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Micro- and Nanopatterning of Surfaces Employing Self Assembly of Nanoparticles and Its Application in Biotechnology and Biomedical Engineering

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1. Introduction

State of the art microelectronics fabrication achieves both high dimensional resolution as well as precision in positioning of structures by using photolithography at relatively high cost / area. There exist, however, numerous applications which only require micro- or nanostructures of well defined dimension without the need for precise positioning. In addition, some of those applications such as filtration membranes or antireflective coatings call for low cost / area, which is not achievable using photolithography. Also, patterning of non-planar surfaces is not feasible by this technology. Materials other than silicon or glass, particularly polymers often are incompatible with solvents and processes employed in conventional micro fabrication.

Diverse and commercially important applications are currently being pursued such as filtration membranes (Fuchsberger, Burkhardt et al.), biosensors (Musil, Jeggle et al. 1995; Neugebauer, Müller et al. 2006; Lohmüller, Müller et al. 2008), optical filters based on plasmon resonance of metallic nanoparticles (Jensen, Duval et al. 1999; Jensen, Schatz et al. 1999; Jensen, Malinsky et al. 2000; Traci R. Jensen 2000; Malinsky, Kelly et al. 2001), model catalysts (Gustavsson, Fredriksson et al. 2004), antireflective coatings (Lohmüller, Helgert et al. 2008; Min, Jiang et al. 2008; Xu, Lu et al. 2008), and model surfaces to study cell / substrate interaction on well defined surface topologies (Hanarp, Sutherland et al. 1999; Dalby, Berry et al. 2004).

Consequently, self assembly of nanoparticles as a means to create nanostructures on surfaces has been investigated by numerous research groups and great effort has been dedicated to devising reproducible deposition techniques as well as to elucidating the physico-chemical effects involved (Denkov, Velev et al. 1992; Adamczyk, Siwek et al. 1994; Kralchevsky & Denkov 2001; Goedel 2003; Hanarp, Sutherland et al. 2003)

Polymers, metals or even liquids may be used as substrates. Chemical functionalization of substrates may be applied to aid in the attraction and assembly of particles.

Electrostatic, van der Waals, capillary, and steric interactions control particle adhesion and density. Capillary forces (Denkov, Velev et al. 1992; Adamczyk, Siwek et al. 1994; Kralchevsky & Denkov 2001) occurring during drying tend to cause aggregation of particles.

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Electrostatic forces (Serizawa, Takeshita et al. 1998; Snyder, Yake et al. 2005) depend on the charge density of particles and surface as well as on the ionic strength of the particle suspension. Van der Waals forces (Hiemenz & Rajagopalan 1997) may cause formation of stable particle micro aggregates in the suspension or on the surface which may induce defects when the monolayer / aggregate structure is transferred to the substrate.

Upon the application of a suspension of these particles or immersion of the substrate into a particle suspension a mono- or multilayer of particles forms on a surface. Adsorption from a particle suspension onto a surface or spin coating procedures have been reported as well. Parameters to achieve homogeneous and defect free particle mono- or multilayers have been elaborated. Yet, although a large number of reports on nanosphere lithography (NSL) may be found in the scientific literature, only very few of them actually demonstrate large scale defect free patterning and are able to quantify the degree of perfection. In most cases, SEM images show a small section of a substrate which - while illustrating the basic principles of the procedure - would be too small to serve any practical purpose. Therefore, particular emphasis will be placed on such technologies holding promise for robust, low defect patterning of large surface areas by NSL.

Once arranged on the surface, particles have been used in a variety of ways to produce nanostructures.

Firstly, particles may serve as shadow masks during the deposition of an etching mask (Musil, Jeggle et al. 1995; Haginoya, Ishibashi et al. 1997; Burmeister, Schäfle et al. 1998; Choi, Yu et al. 2003; Choi, Jang et al. 2004; Lohmüller, Helgert et al. 2008; Lohmüller, Müller et al. 2008). After removal of the particle layers a porous etching mask is obtained having micro- or nanopores at the prior location of the particles. Subsequently, the resulting pattern can be transferred into the bulk material by plasma or wet etching processes. The choice of the material employed for the etching mask depends on the etching process. For example, silicon nitride, titanium or other so-called hard masks will withstand oxygen plasma as is employed to etch polymer substrates. On the other hand, a metallic etching mask may be used to protect silicon oxide surfaces during CF_4 plasma etching. For some applications etching processes need to achieve a considerable aspect ratio. For example nanoporous membranes need to provide sufficient thickness and stability to be of practical use (cf. chapter 6).

Secondly, the particle layer itself may be employed as mask during the deposition of metals to generate arrays of nanoparticles with diverse types of shapes (Hulteen & van Duyne 1995; Burmeister, Schäfle et al. 1998; Hulteen, Treichel et al. 1999; Jensen, Schatz et al. 1999; Jensen, Malinsky et al. 2000; Traci R. Jensen 2000; Haynes & van Duyne 2001; He, Yao et al. 2001; Bullen & Garrett 2002; Gustavsson, Fredriksson et al. 2004; Kosiorek, Kandulski et al. 2004; Ormonde, Hicks et al. 2004; Shemaiah M. Weekes 2004; Yang, Jang et al. 2006). Size and shape of these nanoparticles govern their optical properties. In order to obtain tailor-made particle shapes, complex fabrication schemes comprising the deposition of several layers of nanospheres, etching in plasma, and metallization steps have been devised (Yang, Jang et al. 2006).

After a discussion of general principles of NSL, three application examples will be discussed in detail:

Firstly, optical effects achievable by NSL, secondly, a nanoporous electrode system enabling a considerable enhancement of sensitivity in an electrochemical detection scheme by redox cycling, and thirdly the generation of polymer membranes for ultra filtration.

Finally, technological details of a procedure enabling truly large scale patterning of a polymer membrane by NSL will be discussed and potential future applications of NSL are anticipated.

2. Self assembly of particle monolayers on surfaces

The fundamental challenge for NSL consists in the assembly of mono- or multilayers of particles at fairly even and controllable distribution on a planar or non-planar surface consisting of polymer, oxide or metallic materials. In addition, many applications require large areas and low defect concentration.

In order to devise procedures to achieve this, an in depth understanding of the forces driving the self-assembly process is critical and in fact has been studied over the past 2 decades (Denkov, Velev et al. 1992; Adamczyk, Siwek et al. 1994; Hanarp, Sutherland et al. 2003). Fig. 1 schematically depicts the forces involved.

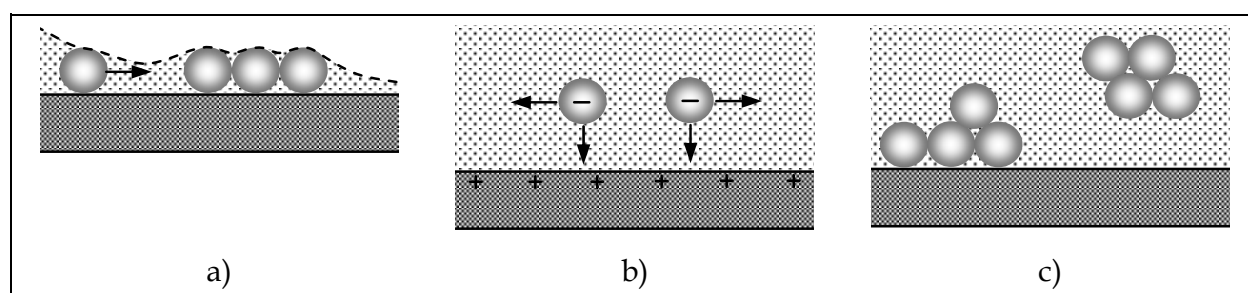


Fig. 1. Forces involved in the formation of particle layers on surfaces: a) when the solvent layer thickness becomes smaller than the particle diameter, capillary forces arise pulling particles together in effect forming 2D crystals. b) Electrostatic interaction results in repulsion between like charged particles and their attraction to an oppositely charged surface. c) Van der Waals forces occur at very low distances and play a role in the formation and stabilization of particle aggregates and 2D crystals

Firstly, long-range electrostatic interaction is observed as a consequence of charged surfaces of both the particles and the substrate. It results in the repulsion of like charged particles and the attraction of particles to a surface bearing a charge density with opposite sign. Charge density of both particles and substrate as well as ionic strength of the buffer solution in which particles are immersed are critical parameters controlling strength and range of electrostatic interaction. Both are reduced by mobile ions present in the buffer solution which will screen the surface charge of particles and substrate. For example, polystyrene particles exhibit negative surface charge due to sulfonate groups stemming from polymer synthesis. Hanarp et.al. (Hanarp, Sutherland et al. 2003) and Semmler et.al. (Semmler, Mann et al. 1998) demonstrated how particle coverage may be controlled by variation of salt concentration. In effect, repulsion of like charged particles is reduced or suppressed at all by addition of mobile ions. While the kinetics of adsorption depends on particle concentration the surface coverage ultimately attained upon saturation seems to be a function of only the ionic strength. If interparticle distance falls below a critical limit short range van der Waals interactions come into play. Then, particles will attract each other and tend to form aggregates. In case of aggregation, interparticle distance is given by the particle size itself. These mechanisms have been studied intensely in colloid physics and have been used to devise stable colloid formulations or to enable formation of colloidal crystals, respectively

(Hiemenz & Rajagopalan 1997). The influence of the surface charge of the substrate on particle assembly has also been studied. Serizawa et.al. investigated both kinetics of and coverage obtained from adsorption of polystyrene particles on substrates coated with ultra thin polymer layers (Serizawa, Takeshita et al. 1998; Serizawa, Kamimura et al. 2000). Surface charge density thereof was modulated by variation of ionic strength of the buffer used during the deposition of polyelectrolyte multilayers. Interestingly, adsorption proceeded faster and resulted in higher coverage onto polyelectrolyte multilayers that had been prepared using higher salt concentration in the buffer. As expected, no particle adsorption was observed on surfaces bearing like signed charge as the particles. Surface charge may also be modulated by variation of the pH if an appropriate substrate material is used. This was shown by Antelmi et.al. (Antelmi & Spalla 1999) with sapphire substrates and by Semmler et.al. with mica substrates (Semmler, Mann et al. 1998). At the point of zero surface charge density (PZC) no particle adsorption was observed.

Capillary forces (Fig.1a) act on particles as a result of the surface tension between the solvent and the particle material (Denkov, Velev et al. 1992; Kralchevsky & Denkov 2001). After application of a droplet of a particle suspension onto a substrate (Denkov, Velev et al. 1992; Burmeister, Schäfle et al. 1997; Burmeister, Badowsky et al. 1999), during the controlled withdrawal of a sample from a particle suspension (Choi, Jang et al. 2004; Prevo & Velev 2004), during spin coating (Denis, Hanarp et al. 2002; Choi, Jang et al. 2004; Jiang & McFarland 2004) or after adsorption of particles to a substrate in a particle suspension (Semmler, Mann et al. 1998; Serizawa, Takeshita et al. 1998; Antelmi & Spalla 1999; Serizawa, Kamimura et al. 2000; Hanarp, Sutherland et al. 2003) the evaporation of the solvent plays a critical role with respect to the structure of the particle layer. As the thickness of the solvent layer becomes comparable to the particle diameter, attractive forces arise pulling particles together to form 2D crystals. Depending on the application pursued this may or may not be desirable. For example densely packed 2D crystals have been employed as masks during a metallization process leading to a regular arrangement of separated metal particles (Hulteen & van Duyne 1995; Hulteen, Treichel et al. 1999; Jensen, Malinsky et al. 2000; Haynes & van Duyne 2001; Bullen & Garrett 2002). Hard core repulsion between particles results in maximum packing density with a lattice constant corresponding to the particle diameter. On the other hand, well separated pores are for example required to provide for sufficient mechanical stability of a filter membrane. To this end, a homogeneous distribution of separated particles has been achieved by freeze drying (Lohmüller, Müller et al. 2008). After preparation of a monolayer of homogeneously distributed particles, while the thickness of the solvent layer is still much larger than the particle diameter so that electrostatic interactions between particles and substrate are predominant, the substrate is cooled below freezing point of the solvent, followed by sublimation of the frozen solvent in a vacuum chamber. Hanarp et.al. explored heat treatment of polystyrene particles and co-adsorption of smaller silica nanoparticles in order to prevent aggregation of polystyrene particles during the drying process (Hanarp, Sutherland et al. 2003). Also, the choice of a solvent with lower surface tension or the addition of surfactant may aid in the reduction of capillary forces. Also, swelling of particles in an appropriate solvent during the deposition process or etching of a 2D particle crystal in oxygen plasma will produce monolayers of separated particles as will be described in detail below.

Repulsive interaction between nanoparticles can be achieved through polymer chain interaction, i.e. stochastic processes. For this purpose metallic nanoparticles were

functionalized with hydrogel polymers such as polyethylene glycol. Thus, monolayers of homogeneously distributed metallic particles were obtained (Lohmüller, Helgert et al. 2008).

3. Preparation of particle mono- and multilayers

A large variety of substrates has been used in NSL. However, general principles apply when large scale high quality particle layers shall be produced.

Often, polymeric particles such as polystyrene particles which are intrinsically negatively charged, silica particles or even metallic nanoparticles bearing charges due to specific surface functionalization are employed in NSL. In order to induce particle adhesion, particles and substrate surface have to bear opposite charges. In case of the substrate this has been achieved by choice of an appropriate material such as an oxide or mica (Semmler, Mann et al. 1998; Antelmi & Spalla 1999) or by deposition of synthetic or biological polyelectrolyte mono- or multilayer coatings (Serizawa, Takeshita et al. 1998; Serizawa, Kamimura et al. 2000; Lohmüller, Müller et al. 2008), which can be deposited under well controlled conditions yielding reproducible results. The charge density of such a polymer layer can be tuned within a certain range by the choice of the salt concentration of the polymer solution during deposition. As has been shown by Serizawa et al., this will affect final particle density as well as adhesion kinetics (Serizawa, Takeshita et al. 1998; Serizawa, Kamimura et al. 2000). Other synthetic and biological polymers such as polyethylene-imine and bovine serum albumin, respectively, which provide for a positive charge density at neutral pH have been used to coat substrates in order to promote electrostatic interaction with negatively charged polystyrene particles (Lohmüller, Müller et al. 2008). Polyimide membranes were successfully modified using diethylene triamine (DETA) to introduce positive charges and provide for favourable wetting properties (Santoso, Albrecht et al. 2003).

Spreading of suspensions of functionalized particles at the air / water or water / oil interface has been used to generate 2D particle assemblies (Aveyard, Clint et al. 2000; Xu & Goedel 2003; Cayre & Paunov 2004; Xu, Yan et al. 2005). Gödel et.al. used functionalized silica particles in a suspension containing polyisoprene (Xu & Goedel 2002). After generation of a monolayer consisting of hydrophobized silica particles and polyisoprene at the air water interface, cross linking of the polymer layer was induced by UV illumination. Silica particles were dissolved using HF and polymer membranes with a regular arrangement of pores were obtained.

As has been pointed out earlier, capillary forces in combination with evaporation play a dominant role in the arrangement of particles if samples are allowed to dry following the addition of a particle suspension. Special emphasis therefore has been put on the design of procedures and instrumentation for controlled deposition of particles.

According to the model proposed by Denkov et.al. (Denkov, Velev et al. 1992) capillary forces and convective flow contribute to the assembly process. Due to evaporation the solvent layer eventually becomes thinner than the particle diameter giving rise to capillary forces pulling particles into close contact with each other in effect forming 2D crystal while at the same time convective flow transports particles from areas exhibiting thicker solvent layers towards the 2D crystal.

Based on this model, refined procedures using heating stages, evaporation chambers to control evaporation have been devised (Denkov, Velev et al. 1992; Burmeister, Schäfle et al. 1997; Burmeister, Badowsky et al. 1999; Zhen Yuan 2006) which, however, prove to be quite

time consuming. In a refined procedure Prevo et al. employ a meniscus between the substrate and a moving plate to generate a controllable evaporation zone (Prevo & Velev 2004).

Finally, spin coating has been used in an attempt to provide a fabrication method which would both be compatible to conventional micro fabrication technology and enable generation of large scale 2D and 3D colloid crystals (Denis, Hanarp et al. 2002; Jiang & McFarland 2004). However, data reported generally show defects such as dislocations, voids and aggregates.

4. Properties of particle monolayers

Figure 2 shows micrographs obtained by scanning electron microscopy of typical results obtained by NSL and is intended to visualize commonly observed defect structures. 2D crystals are always imperfect in that dislocations and unoccupied lattice positions are present. Rarely, long range order exceeds more than $\sim 100 \mu\text{m}$ (Fig.2a). While electrostatic interaction between nanospheres and surface usually result in a homogeneous distribution of well separated particles, upon drying of the surface capillary forces draw particles together to form small 2D aggregates and voids (Fig.2b). As Fig.2b shows compression may be strong enough to even cause deformation of particles (arrow). A third type of defect observed in NSL is 3D particle aggregates of different sizes (Fig.2c). Presumably, these aggregates are already present in the suspension employed in NSL and adsorb to the substrate surface along with individual nanospheres by electrostatic interaction.

5. Applications of surfaces patterned using NSL

5.1 Optical applications: surface plasmon resonance and optical filters

Haynes et al. used NSL to produce 2D crystals of polystyrene particles which were used as shadow masks during the deposition of Ag on mica substrates (Haynes & van Duyne 2001). Regular 2D patterns of discrete Ag nanoparticles of various shapes were fabricated and investigated with respect to their optical properties. Metallic nanoparticles give rise to localized surface plasmon resonance (LSPR). This phenomenon has two consequences with potentially interesting applications. Firstly, light in a certain spectral region is absorbed providing optical filter properties. Secondly, electric field strength in close vicinity of the particle is enhanced. This is useful in sensor applications where molecules in close contact with these particles can be probed with superior sensitivity by surface enhanced Raman spectroscopy (SERS) to obtain chemical information about individual molecules (Kneipp, Wang et al. 1997; Nie & Emory 1997). Through an appropriate choice of the particle diameter used for NSL and deposition parameters a variety of shapes of metallic nanoparticles was demonstrated. In particular, by introduction of a tilt angle between the surface normal and the direction of evaporation, asymmetric particle shapes were obtained. While nanospheres showed extinction wavelength around 300 nm, strongly asymmetric nanotriangles exhibited absorptions in the mid-IR range, demonstrating the ability to tune the optical properties of nanoparticles by variation of their shape. In addition to devising fabrication procedures Haynes et al. studied the effect of nanoparticle material, size, shape, interparticle spacing, external dielectric medium, thin film overlayer, substrate dielectric constant and molecular adsorbates on the optical properties of nanoparticle arrays. Finally, the sensitivity towards thin adsorbate layers is demonstrated by measurement of the

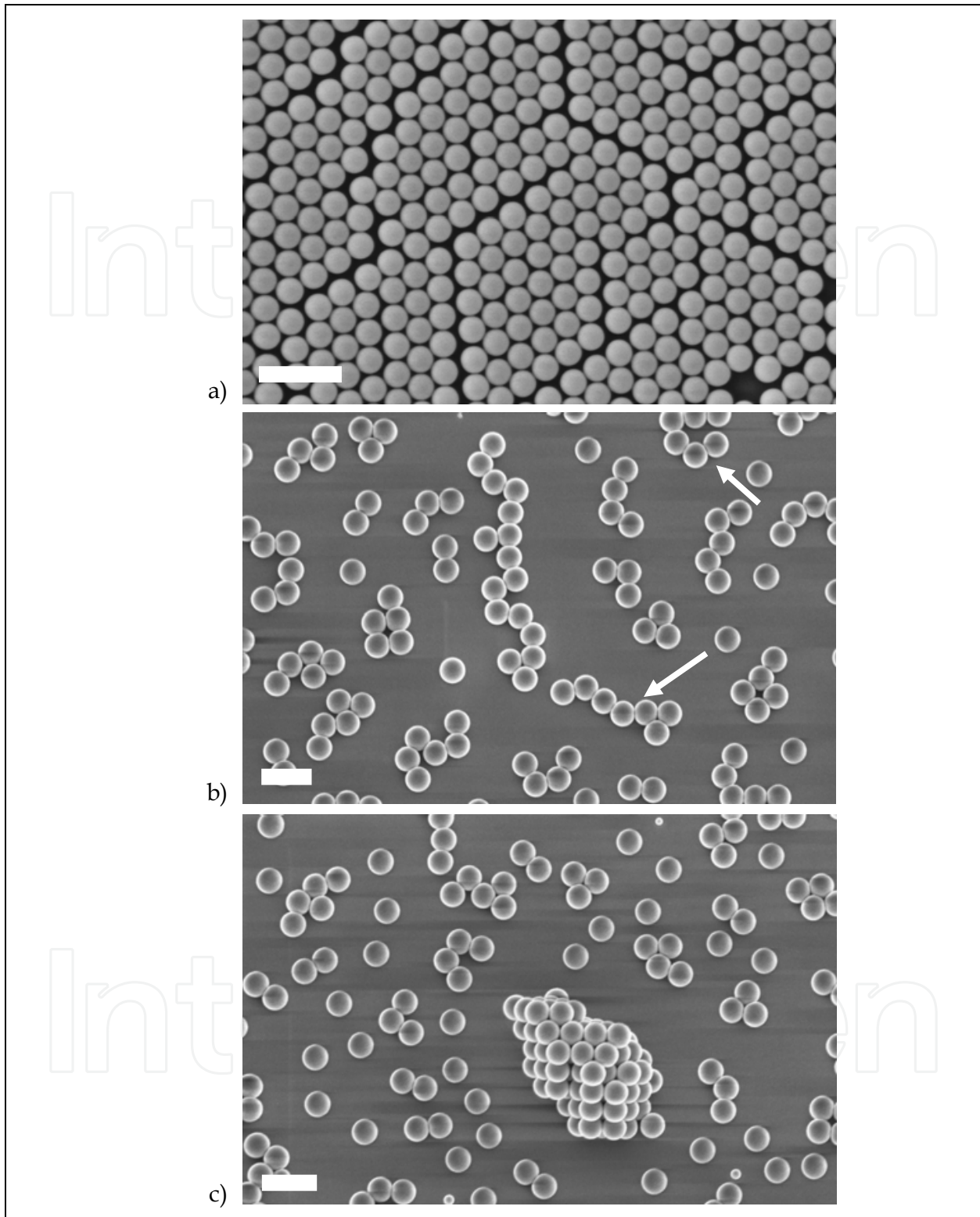


Fig. 2. typical morphology of particle monolayer and commonly observed defect structures: a) cracks, dislocations and voids in 2D nanosphere crystal. b) small 2D aggregates separated by voids, generated by capillary forces during the drying process. c) 3D nanosphere aggregates, presumably already present in the suspension used for NSL. Bar corresponds to $1\mu\text{m}$.

adsorption of polylysine to Ag nanoparticles that had been functionalized with a carboxy-terminated alkane thiol (McFarland & Van Duyne 2003). A comprehensive review of this particular application was published by Haes et.al. (Haes & Van Duyne 2004; Stuart, Haes et al. 2004).

In addition, van Duyne et al. published a number of studies exploring NSL as a means to fabricate arrays of metallic nanoparticle of different shapes and their relationship to their optical properties which were mostly measured by UV-VIS spectroscopy (Hulteen & van Duyne 1995; Jensen, Duval et al. 1999; Jensen, Schatz et al. 1999; Jensen, Malinsky et al. 2000; Traci R. Jensen 2000; Malinsky, Kelly et al. 2001; Ormonde, Hicks et al. 2004) and related their results to theoretical considerations (Jensen, Duval et al. 1999; Jensen, Schatz et al. 1999; Haynes & van Duyne 2001).

NSL also has been employed to provide a low cost large scale etching mask on glass and silicon substrates to produce nanoporous surfaces which exhibit reduced reflectivity in the UV and visible spectrum by utilizing the moth eye effect (Lohmüller, Helgert et al. 2008), (Xu, Lu et al. 2008). A reduction of reflectivity results in an improved efficiency of solar cells. Also, optical throughput of UV optics can be improved in this way.

5.2 Sensors

NSL already has found significant applications in sensor devices. Van Duyne and co-workers demonstrated biosensors based on surface enhanced Raman spectroscopy on metallic nanoparticles deposited through a mask fabricated by NSL (Haynes & van Duyne 2001; Haes & Van Duyne 2004; Stuart, Haes et al. 2004). Upon adsorption or binding of molecules to the nanoparticles, a spectral shift in the absorption maximum is observed and chemical signatures of molecules may be observed in the spectrum obtained by surface enhanced Raman spectroscopy.

Porous metal layers have been proposed as transducers for electrochemical biosensors as they allow for the deposition of the biological recognition elements in close proximity to the sensing element. Musil et al. used NSL, deposited a thin metal layer by evaporation or plasma enhanced chemical vapour deposition (PECVD) and subsequently removed the particles to obtain a sensor element having a nanoporous, yet laterally connective metal layer (Musil, Jeggler et al. 1995). Though not demonstrated in this particular publication, it is easily conceivable how molecules may be selectively either bound to the surface exposed in the pores employing silane chemistry or to the gold electrode using thiol groups.

Electrochemical sensors are widely employed for immunosensing applications (Marquette & Blum 2006; Wang, Xu et al. 2008). In order to enhance sensitivity and/or signal strength, so-called redox cycling may be employed (Aoki 1989; Niwa, Xu et al. 1993). In this particular detection scheme, redox molecules generated by the enzyme label of the immuno assay may be oxidized and reduced several times giving rise to an increased current signal. However, this requires very closely spaced electrodes in order to obtain a reasonably high number of cycles (Shim, Rust et al. 2008). While this may be achieved with interdigitated electrode arrays (IDE) using conventional photolithography or e-beam patterning, the costs associated with using these technologies are incompatible with the requirements of the diagnostic market.

As a cost effective alternative, nanoporous metal - insulator - metal electrode systems (Fig.3) have been developed and were shown to exhibit superior redox-cycling properties (Neugebauer, Müller et al. 2006; Lohmüller, Müller et al. 2008). Amplification ratios of up to

100 fold have been demonstrated. Deposition of a first gold layer creates the bottom electrodes and their connecting leads. Shadow masks may be used to pattern the relatively coarse structures of the sensor pads and the connecting leads. Subsequently, an insulation layer of 100 - 200 nm thickness is deposited and NSL using polystyrene particles with a diameter ranging from 200 nm to 1 μm is carried out. A second gold layer is deposited onto this substrate. After removal of the particles the porous top electrode is used as an etching mask during a plasma etching process to expose the bottom electrode in the area of the pores (Fig. 3). In this way, a large number of electrically connected electrochemical nano-

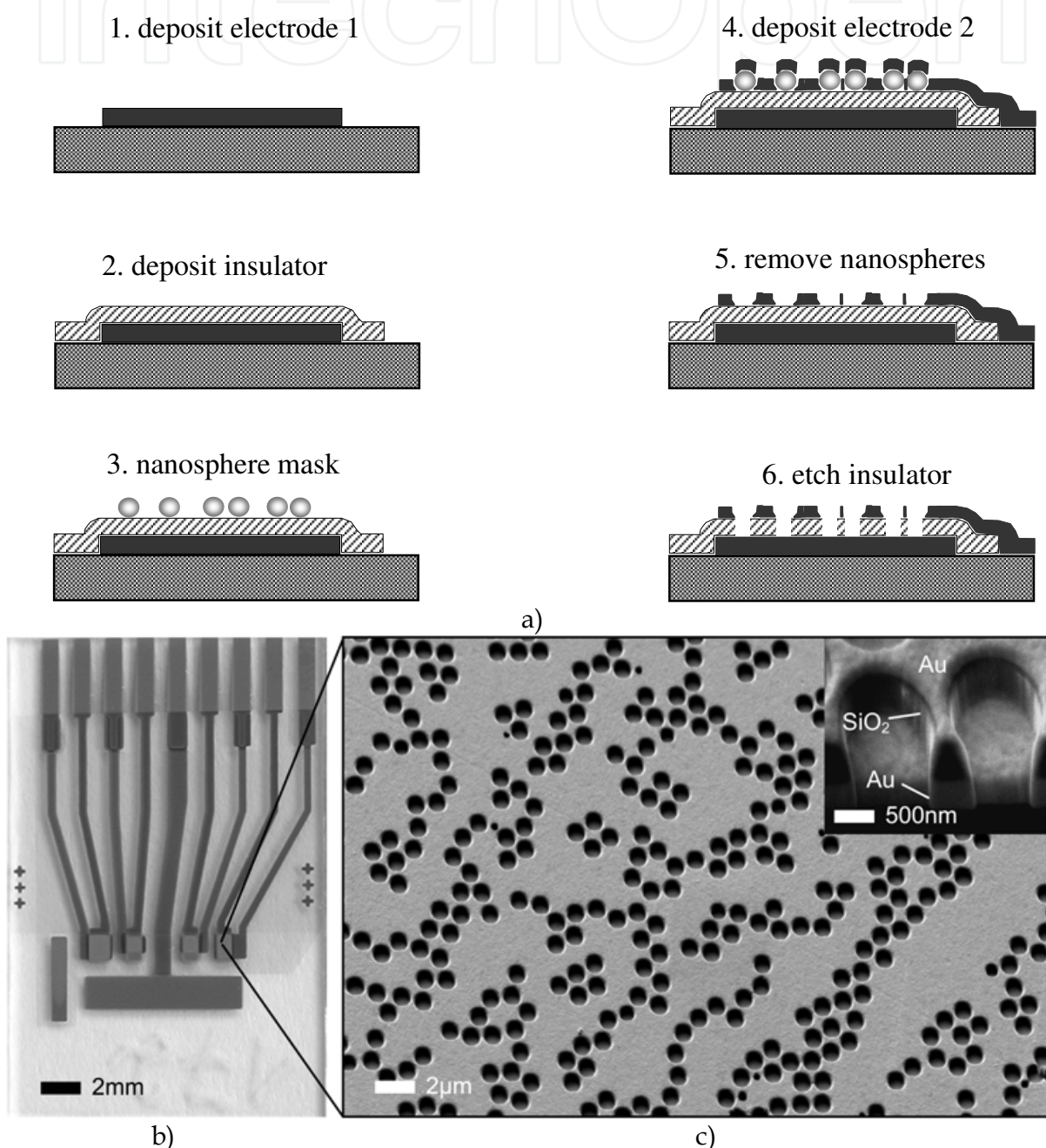


Fig. 3. NanoBioPore sensors: a) fabrication process, b) sensor with four sensor pads, c) SEM image of sensor surface showing pores and cross-sectional view of the porous metal - insulator - metal electrode system (insert).

cells are created and upon application of oxidizing and reducing potentials to top and bottom electrodes, respectively, a large signal due to repeated oxidation and reduction of molecules in the nanopores is observed. Here, the thickness of the insulation layer defines the electrode spacing. As it is quite easy to produce insulation layers with a thickness as small as 100 – 200 nm, highly efficient redox - cycling devices may be fabricated at relatively low cost when compared to IDE sensors.

While homogeneous pore distribution in principle is not very important in this application, it was observed that 2D aggregates may contribute to short circuits, when small electrode portions are destabilized by under-etching during the pore development (Lohmüller, Müller et al. 2008). Also, back sputtering of metal from the bottom electrode to the pore walls due to prolonged pore etching was discussed as another possible cause for short circuits between top and bottom electrodes.

5.3 Filter membranes

Ultra filtration membranes are used in such diverse applications as for filtration of fermenter suspensions to remove virus or bacterial contamination or to filter solvents in micro fabrication technology. Conventional ultra filtration membranes are manufactured by phase inversion technology. A polymer is dissolved in an organic solvent which evaporates as a thin film is continuously drawn on an air/water interface. Porosity, thickness and effective pore diameter depend on process parameters and require careful control of parameters such as temperature, humidity, and drawing speed.

Usually, thickness is on the order of 100 - 200 μm both to provide mechanical stability as well as to obtain the required filtration properties through the joint effect of the micro- or nanoporous polymer mesh making up the membrane. However, particularly for very small pore sizes, fluidic resistance of these membranes become exceedingly high thus limiting flux and ultimately the productivity of the filtration process (DiLeo, Allegranza et al. 1992; van Reis & Zydney 2001).

In contrast, a membrane manufactured by a combination of NSL and plasma etching technology should exhibit much larger flux and possibly a narrower pore size distribution. The requirements are quite demanding, though: the reduction ratio for virus filtration for example should be $>10^6$. This requires an extremely low defect density in NSL. In particular, aggregate deposition or formation has to be avoided by all means. At the same time continuous reproducible and reliable NSL on very large surface areas is critical.

The Nanohybrid project employed polyimide as membrane substrate, a polymer which even at a thickness of only 5 μm provides sufficient mechanical stability to be useful as filtration membrane. At this thickness combined with a porosity on the order of 20 – 30 % theoretical calculations predict an increase of flux by up to 100 fold when compared to conventional membranes. Results obtained by an optimized fabrication procedure based on NSL are presented in chapter 6.

5.4 Applications of NSL in biology and biotechnology

NSL has been used to generate surfaces to study the effect of well defined nano-topologies and chemistries on cellular functions such as adhesion (Dalby, Berry et al. 2004; Dalby, Riehle et al. 2004; Graeter, Huang et al. 2007; Huang, Graeter et al. 2009), proliferation, endocytosis (Dalby, Berry et al. 2004), differentiation (Steinberg, Schulz et al. 2006), apoptosis (Ranzinger, Krippner-Heidenreich et al. 2009) and gene regulation. In particular,

the group of Spatz et.al. showed the deposition of polymer-functionalized gold colloids on substrates followed by an etching step to remove polymer ligands. This results in regular arrays of nano-sized anchoring sites for biochemical functionalization via thiol chemistry. Control of spacing, order and biochemical function immobilized onto gold nanospots allowed for in depth studies of cellular functions (Spatz, Mössmer et al. 2000; Roos, Ulmer et al. 2005; Steinberg, Schulz et al. 2006; Graeter, Huang et al. 2007; Huang, Graeter et al. 2009; Ranzinger, Krippner-Heidenreich et al. 2009).

The fabrication of nanopatterned films of protein by NSL yielding ring shaped structures has been demonstrated (Garno, Amro et al. 2002; Li, Henry et al. 2006). In particular it was shown that proteins deposited in this manner retained the capability to bind specifically to immunoglobulin molecules (Garno, Amro et al. 2002). Results obtained from this research are expected to result in novel biomaterials provided with tailor made surface topologies and chemical composition to induce specific tissue responses.

6. Origin of defects in NSL ultra low defect & large scale patterning for filter membranes

As pointed out in Chapter 4, typical defect structures found in NSL involve crystal defects in 2D crystals as well as 2D and 3D aggregates where a homogeneously array of separated particles was intended.

A robust fabrication process involving NSL to produce nano-porous filtration membranes was developed. Defect densities on the order of 10^{-5} or smaller were achieved. Particular care was taken to devise and apply such process steps that would be scalable and

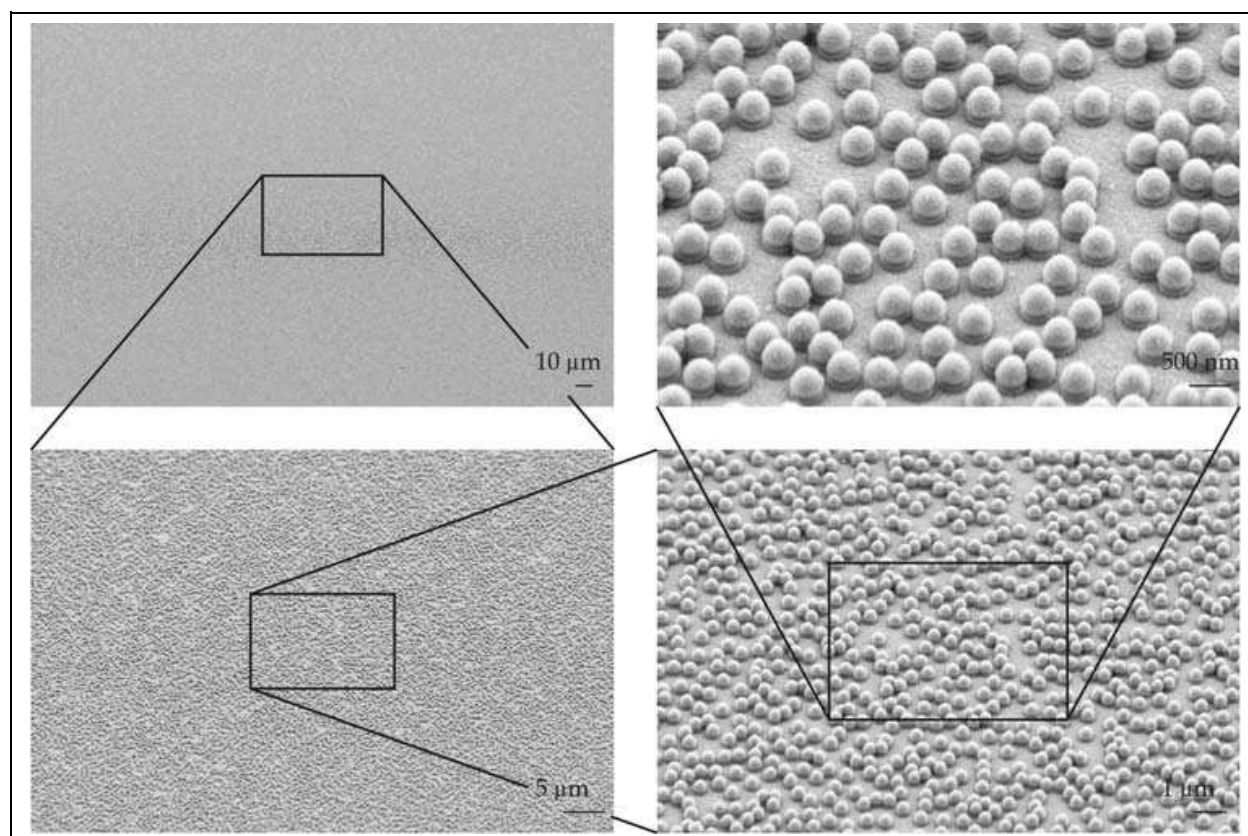


Fig. 4. Large area ultra low defect NSL on polyimide membranes

compatible with state of the art production technologies. Details of this process will be published elsewhere (Fuchsberger, Burkhardt et al.).

Briefly, polyimide was used as substrate because of its favourable mechanical and chemical properties. Even at 5 μm , polyimide membranes exhibit sufficient mechanical stability to produce filter membranes. After deposition of nanospheres (Fig.4), an etching mask was deposited, nanospheres were removed and the nanostructure was transferred into the polyimide membrane by plasma etching in an oxygen / argon plasma.

In conclusion, this method opens up the possibility to employ NSL to pattern pores with a diameter of less than 100 nm at very high aspect ratios which was previously not possible (Fig.5).

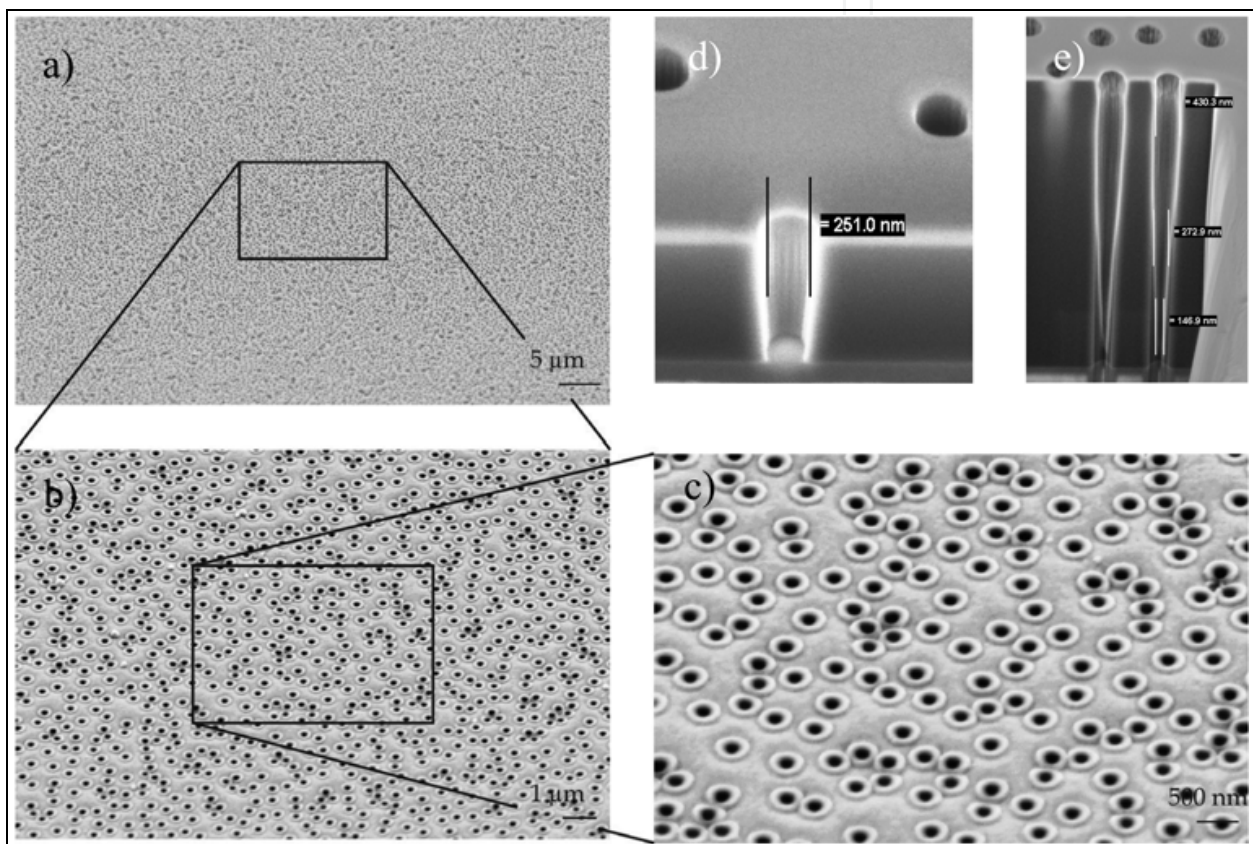


Fig. 5. Membrane comprising well separated nanopores (a-c). Cross-section of a porous membrane with a thickness = 600nm (d) and 6 μm (e), respectively, demonstrates high aspect ratios of up to ≈ 15 with a small degree of conicity.

7. Conclusion

NSL has been studied intensely as it provides a cost effective means to generate well defined nanostructures where positional order is not required. Numerous applications have been proposed and investigated in optics, sensors and membrane technology. However, in spite of broad knowledge about forces governing the self-assembly of nanospheres on surfaces, widespread application of NSL has been severely hampered by typical defect structures, namely dislocations and voids in 2D crystals as well as 2D and 3D aggregates where a homogeneous monolayer of well separated nanospheres would be required. Very few if any

patterning procedures are currently available which actually have been demonstrated on large ($>cm^2$) areas.

To this end, a comprehensive process scheme was devised comprising all necessary steps from preparation of surfaces and pure particle suspensions, application of nanospheres to surfaces up to pattern transfer into polymeric membranes. Defect densities below 10^{-5} have been demonstrated and nanoporous filter membranes exhibiting pores with an aspect ratio of >15 were fabricated.

We believe that these developments open the door for more widespread application of NSL in industrial fabrication.

8. Acknowledgements

Helpful discussions with Volkmar Thom, Sartorius Stedim, are acknowledged. Funding for this research was in part obtained from the German ministry for education and research through grant 13N9122.

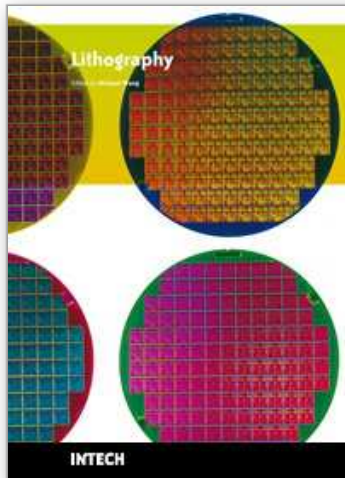
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Lithography, the fundamental fabrication process of semiconductor devices, plays a critical role in micro- and nano-fabrications and the revolution in high density integrated circuits. This book is the result of inspirations and contributions from many researchers worldwide. Although the inclusion of the book chapters may not be a complete representation of all lithographic arts, it does represent a good collection of contributions in this field. We hope readers will enjoy reading the book as much as we have enjoyed bringing it together. We would like to thank all contributors and authors of this book.

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