

To whom it may concern,

This letter is in support of Dr. Marinescu's application for permanent residency in the United States. Dr. Marinescu is an scientist of extraordinary talent with an outstanding reputation, and among the most productive and innovative figures in the field of medical Artificial Intelligence (AI).

I am Professor in XX at the Department of XX at the XXX XXX, XX, and full Professor of XX at the Institute of XXXX. [...] I am the Scientific Director of XXX, involved in the analysis of multicentre drug trials. I serve on the Editorial boards of multiple journals, including XXXXX. My research interests focus on Multiple Sclerosis, on dementias such as Alzheimer's disease, and on the normal ageing process.

Through these research activities I have come in contact with Dr. Marinescu on scientific research, being a scientific advisor for the TADPOLE Challenge that he conducted. TADPOLE is the leading international challenge and benchmark of computational models for predicting subjects at risk of Alzheimer's disease. The challenge received a lot of interest from researchers, media and institutions around the world: more than 30 international teams participated with almost 100 different prediction models, was widely featured in the media and received sponsorship from the three main Alzheimer's disease charities Alzheimer's Association, The Alzheimer's Society, and Alzheimer's Research UK. In addition, the contribution of TADPOLE towards the field was immense. In particular, the most surprising result was that while the models could predict the clinical diagnosis and measures from MRI, they could not reliably predict cognitive scores that are routinely used in clinical trials of Alzheimer's disease. This finding has important implications for clinical trials, and also highly impacted the field: many researchers are now working on improving the predictions models for cognitive tests.

Dr. Marinescu has also made highly original contributions in the field of disease progression modelling, having authored and co-authored more than 11 scientific articles on this topic. One of his landmark contributions, the DIVE model, estimated the progression of Alzheimer's brain pathology markers at each location in the brain. In another landmark study Dr. Marinescu co-authored with Dr. Eshaghi, they applied such disease progression models on the largest cohort to date of subjects with Multiple Sclerosis, and found that the brain gray matter is affected in a specific sequence of events that they described. The publications are both well cited, and their models widely used in the research community, with DIVE and its precursor having more than 37 citations, while the Multiple Sclerosis study already receiving more than 104 citations. As one of the world experts in Multiple Sclerosis and Alzheimer's disease, I can confirm that such models are

of crucial importance for identifying the right subjects for clinical trials, and I am aware that pharmaceutical companies are already using their models for the analysis of their imaging data in Alzheimer's disease and Multiple Sclerosis drug trials.

Dr. Marinescu has further made landmark contributions to the study of Posterior Cortical Atrophy, a recently recognized variant of Alzheimer's disease that affects the visual cortex. Dr. Marinescu, through his scientific article published in the journal *Brain* as well as his PhD thesis, elucidated the temporal progression of Posterior Cortical Atrophy, and showed that it is indeed distinct from that of Alzheimer's disease. He further analysed the progression patterns in three different subgroups of Posterior Cortical Atrophy with different clinical presentations, and showed that these subgroups again have different progression profiles of brain atrophy. These contributions are fundamental for clinical trials in Posterior Cortical Atrophy, and will help the management of all patients suffering from this disorder (~2.5 million people worldwide).

The journals Dr. Marinescu has published in are the leading journals in the field. For example, the journal XXX, [...], has a very high acceptance standard, and only the leading scientific articles with major impact to the field are accepted. Other journals such as *Nature Communications* and *NeuroImage* also have a similarly high standard. Similarly, the leading international conferences in medical AI, Medical Image Computing and Computer Assisted Intervention (MICCAI) and Information Processing in Medical Imaging (IPMI), also only accept truly novel contributions. In addition, in contrast to conferences that only require abstract submissions, these conferences require articles fully describing the methods and results in their entirety, so publications in MICCAI and IPMI are often comparable to journal publications in their own right.

Dr. Marinescu is a scientific leader of extraordinary ability, who has risen to the very top of the field of medical Artificial Intelligence. His pioneering work on disease progression modelling has influenced many later developments and have led to a better understanding of many neurodegenerative diseases such as Alzheimer's disease, Posterior Cortical Atrophy and Multiple Sclerosis. In addition, through his TADPOLE project, he helped push forward the state-of-the-art AI models for the prediction of Alzheimer's disease. As a XXXX[anonymized role], I can confirm that Artificial Intelligence models such as those developed by Dr. Marinescu will play a pivotal role in future healthcare.

In summary, Dr. Marinescu has made many original contributions of major significance to the field, and will continue to do so in the future. It would thus greatly benefit the United States to have Dr. Marinescu as a permanent resident, and I give my full support to his petition.

Sincerely,