

Porous silicon nanoparticles for target drug delivery: structure and morphology

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Abstract. Nanoparticles of porous silicon were obtained by electrochemical anodic etching. Morphology and structure of the particles was investigated by means dynamic light scattering and scanning electron microscopy. The influence of technological conditions of preparation on geometrical parameters of the porous silicon particles (particle size distribution, pore shape and size, the specific surface area of the porous silicon) is discussed.

1. Introduction

Porous silicon (por-Si) and nanocomposites based on it offers many properties useful for various fields as micro- and nanoelectronics, solar and hydrogen energies as well as in biomedical technology [1-8]. For example, ultra-thin layers consisting of monodisperse por-Si nanoparticles due to photoluminescence properties of por-Si could dramatically improve the efficiency of photovoltaic solar cells, including cells obtained by hydro-chemical deposition [9-11]. At the moment application of por-Si in biomedicine is the most actively developing area [12-22], namely:

- support material for targeted drug delivery (both single and multiple drugs simultaneously);
- photosensitizers in photodynamic therapy;
- tissue engineering;
- biosensors of various types;
- biomedical imaging, including tumor imaging;
- treatment of eye diseases and etc.;

The great attention to the por-Si for applications in biomedicine caused by following important properties:

- biocompatibility i.e. ability to be incorporated into the body, without causing side effects, and the ability to induce a cellular or tissue response necessary to achieve optimum therapeutic effect;
- biodegradability (i.e., the ability to dissolve and be absorbed);
- processability;



- possibility to control the parameters of the porous structure (porosity, pore diameter, surface development, hydrophobicity / hydrophilicity) and properties (surface charge state, the local distribution of charges and m. p.) in a rather wide range;
- multifunctional (not only the carrier matrix, and simultaneously the sensor, marker and so on).

Advantages of por-Si as carriers of drugs due are also the high surface area and large pore volume.

Nanosystems based on por-Si exhibit improved parameters needed for drug delivery: increase the solubility of the test drug, high stability in vitro, low cytotoxicity, and others. So, nanoparticles of porous silicon can effectively deliver antiviral drugs to infected cells. In [23] investigated the possibility of increasing the solubility of saliphenylhalamide (SaliPhe) by loading the compound into nanoparticles thermohydrocarbonized porous silicon (THCPSi). Nanoparticles loaded SaliPhe, were further tested for ability to inhibit influenza infection. It was shown that after release from THCPSiSaliPhe inhibit influenza infection in vitro and reduces the number of progeny in influenza virus-infected cells. In [24] described the preparation of biodegradable porous silicon nanoparticles functionalized with antibodies that target cancer cells and the loaded hydrophobic anticancer drug camptothecin. Successful targeting demonstrated by flow cytometry and immunocytochemistry, both cell lines and primary cells. The analysis of cells after incubation for viability confirmed the selective destruction of cancer cells.

An important task is the creation of drug delivery systems capable of carrying multiple loads simultaneously, for example, the simultaneous delivery of small molecule drugs and relatively large peptides [18]. In [18] investigated the possibility of simultaneous delivery of multiple drugs with the joint loading of hydrophobic and hydrophilic peptide indomethacin human YY3-36 (PYY3 -36). The authors argue that the startup sequence of these two drugs in porous silicon nanoparticles increases the rate of release of each drug. Loading PYY3-36 also significantly improved compatibility cytological nanoparticles spanning. Conformational analysis showed that after the release of por-Si nanoparticles, PYY3-36 drug exhibits bioactivity and the ability to penetrate the intestinal cells.

Currently, porous silicon and porous SiO₂ were used to demonstrate the release of the steroid dexamethasone, ibuprofen, Peyronie chloride, doxorubicin and many other drugs. Note that the nanoparticles themselves spanning can have bioactivity [25].

In the preparation of nanoscale powders of porous silicon on the one hand, there is a need for the development of processing methods for the preparation of porous silicon nanopowder, separating them by size and choice of storage conditions. On the other hand, need information about the properties, composition and the evolution of the time properties of individual particles of porous nanosized powders, as well as the impact on their properties or environmental conditions (temperature, light, composition, medium). It is also important to investigate the effect of nanoparticles Spanking (especially modified other substances) from the point of view of safety of living organisms.

This work is devoted to characterization of the structure and morphology of por-Si nanoparticles as well as the study of the influence of various dispersion media.

2. Experiment

Preparation of porous silicon nanoparticles was performed in several stages [8, 12, 26]. First, porous silicon layers very obtained by electrochemical etching using the single electrochemical cell (Figure 1). Such configuration of the electrochemical cell allows the formation of por-Si on both sides of the original silicon wafer (rather than only in one side as in the conventional cells). Thus, it leads to increasing productivity of the method. The electrolyte is an aqueous solution of hydrofluoric acid with the addition of isopropanol and hydrogen peroxide. There were studied three series of por-Si powders which were differ anodizing current density, resistivity silicon substrate. The anodization conditions are shown in Table 1. In a second step the samples were placed in a vessel containing isopropanol and sonicated for 30 min. Thus it was obtained the porous silicon powder dispersion in isopropanol media.

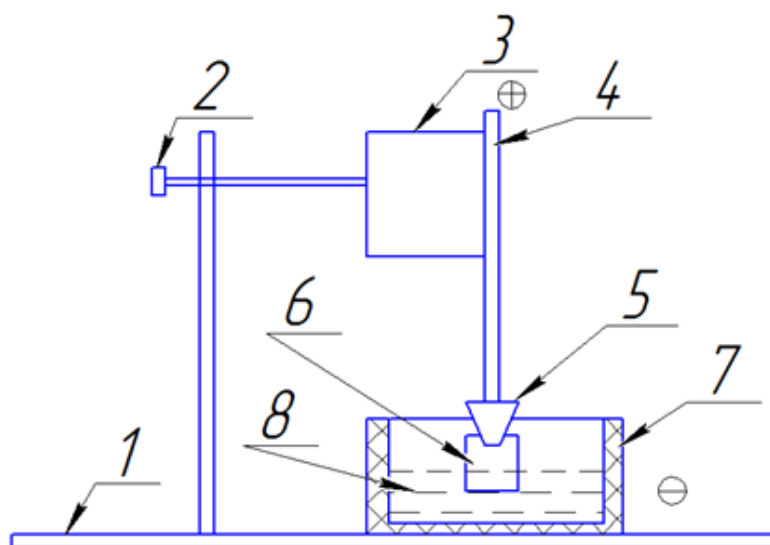


Figure 1. Schematic representation of laboratory stand for porous silicon powder preparation: 1-tripod with stand; 2- knob position of the sample; 3-holder; 4- metal rod (anode); 5 - copper holder; 6 - silicon sample; 7 - glassy carbon crucible (cathode); 8- electrolyte

Table 1. The anodizing process parameters for the obtained por-Si nanoparticles

Series	Si parameters	Si resistivity, $\Omega\cdot\text{cm}$	Anodizing time, min.	Current density J_A , mA/cm^2
I	n-Si (111)	1,0	20	30
II		1,0		70
III		0,3		70

Subsequently, the por-Si dispersions were used to study the distribution of particle size by dynamic light scattering using Photocor mini (Scientific Laboratory UrFU named after the first President of Russia Boris Yeltsin). The device is designed according to the traditional scheme of dynamic light scattering spectrometer. It allows multi-angle measurements both for dynamic and static light scattering. The dynamic light scattering allows determining the diffusion coefficient of the particle in the fluid by analysis fluctuations of the correlation function scattered light intensity. Further, from the diffusion coefficient is calculated the radius of the nanoparticles. Directly before measuring the dispersion of porous silicon powders in isopropyl alcohol were additionally sonicated.

The structure and morphology of porous silicon particles were studied using Tescan MIRA II scanning electron microscope. For scanning electron microscopy the samples were prepared as follows: dispersion droplets were deposited on the prewashed monocrystalline silicon substrate by dispenser, and then were dried.

3. Results and discussion

Figure 2 shows typical SEM micrographs of porous silicon particles for series I-III. As expected, the por-Si powders are consisting of particles of different size, which is obviously due to the grinding method of por-Si layers. The lowest number of large particles observed in the sample №1, the largest number in the sample №2. Por-Si particle of series II and III are sharp, but in I series particles more smooth and round, and of smaller sizes generally. Por-Si Series I and II are of mixed type and contain meso- and micropores as was expected by previous studies [27]. Thus, by the capillary condensation it has been found that por-Si particles are present in the pores with the diameter less than 5 nm (the proportion of which was 42.4% of the total pore fraction) and rather larger mesopores with sizes of 10-

20 nm and 50 nm [27]. Mesopores for Series II might be distinguished on Fig. 2, e. Observation of micropores by conventional SEM is extremely difficult. For por-Si particles of Series I, which are obtained at a lower current density, are expected even smaller pores [28].

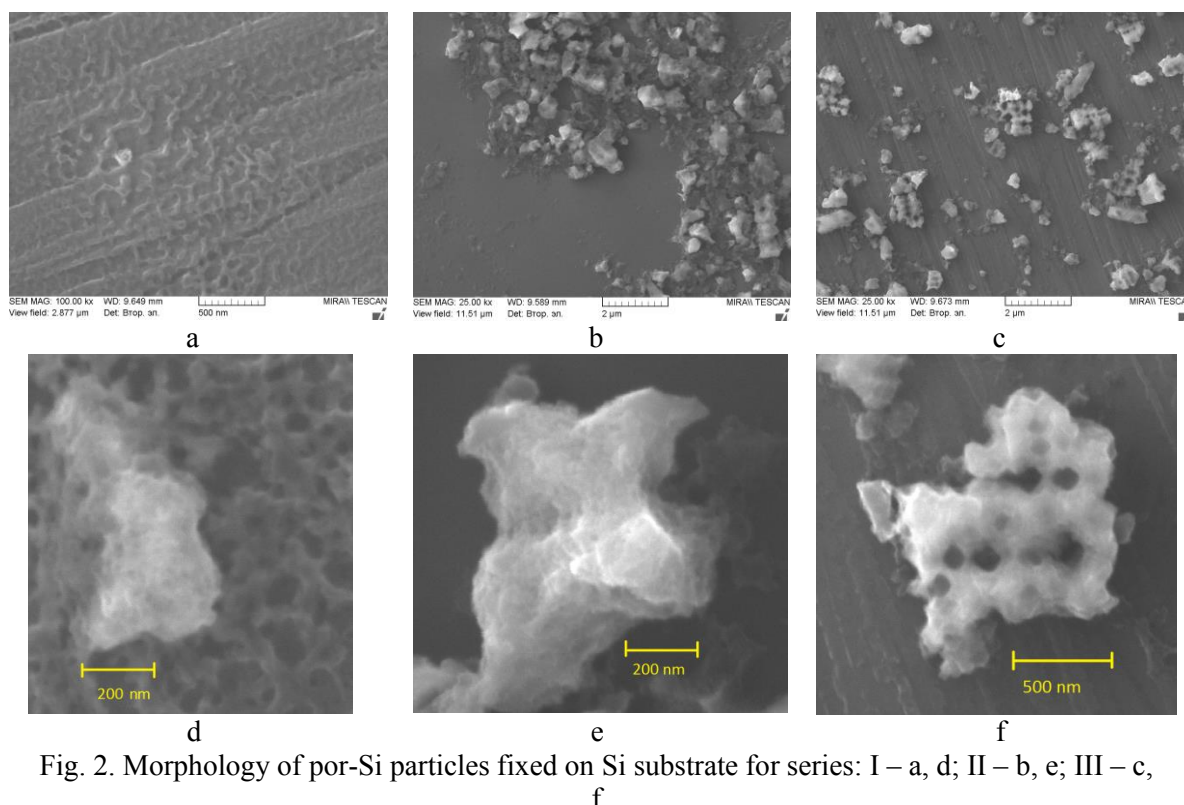


Fig. 2. Morphology of por-Si particles fixed on Si substrate for series: I – a, d; II – b, e; III – c, f

According to Fig. 2, a and 2, d, it may be assumed that in the series I contains a significant proportion of smaller particles of porous silica, which aggregate to form a porous layer consisting of porous particles on the surface of the silicon substrate. It has been found by means of SEM, so that a porous layer made of por-Si particles series I covers almost the entire silicon substrate. Thus a "secondary" porous layer is a macro- and mesoporous with typical pore diameter of about 20-150 nm. A typical thickness of the "secondary" porous skeleton is of the order 20-40 nm. It can be assumed that a vivid manifestation of aggregation effects in dispersions series I due to the fact that the particles of porous silicon in this series have a large specific surface area and tend to minimize the surface energy through the formation of aggregates. Also, there are large particle with a size of 200-400 nm.

Samples Series III contains preferably macropores of 50-100 nm and less sizes with a square shape of the pore channels; the skeleton of porous silicon perhaps retains monocrystalline (Fig. 2, c, f). This form and the geometry of the pore channels corresponds to the propagation channel along the crystallographic directions $\langle 100 \rangle$, characterized maximal etch rate for single crystal silicon [29].

The estimates of distribution for por-Si dispersions obtained by the method of dynamic light scattering showed the following (Table 2). In general, the data for estimating the size of particles and its size distribution obtained according to the dynamic light scattering are consistent with SEM data for the same samples: in all studied samples present por-Si particle with size of tens and hundreds of nanometers in varying proportions. Also, common to all studied sample series is that the main contribution – more than 50%, was given by particles of 100-200 nm sizes. In contrast to the series II and III, a series I possesses quite large contribution of particles of about ≈ 14 -20 nm sizes – about 40%. Evidently, the porous layer observed in Fig. 2, a and 2, d, is composed of such particles.

Table 2. Estimation of por-Si particle size and percentage of particles in the dispersions according to the dynamic light scattering

Series	Media	The particle size and its accuracy, nm	The percentage of particles in dispersion
I	Isopropanol	17.8±3.3	40.6
		194.1±42.4	59.4
II	Isopropanol	18.4±1.7	11.8
		197.2±29.1	73.9
		691.9±81	14.3
III	Isopropanol	9.3±0.6	7.4
		94.7±12.2	53.1
		609.4±67.6	39.5

4. Conclusions

Particles of porous silicon were obtained by electrochemical anodic etching of n-Si (111) under different technological conditions: 30 and 70 mA/cm² of current density, 1.0 and 3.0 Ω·cm of specific resistivity of initial n-Si. Por-Si particles of series II and III are sharp, but in I series particles more smooth and round, and of smaller sizes generally. ion current density, 0.3 and 1.0 Ω·cm of specific resistivity of Si. The morphology, texture, sizes and size distribution of porous particles and pore diameter in it were studied by SEM and dynamic light scattering. SEM data revealed pores in all sample series.

It was found that por-Si nanoparticles (Series I and II) are of mixed type and contain mesopores, series III – meso- and macroporous silicon particles (≈50-100 nm). Por-Si particles of series II and III are sharp, but I series particles more smooth and round, and of smaller sizes generally. As could be noticed, the pore diameter increases with increasing doping level of the substrate and with increasing current density anodizing, which is in good agreement with the experimental data of other authors [30]. It was found that por-Si particles of series I unlike the other two series covered the surface of the monocrystalline Si substrate with porous layer in which is difficult to distinguish individual particles (with the exception of large ones order of 100-200 nm). The pore diameter in a "secondary" layer on the order of 20-150 nm, and the cross section of skeletal branches - the order of 20-40 nm. It is assumed that the formation of such layers involves particles aggregation processes in the origin dispersion to minimize surface energy.

Both methods (SEM and dynamic light scattering method) have shown that porous silicon powders are characterized by polydispersity: the main contribution – more than 50%, was given by particles of 100-200 nm sizes. In contrast to the series II and III, a series I possesses quite large contribution of particles of about ≈14-20 nm sizes – about 40%. Apparently this is due to the fact that the particles obtained in one series of lower current density and nonporous be expected with a high degree of porosity. Such layers are typically more mechanically strained, more fragile, so are ground by ultrasound into smaller parts.

From the viewpoint of practical use obtained in this paper por-Si particles are perspective as containers for targeted drug delivery. Thus, the creation of a composed container consisting of porous particles with different morphology and pore sizes are very promising for the target delivery of several types of drugs with different molecular sizes, different properties and so on. Also, porous layers composed of

porous silicon particles of one or more types may be of interest for sensors, considering advantages and simplicity of the technology for producing porous silicon.

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