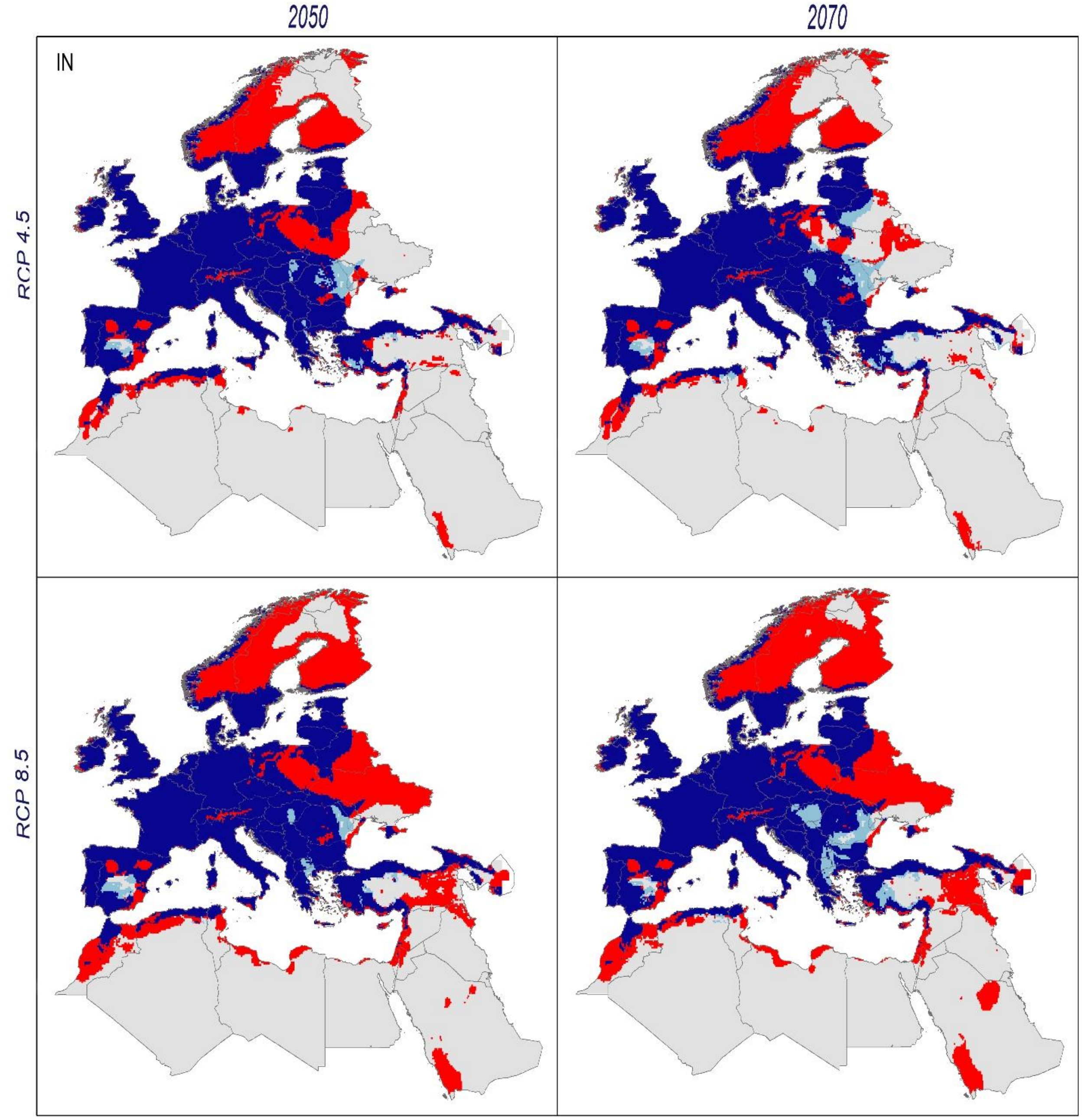
Supplementary fig 7. National Institute of Meteorological Research / Korea Meteorological Administration (HadGEM 2 – AO).



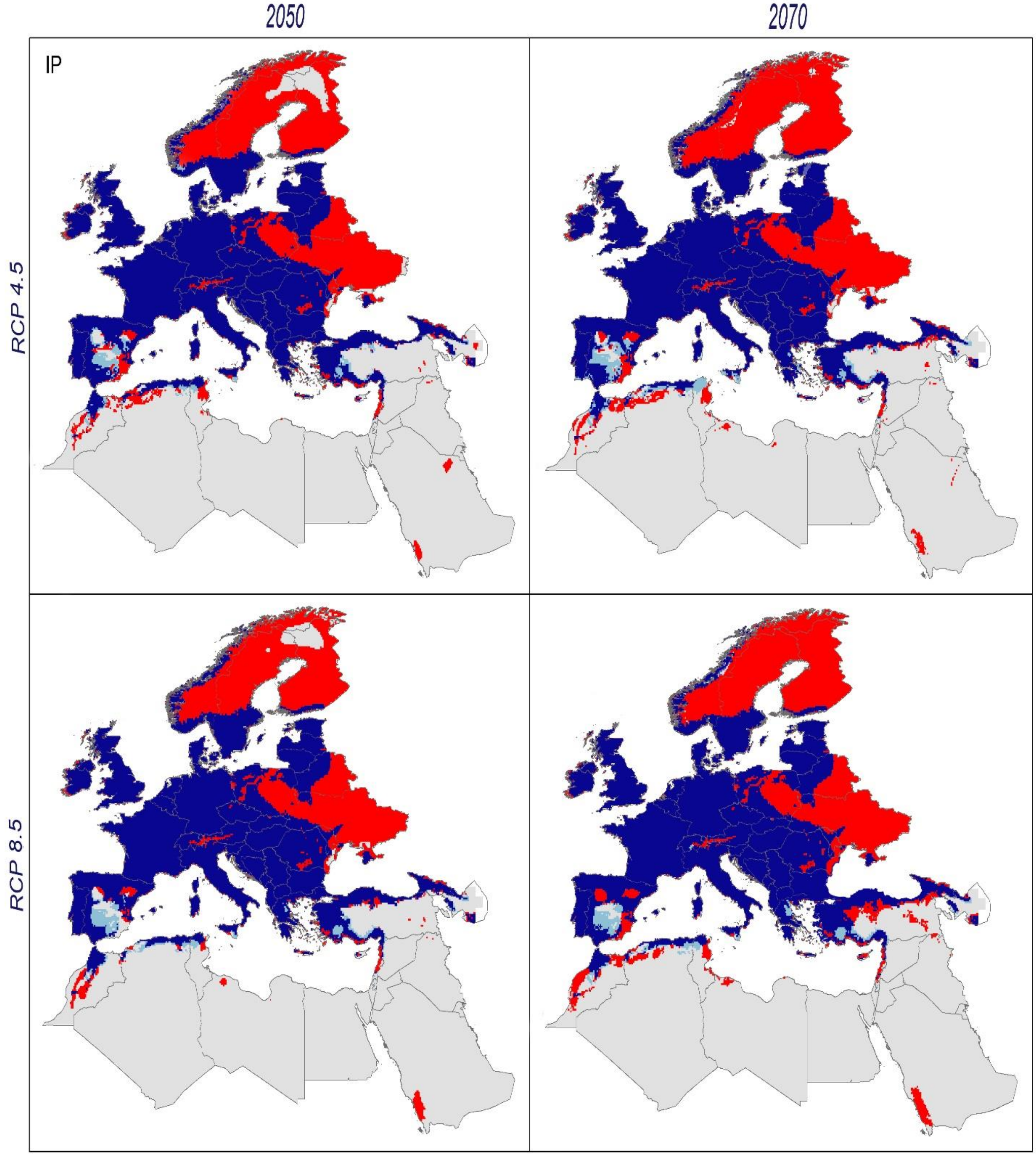
Supplementary fig 8. Met Office Hadley Centre (additional HadGEM2-ES realizations contributed by Instituto Nacional de Pesquisas Espaciais) (HadGEM 2-ES).



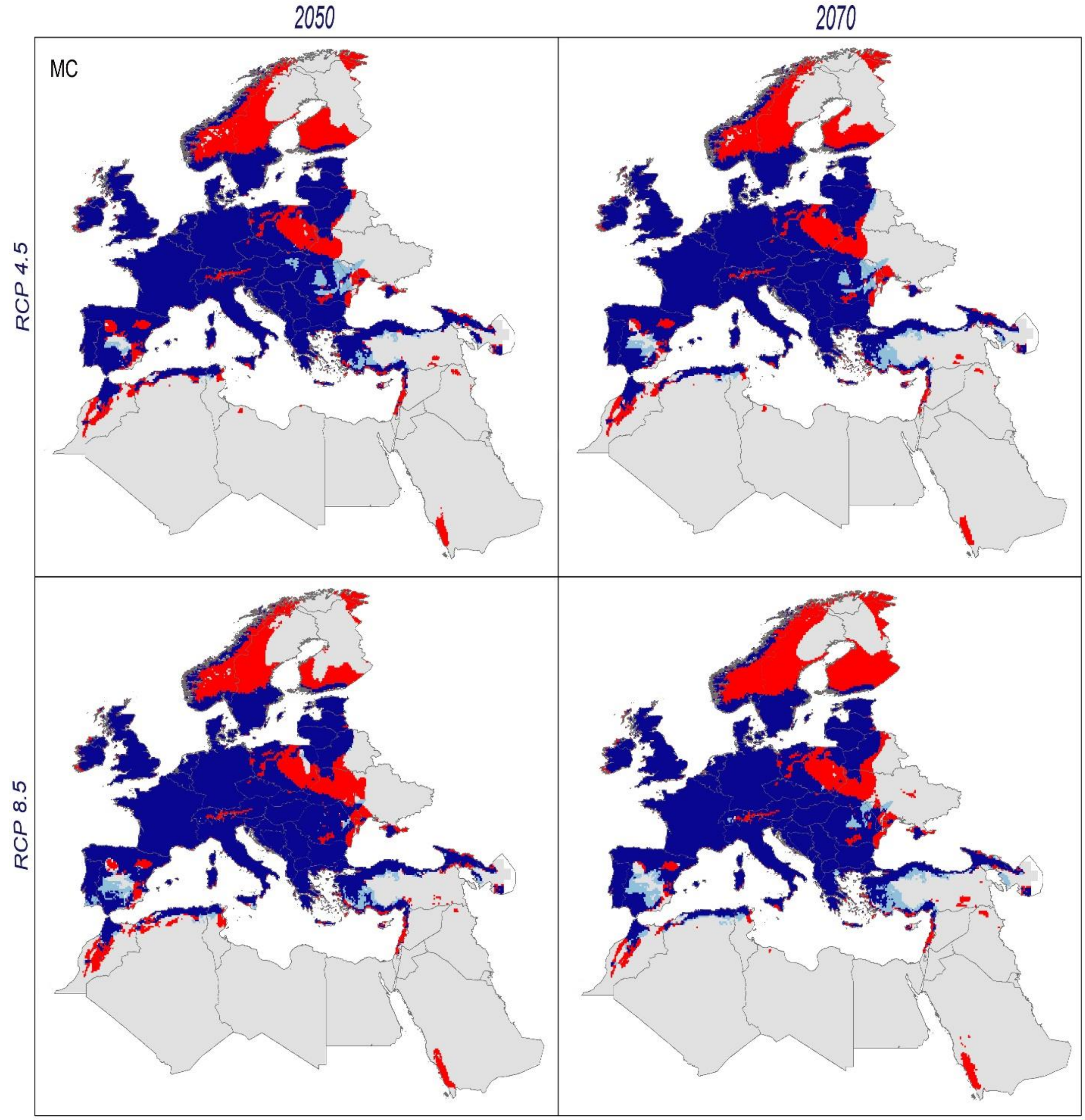
Supplementary fig 9. Met Office Hadley Centre (additional HadGEM2-ES realizations contributed by Instituto Nacional de Pesquisas Espaciais) (HadGEM 2 – CC).



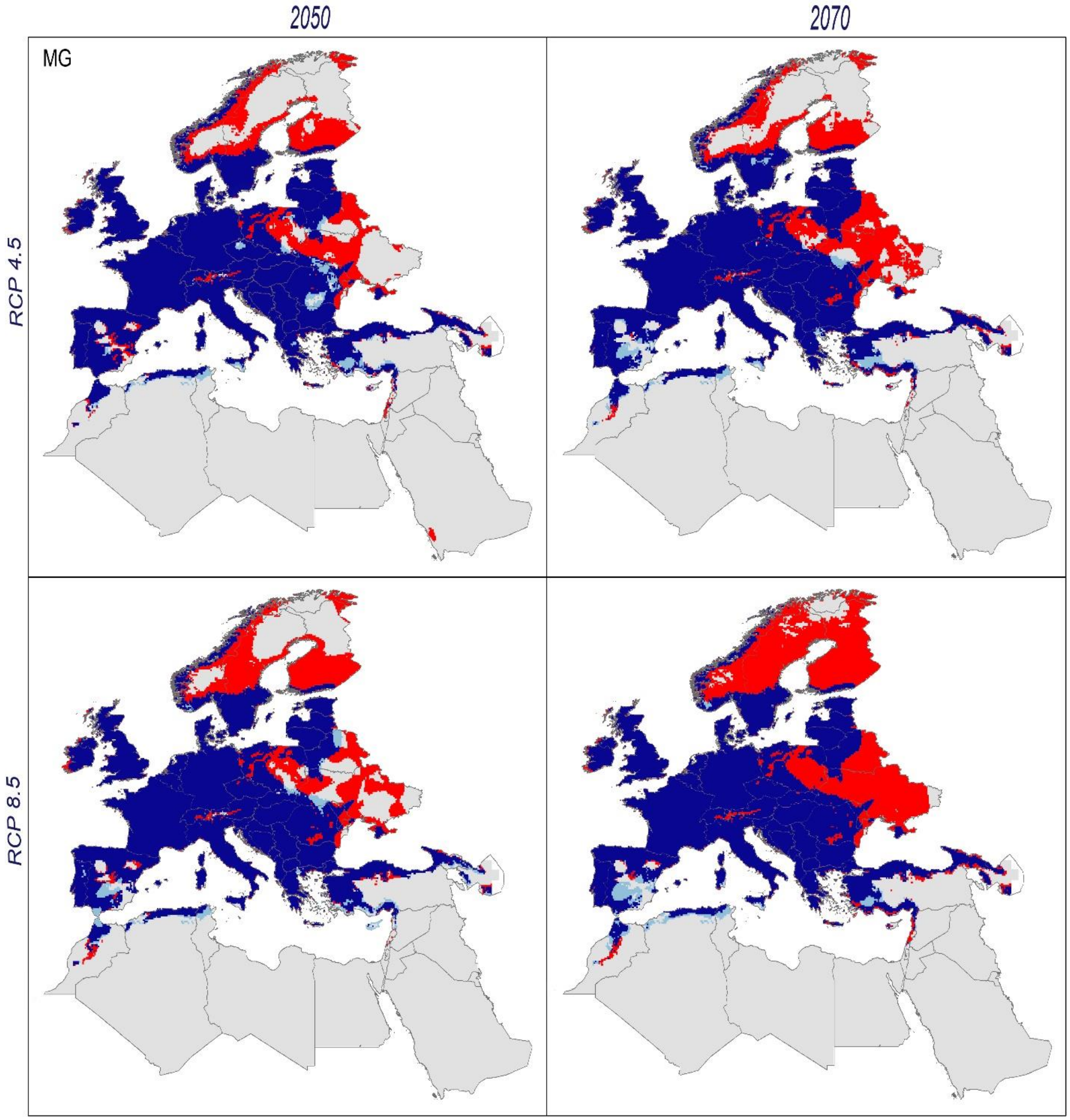
Supplementary fig 10. Institute for Numerical Mathematics (INMCM 4).



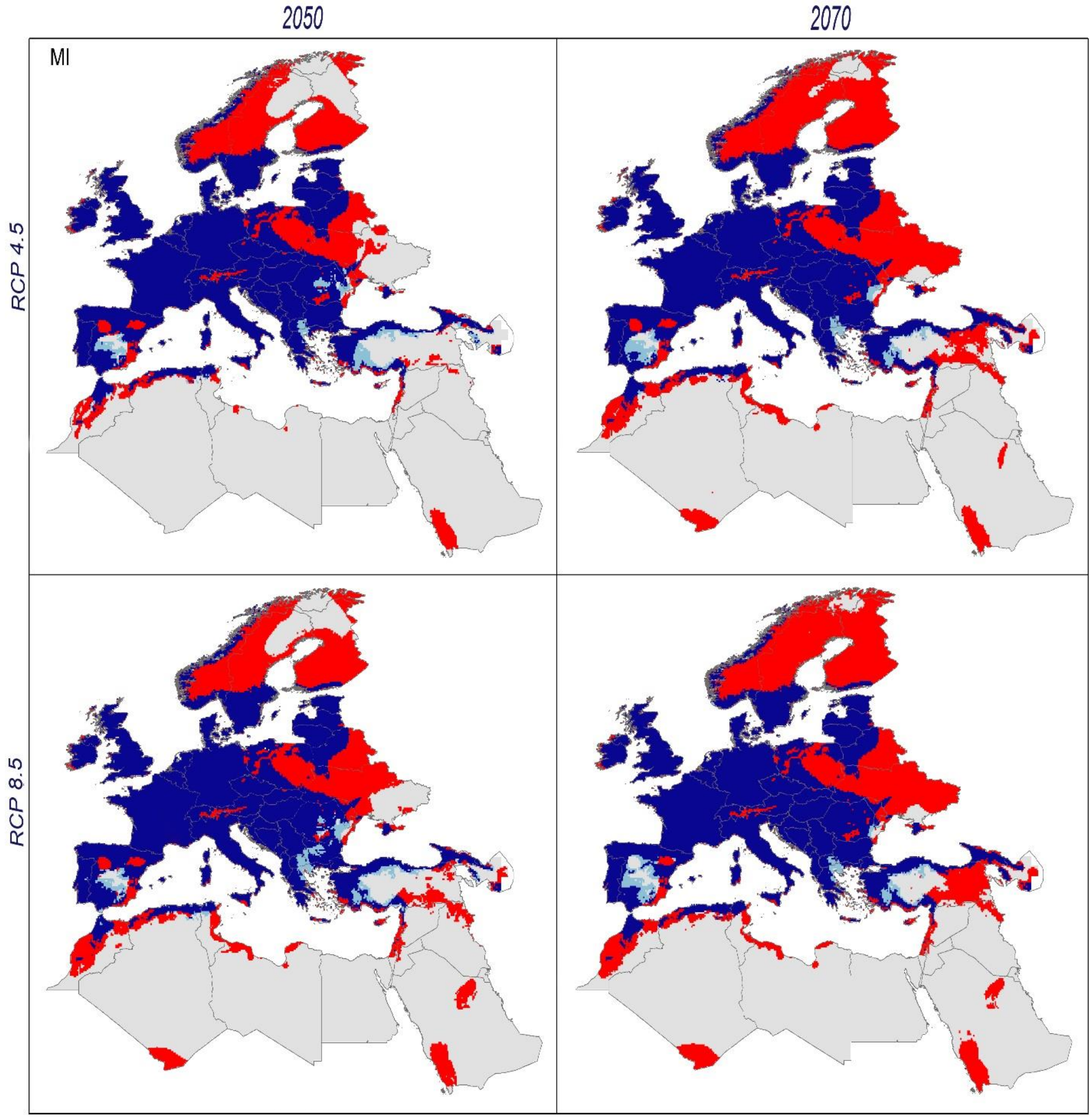
Supplementary fig 11. Institute Pierre-Simon Laplace (IPSL – CM5A – LR).



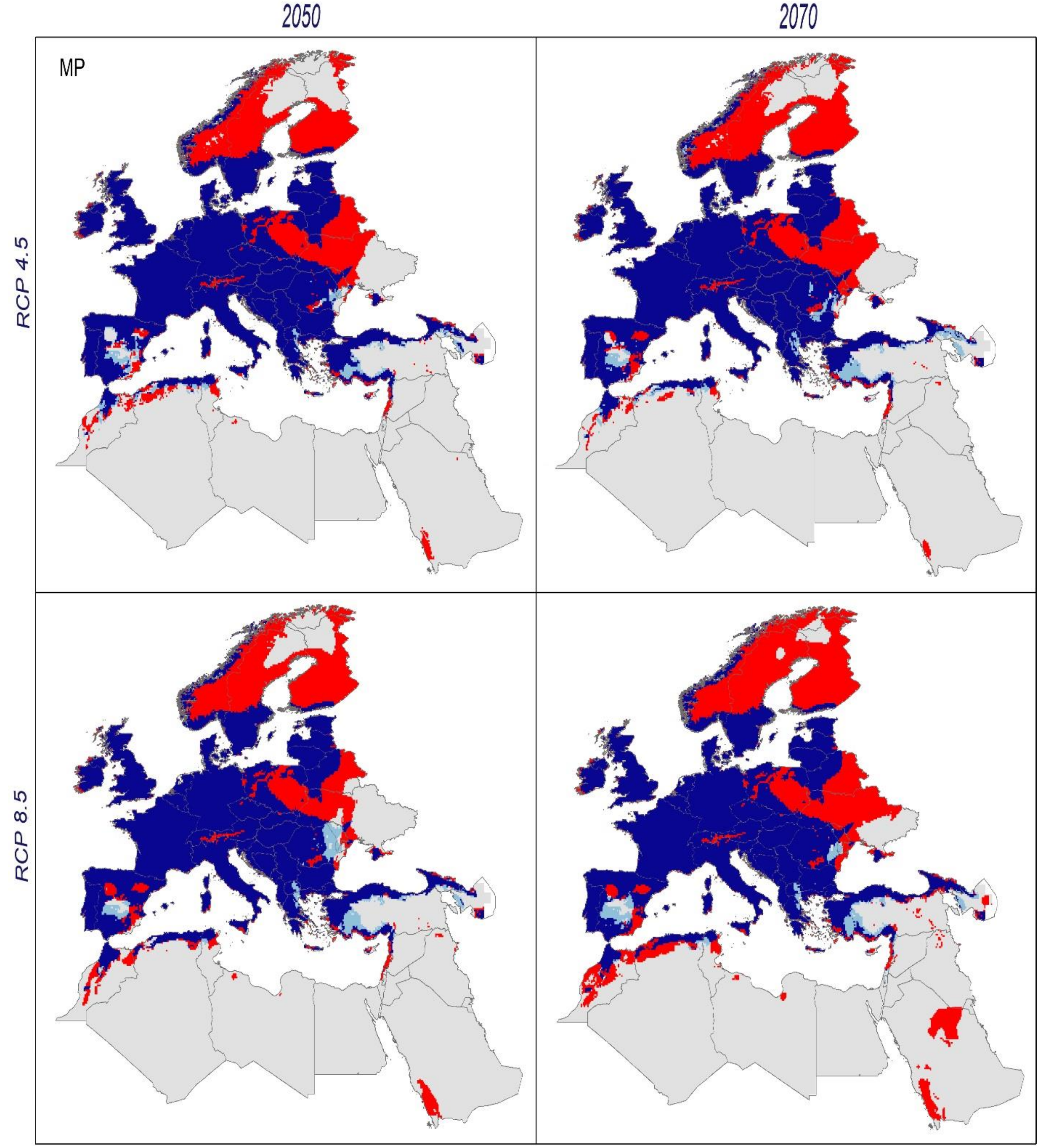
Supplementary fig 12. Atmosphere and Ocean Research Institute (The University of Tokyo), National Institute for Environmental Studies, and Japan Agency for Marine-Earth Science and Technology (MIROC 5).



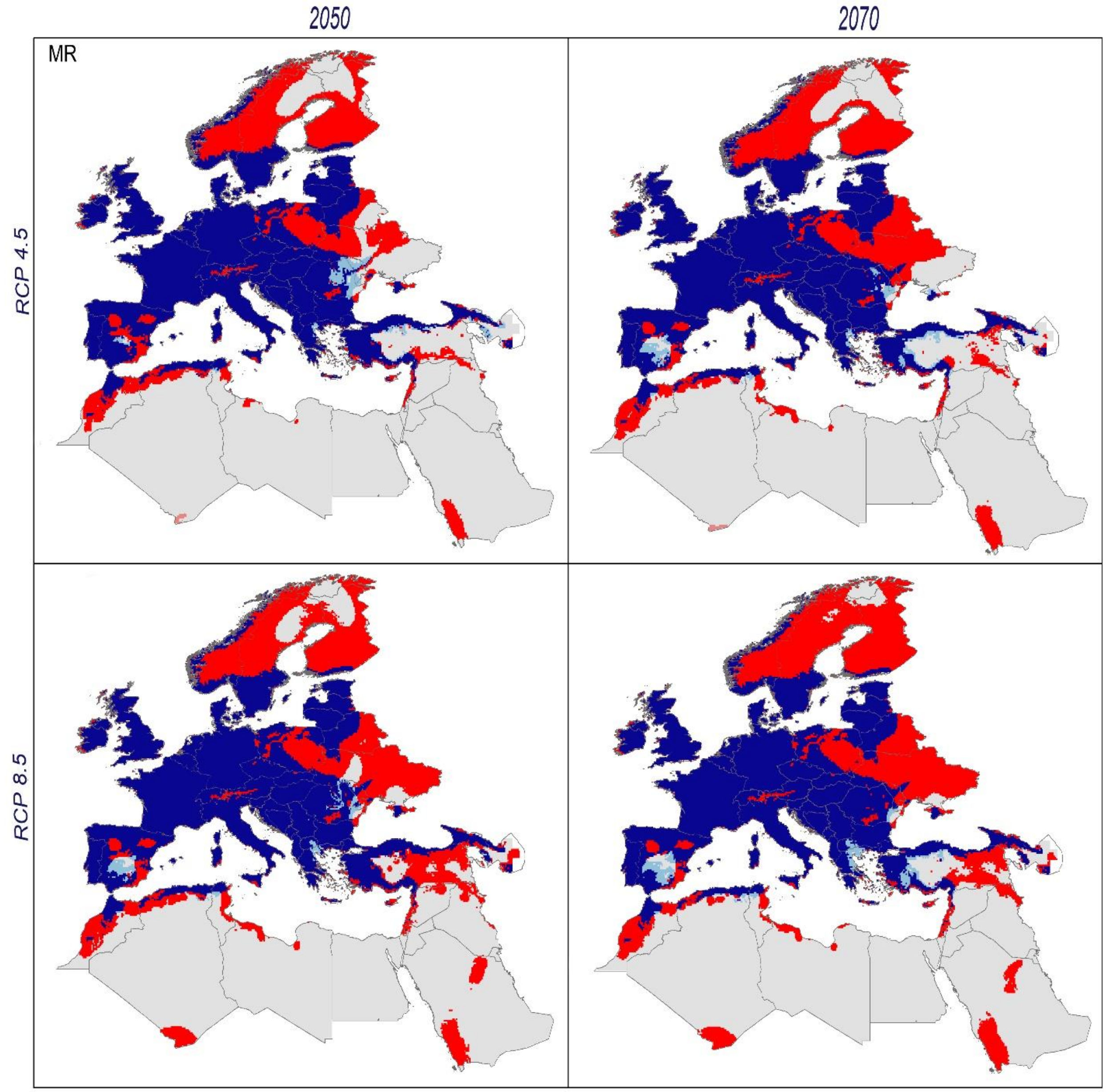
Supplementary fig 13. Meteorological Research Institute (MRI – CGCM 3).



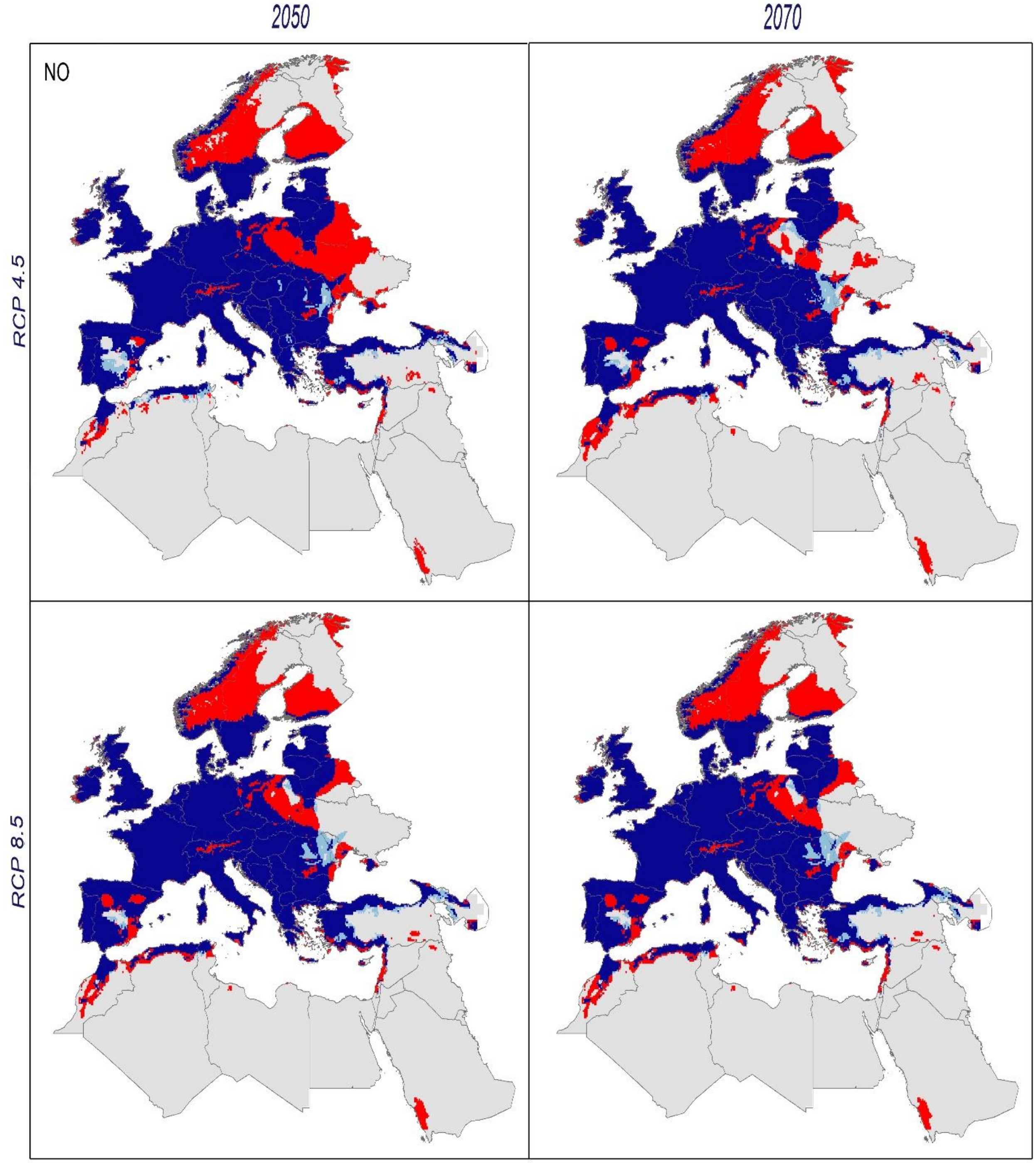
Supplementary fig 14. Japan Agency for Marine-Earth Science and Technology, Atmosphere and Ocean Research Institute (The University of Tokyo), and National Institute for Environmental Studies (MIROC – ESM – CHEM).



Supplementary fig 15. Max-Planck-Institut für Meteorolgie (Max Planck Institute for Meteorology) (MPI – ESM – LR).



Supplementary fig 16. Japan Agency for Marine-Earth Science and Technology, Atmosphere and Ocean Research Institute (The University of Tokyo), and National Institute for Environmental Studies (MIROC – ESM).



Supplementary fig 17. Norwegian Climate Centre (NorESM 1 – M).