

## Technology Offer

### Method for manufacturing a holey film, in particular for electron microscopy applications

#### Introduction

The development of cryogenic (cryo-) EM provided a way to investigate samples in a near-to native condition. For single particle cryo-EM, samples are usually plunge frozen in a cryogen that preserves them in a liquid-like environment (vitrification). Recent advances in detector and software development render cryo-EM an attractive alternative to X-ray crystallography if e.g. protein structures are to be solved. In contrast to lacey carbon films, sample supports providing a defined pattern of holes with respect to both size and pitch facilitate automatized image analysis, especially since many thousand images have to be averaged.

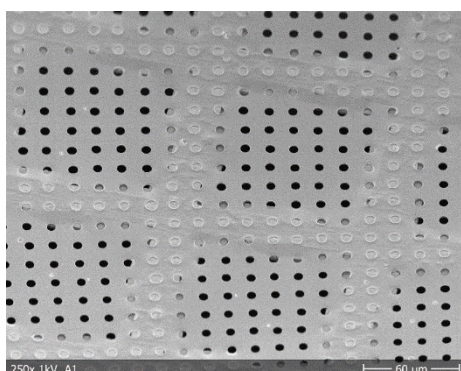
Current manufacturing methods are inflexible with regard to the obtained hole sizes. For each diameter, a separate master has to be manufactured. Some methods have the further disadvantage that release layers need to be present and therefore the substrates are not directly reusable.

#### Invention

The present invention aims to provide a time- and cost-efficient method for manufacturing holey films with a well-defined, yet flexibly adjustable geometry. The method is particularly useful for the manufacture of holey films for TEM applications, especially in the automated analysis of images obtained by single particle cryo-EM or electron cryotomography. Due to the new manufacturing process a dynamic regulation of hole diameters with only one template input diameter can be achieved.

#### Advantages of the invention

By using the invention, the substrate may be recycled multiple times for the purpose of the present method. Several accessible diameters are provided with only one template. Additionally other coatings than carbon (Au or SiO<sub>2</sub>) are possible.



**Figure 1** SEM image of a 10 nm thick patterned carbon film with approximately 5 μm holes recorded at 40 ° tilt.

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#### Areas of application

Single particle cryo-EM,  
electron cryotomography

#### Keywords

holey film manufacturing, cryo-EM

#### Development Status

Prototype

#### Commercial Opportunity

The technology is offered for in-licensing and co-development

#### Patent Status

European patent granted

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