AirPROM

Taking respiratory modelling towards a patient specific model

Funded by the European Union

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European Respiratory Society – Switzerland
European Lung Foundation (ELF) – United Kingdom
European Federation of Allergy and Airways Diseases Patients' Associations (EFA) – Belgium

Creating models to move treatment forward

AirPROM aims to create a virtual model of the lung that can be used by scientists and health professionals to predict disease and match the right treatment to the right patient. This will help us achieve:

- Better measurement of disease progression
- Better monitoring of asthma and chronic obstructive pulmonary disease (COPD)
- More precise matching of the right treatment to the right patient
- Better tools for more targeted research
- Improved quality of life for people with asthma and COPD through personalised treatment

AirPROM will bridge the critical gaps in our clinical management of airways diseases, by providing validated models to predict disease progression, response to treatment, and the platform to translate these patient-specific tools, which can pave the way for the improvement of personalised management of airways diseases.

The multi-scale model will also help predict how the disease will progress and affect the airways, to help monitor the future risk for patients. By gaining an insight into how specific treatments will work, patients can have a better understanding of how to manage their condition in the future, enabling them to take better control of their disease.

Professor Chris Brightling, AirPROM project coordinator, said: *"Current treatments for COPD and asthma adopt a 'one size fits all' approach. People with these respiratory diseases are therefore missing out on the right treatment to help them manage their condition. Our patient-specific models will help us monitor the diseases and how they progress, to make current treatments much more specific and targeted to benefit COPD and asthma patients."*

Bringing European research together to bring modelling forwards

AirPROM is taking data from key European projects, and combining it with new data, to create and validate computational models that predict patient disease evolution and ultimately predict responses to treatment.

These European projects include U-BIOPRED, which is providing clinical, genomics (GWAS) data, and baseline as well as follow up Computed Tomography (CT) scans. The EvA study is also contributing clinical data, CT scans and genomics data, with transcriptomics work being advanced by AirPROM. The British Thoracic Society severe asthma registry group have also contributed clinical and CT scan data.

Alongside these large European projects, data from a number of smaller trials, supported by AirPROM, are also being used, such as a study into the effects of thermoplasty which aims to reduce the smooth muscle mass in the lung by tracking responses to this treatment.

The modelling effort

AirPROM's work on the lung focuses on three areas – sub-cellular and cellular level models, tissue models and whole lung models. To support these models, experiments are carried out at the cellular and tissue level, including the development of electrospun scaffolds at the tissue level. These scaffolds are one way in which cells are directed to replicate, and this can then lead to different cell structures in different patients.

Other re-modelling efforts include:

- Damage to the epithelial layer,
- Increased mucus production,
- Elevated content of sub epithelial collagen,
- Disruption of cartilage,
- Infiltration with immune system cells and angiogenesis.

Both Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans can show us the conditions and developments in the lung where disease is present, but AirPROM aims to create a method to segment the many small airways of the lung so that the images can be accurately reported. The goal is to create a process, using various computational algorithms, in order to support the use of imaging in the clinical environment.

The segmented images are then used by the computational modelers and physical modelers to replicate the biology seen in the lung and how this changes over time. This work also identifies significant changes seen in the lung which can act as a biomarker of disease development.

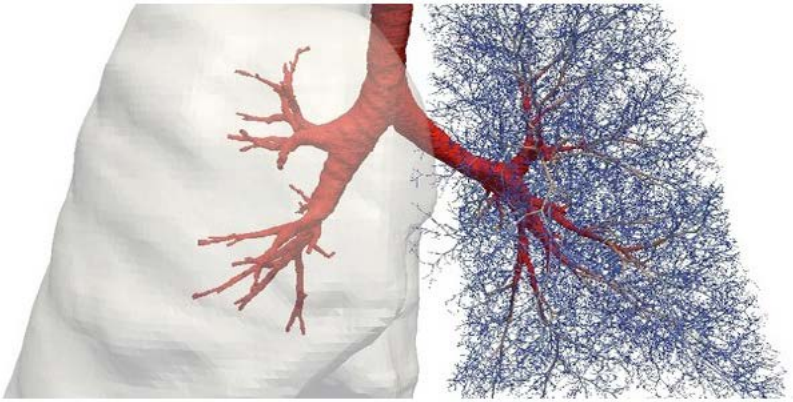
Managing the data

Supporting the research work is the development of a cloud based infrastructure which can host different software from different working groups. This platform is integrated with the AirPROM Knowledge Portal, where smaller datasets are held and where all data is mapped in order to assist researchers in identifying the right data for their work.

The Knowledge Portal currently contains 5 clinical studies with 930 participants and 23 segmentations. A new structure for model descriptions allows for the connection of models with results and data already existing in the system using a weighing and ranking system.

The 3D or physical mode

To understand how lung-conditions affect breathing and validate computational models, patient-specific models of the conducting airways have been created using novel Additive Layer Manufacturing (ALM) techniques (3D printing). The 3-dimensional shape of the airways is provided by the segmented airway images and used to create physical models. Using multi-material ALM physical models are produced that incorporate different elasticity ranging from very flexible in the small airways to quite stiff in the trachea area, thus mimicking the natural composition (cartilage, muscle and soft tissue) of various airway segments. The physical models are then used to study the flow dynamics inside the airways for different airway geometries as well as various airway compositions. This allows e.g. the effect of obstructions in different parts of the lungs to be investigated.



« Courtesy of Rafel Bordas, Computational Biology Group, Department of Computer Science, University of Oxford »

For more details

AirPROM has a good record of reporting its results at a number of conferences, including the leading respiratory conferences hosted by the American Thoracic Society and the European Respiratory Society. The AirPROM website (www.airprom.eu) contains the details of the presentations and posters, and you can sign up for project updates.

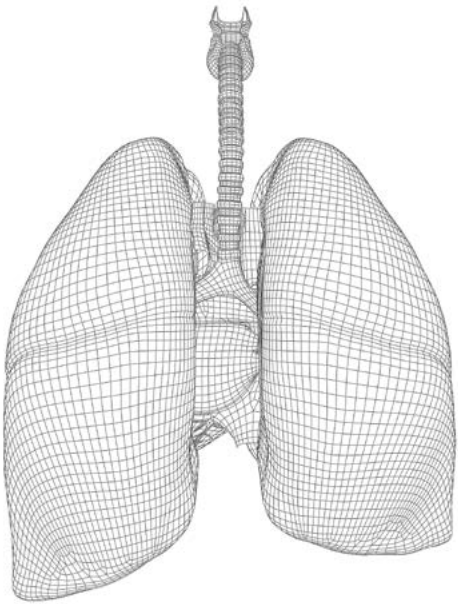
You can follow us on twitter #airprom and connect to our group on LinkedIn linkd.in/1aKScGI.
We are also producing some new video shorts, where researchers explain their work in their own words. These will be available on the website and on YouTube by December 2014.

Integrating the models

A good degree of integration is being seen between various models, with some already well integrated. This is the first step to a multi-scale model. All models have been designed with eventual coupling or integration in mind, which is the ultimate aim of the project.

By involving pharmaceutical companies, the project can make use of their data, taken from clinical trials, to help

- Validate the models with real clinical questions and data
- Demonstrate the validity of the approach



Moving our approach to research forward

Professor Chris Brightling of the University of Leicester leads the AirPROM research consortium and hopes the "one-size-fits-all" approach to managing asthma and COPD can become a thing of the past.

"*The way we define disease is still based on their symptoms but we are learning that underlying the things patients complain about is quite a broad spectrum of biological processes,*" he says.

This means that two people may have similar difficulties breathing but because the fundamental cause of their problem is different giving them the same medication can lead to a good result for one but no improvement in the other person.

"*Recognising this diversity is important if we are to give the right treatment to the right patient and this approach may also guide drug discovery,*" says Prof Brightling.

"*We have models for different parts of the disease. Some treatments may be targeting very specific pathways at a cellular or even subcellular level. Others may be affecting the airway more directly.*"

The more patient data that is added to the system, the more the computer models "learn" and become more accurate in assessing the individual patient. This personalised approach could help identify patients in need to have a series of tests – lung function, blood samples, MRI scans – when they see their doctor, to receive a more accurate diagnosis and monitoring of their disease.

Although the cost of this modelling is not yet clear it may still be cheaper to do the modelling than standard treatment as we would be able to predict which patients will do well, which will do badly, and even which ones are at risk of potential harm beforehand.

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