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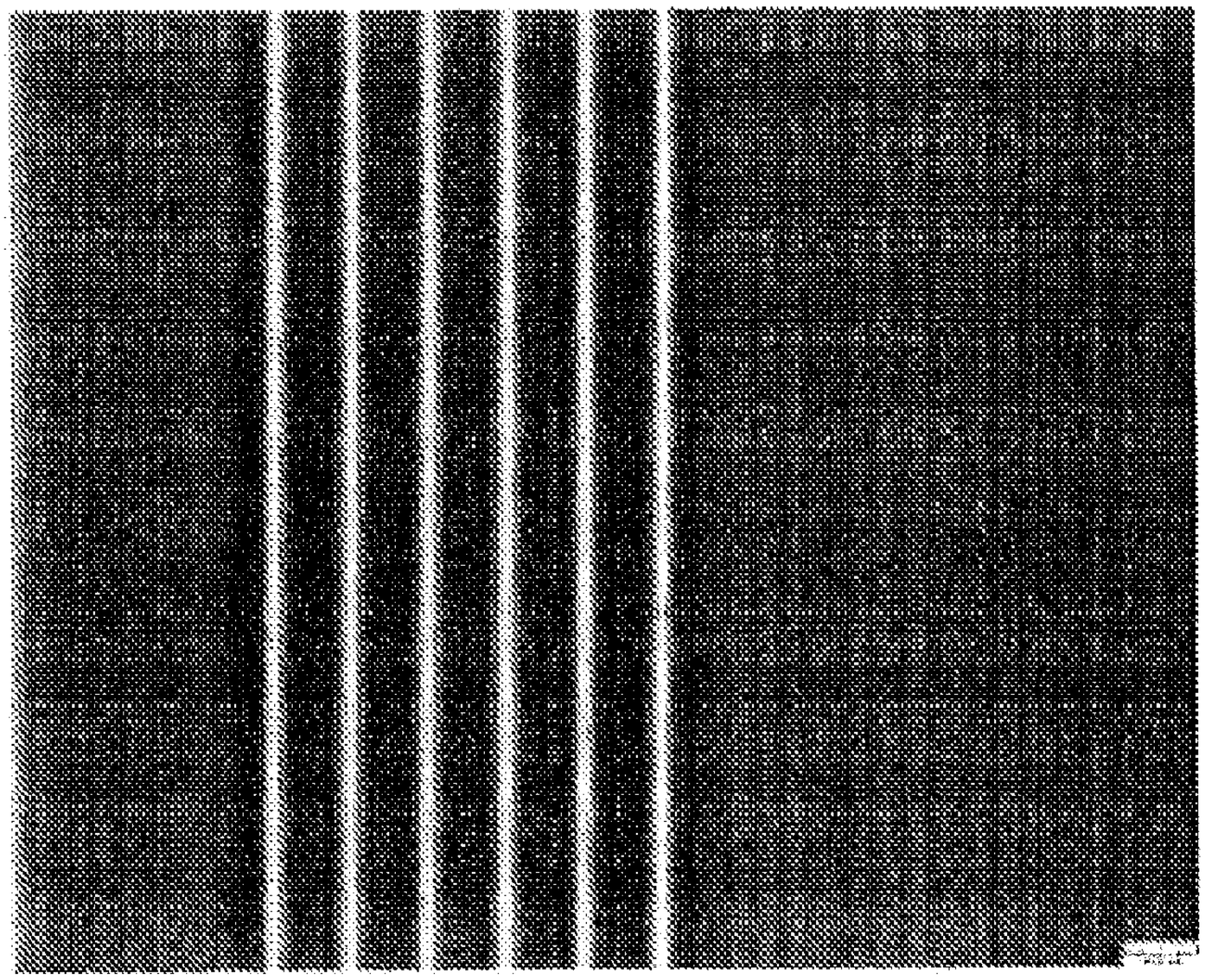
(54) Titre : LENTILLE INTRAOCULAIRE A PHOTOSENSIBILISATEUR ET PROCEDE DESTINE A MODIFIER L'INDICE DE REFRACTION DE LA LENTILLE

(54) Title: INTRAOCULAR LENS WITH PHOTOSENSITIZER AND METHOD FOR MODIFYING THE REFRACTIVE INDEX OF THE LENS



(57) Abrégé/Abstract:
An intraocular lens comprising an optical, polymeric material with predetermine regions that have been irradiated with light from a laser to form refractive structures. The refractive structures are characterized by a change in refractive index within the irradiated regions of the lens with little or no scattering loss. To facilitate the formation of the refractive structures the optical, polymeric material is prepared from at least one monomer having a photofunctional group, the monomer having a two- photon cross- section of at least 10 GM. The invention is also directed to a method for modifying the refractive index of an intraocular lens prior to the surgical insertion of the lens in a human eye. The described irradiation process is used in a manufacturing environment to create refractive structures in the intraocular lens. The method includes irradiating a solvated intraocular lens at predetermined regions with light from a laser to form refractive structures.

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(54) Title: INTRAOCULAR LENS WITH PHOTOSENSITIZER AND METHOD FOR MODIFYING THE REFRACTIVE INDEX OF THE LENS

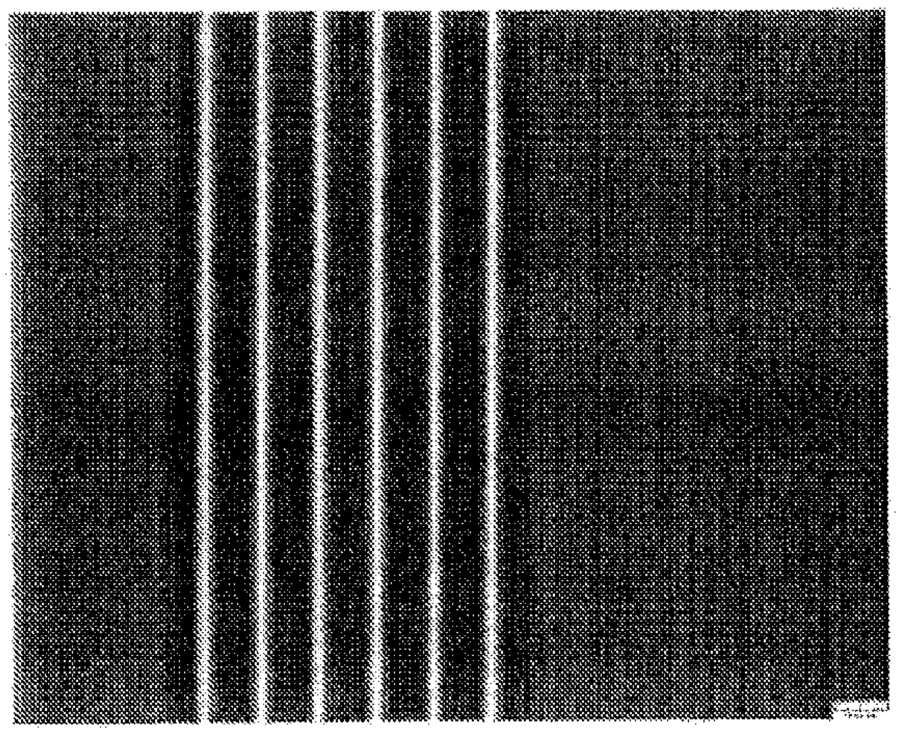

Figure 9B

(57) Abstract: An intraocular lens comprising an optical, polymeric material with predetermine regions that have been irradiated with light from a laser to form refractive structures. The refractive structures are characterized by a change in refractive index within the irradiated regions of the lens with little or no scattering loss. To facilitate the formation of the refractive structures the optical, polymeric material is prepared from at least one monomer having a photofunctional group, the monomer having a two-photon cross- section of at least 10 GM. The invention is also directed to a method for modifying the refractive index of an intraocular lens prior to the surgical insertion of the lens in a human eye. The described irradiation process is used in a manufacturing environment to create refractive structures in the intraocular lens. The method includes irradiating a solvated intraocular lens at predetermined regions with light from a laser to form refractive structures.

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INTRAOCULAR LENS WITH PHOTOSENSITIZER AND METHOD FOR MODIFYING THE REFRACTIVE INDEX OF THE LENS

The present invention relates to a method of using a laser to modify the refractive index of an intraocular lens that includes an optical polymeric material, and the resulting intraocular lens.

Background of the Invention

In general, there are two types of intraocular lenses. One type replaces the eye's natural lens, usually to replace a cataractous lens. The other type is used to supplement an existing lens and functions as a permanent corrective lens. This type of lens (referred to as a phakic IOL) is implanted in the anterior or posterior chamber to correct refractive errors of the eye. The power of the lens, i.e., the point focus on the retina from light originating at infinity, to be implanted is determined based on pre-operative measurements of ocular length and corneal curvature of each patient. The pre-operative measurements are conducted with the hope that the patient will need little, if any, vision correction following the surgery. Unfortunately, due to errors in measurement, variable lens positioning or wound healing, most patients undergoing cataract surgery will not enjoy optimal vision without some form of vision correction following the surgery. Brandser et al., *Acta. Opthalmol. Scand.* 75:162 165 (1997); Oshika et al., *J. Cataract Refract. Surg.* 24:509 514 (1998). In-part because the power of present IOLs is typically fixed across the optic many patients will require corrective lenses such as eye glasses or contact lenses following surgery.

U.S. Patent No. 6,450,642, hereafter referred to as the Calhoun Patent, describes a light-adjustable lens that is said to comprise (i) a first polymer matrix and (ii) a refraction modulating composition (RMC) that is capable of stimulus-induced polymerization. As stated, when a portion of the described lens is exposed to light of sufficient intensity, the RMC forms a second polymer matrix. The process is said to result in a light adjusted, power-modified lens.

As described in the Calhoun Patent, the first polymer matrix and the RMC are selected such that the components that comprise the RMC are capable of diffusion within the first polymer matrix. Put another way, a loose first polymer matrix will tend to be paired with larger RMC components and a tight first polymer matrix will tend to be paired with smaller RMC components. Upon exposure to an appropriate energy source

(e.g., heat or light), the RMC typically forms a second polymer matrix in the exposed region of the optical element. After exposure, the RMC in the unexposed region will migrate into the exposed region over time. The amount of RMC migration into the exposed region is said to be time dependent and controllable. If enough time is permitted, the RMC components will re-equilibrate and redistribute throughout the lens material (i.e., the first polymer matrix, including the exposed region). When the region is re-exposed to the energy source, the RMC that has since migrated into the region polymerizes to further increase the formation of the second polymer matrix. This process (exposure followed by an appropriate time interval to allow for diffusion) may be repeated until the exposed region of the optical element has reached the desired property (e.g., power, refractive index, or shape). The entire optical element is then exposed to an energy source to "lock-in" the desired lens property by polymerizing the remaining RMC in the lens material. Overall, the power of the lens is changed by a shape change caused by the migration of the RMC and subsequent polymerization(s).

One obvious disadvantage to the Calhoun process is the time it takes to actually provide a custom-fit intraocular lens. For example, it can take several days or perhaps a week or so for the RMC to migrate to the previously exposed irradiated regions. Accordingly, the Calhoun process is unacceptable for the manufacture of custom-fit intraocular lenses.

U.S. Patent No. 7,105,110 describes a method and instrument to irradiate a light adjustable lens as described in the Calhoun Patent with an appropriate amount of radiation in an appropriate pattern. The method is said to include aligning a source of the modifying radiation so as to impinge the radiation onto the lens in a pattern, and controlling the quantity of the impinging radiation. The quantity of the impinging radiation is controlled by controlling the intensity and duration of the irradiation.

There exists an ongoing need for new materials and processes to improve a patient's vision following cataract surgery. Accordingly, there is a need for an intraocular lens whose refractive power can be modified by a change in the refractive index of a lens material prior to the surgical implantation of the lens as well as post-operative corrections. There is also interest in the ophthalmic community for an IOL that provides a patient with an extended depth of field or with a multifocal modality to improve a patient's visual acuity at variable distances.

Summary of the Invention

The invention is directed to an intraocular lens comprising an optical, polymeric material with predetermined regions that have been irradiated with light from a laser to form refractive structures. The refractive structures are characterized by a change in refractive index within the irradiated regions of the lens with little or no scattering loss. The irradiation is conducted by scanning predetermined regions of the polymeric material with the laser. To facilitate the formation of the refractive structures the optical, polymeric material is prepared from at least one monomer having a photofunctional group, the monomer having a two-photon cross-section of at least 10 GM.

In one instance, the irradiated region is defined by a three-dimensional refractive structure in the form of a positive or negative lens element.

The invention is also directed to a method for modifying the refractive index of an intraocular lens prior to the surgical insertion of the lens in a human eye. The described irradiation process is used in a manufacturing environment to create refractive structures in the intraocular lens. The method includes irradiating a solvated intraocular lens at predetermined regions with light from a laser, the light having a wavelength from 600 nm to 900 nm to form refractive structures. The refractive structures are characterized by a change in the refractive index within the irradiated regions of the lens with little or no scattering loss.

To facilitate the formation of the refractive structures the optical, polymeric material includes a photosensitizer. In one instance, the polymeric, optical material is prepared from at least one monomer having a photofunctional group, the monomer having a two-photon cross-section of at least 10 GM. In another instance, the polymeric, optical material is solution-doped with a photosensitizer having a two-photon cross-section of at least 10 GM.

Brief Description of the Drawings

The invention will be better understood from the following description and in consideration with the accompanying figures. It is to be expressly understood, however, that each of the figures is provided to further illustrate and describe the invention and is not intended to further limit the invention claimed.

Figure 1A is a microscope photograph of a line grating written in an optical, polymeric material produced by laser irradiation;

Figure 1B is a schematic representation of the microscope photograph of Figure 1A;

Figure 2A is a microscope photograph of a line grating written above and orthogonal to another line grating in an optical, polymeric material produced by laser irradiation;

Figure 2B is a schematic representation of the microscope photograph of Figure 2B;

Figure 3A is a microscope photograph of an array of cylinders etched in an optical, polymeric material produced by laser irradiation;

Figure 3B is a schematic representation of the microscope photograph of Figure 3A;

Figure 4A is a microscope photograph of one array of cylinders (20 x 20) etched above and slightly offset to another array of cylinders (20 x 20) in an optical, polymeric material produced by laser irradiation;

Figure 4B is a schematic representation of the microscope photograph of Figure 4A;

Figure 5 is a schematic representation of a three-dimensional structure in an optical, polymeric material that can be produced by laser irradiation;

Figure 6 is a schematic representation of creating a convex, plano or concave structure in an optical, polymeric material to yield a positive or negative correction;

Figure 7 is a schematic representation of the laser and optical system used to write the structures shown in Figures 1 to 4, 9, 10 and 12;

Figure 8A is a transmission spectrum of a hydrated Akreos® IOL without photosensitizer;

Figure 8B is a transmission spectrum of a hydrated Akreos® IOL doped with a solution containing 17 wt.% coumarin-1;

Figure 9A is phase contrast photograph of a hydrated Akreos® IOL without photosensitizer micromachined at a scan rate of 50 μm/s and 160 mW average power;

Figure 9B is phase contrast photograph of a hydrated Akreos® IOL doped with a solution containing 17 wt.% coumarin-1micromachined at a scan rate of 50 μm/s and 160 mW average power;

Figure 10A is phase contrast photograph of a hydrated Akreos® IOL doped with a solution containing 17 wt.% coumarin-1 micromachined at a scan rate of 1 mm/s and 160 mW average power;

Figure 10B phase contrast photograph of a hydrated Akreos® IOL doped with a solution containing 17 wt.% coumarin-1 micromachined at a scan rate of 1 mm/s and 60 mW average power.

Figure 11A is a transmission spectrum of a hydrated Pure Vision® silicone hydrogel without photosensitizer;

Figure 11B is a transmission spectrum of a hydrated Pure Vision® silicone hydrogel doped with 0.17 wt.% fluorescein;

Figure 12A is phase contrast photograph of a hydrated Pure Vision® silicone hydrogel without photosensitizer micromachined at a scan rate of 0.5 μm/s and 60 mW average power;

Figure 12B is phase contrast photograph of a hydrated Pure Vision® silicone hydrogel doped with 0.17 wt.% fluorescein micromachined at a scan rate of 5.0 μm/s and 60 mW average power;

Figure 13 is a plot of change in refractive index vs. scan rate in balafilcon A films (undoped and doped with fluorescein and coumarin-1;

Figure 14 are the transmission spectra of the hydrogel materials of Example 5;

Figure 15 is a plot of the measured change in refractive index at different scan rates for the hydrogel materials of Example 5;

Figure 16A and 16B are plots of the measured change in refractive index at various wavelengths at average pulse energies of 1.5 nJ and 2 nJ, respectively, for the hydrogel materials of Examples 5A and 5E;

Figure 17 is a plot of the measured change in refractive index at various wavelengths, an average pulse energy of 1.5 nJ and a scan rate of 1 mm/s for the hydrogel materials of Examples 5A and 5E;

Figure 18 is a plot of the measured change in refractive index for hydrogel materials with variable water content; and

Figure 19 is a plot of the measured change in refractive index at various wavelengths for hydrogel materials with variable water content.

Detailed Description of the Invention

If very short laser pulses of sufficient energy are used to irradiate an optical, solvated polymeric material, the intensity of light within the irradiated region (i.e., focal volume) causes a nonlinear absorption of photons (typically multi-photon absorption) and leads to a change in the refractive index of the material within the focal volume. Moreover, portions of the material just outside the focal volume is minimally affected by the laser light. The femtosecond laser pulse sequence used in the experiments operates at a high repetition-rate, e.g., 80MHz, and consequently the thermal diffusion time (>0.1μs) is much longer than the time interval between adjacent laser pulses (~11ns). Under such conditions, absorbed laser energy can accumulate within the focal volume and increase the local temperature. We believe that this thermal mechanism likely plays a role in the formation of laser-induced refractive structures in optical, solvated polymeric materials. The presence of a solvent, e.g., water or an organic solvent such as an alcohol, in the polymeric material is very important, and is believed to profoundly influence the formation of the refractive structures.

Accordingly, the invention is directed to a method for modifying the refractive index of an optical, polymeric material that comprises a photosensitizer. The method comprises irradiating select regions of an optical, solvated polymeric material with a laser. The irradiated regions exhibit little or no scattering loss, which means that the resulting refractive structures that form in the focal volume are not clearly visible under appropriate magnification without phase contrast enhancement. In other words, the refractive structures are virtually transparent to the human eye without some form of image enhancement.

To facilitate the formation of the refractive structures, the optical, polymeric material comprises a photosensitizer. The presence of the photosensitizer permits one to form the refractive structures using greater scan rates and low average laser power relative to a base polymeric material without the photosensitizer. For example, the presence of the photosensitizer permits one to set a scan rate to a value that is at least fifty times greater, or at least 100 times greater, than a scan rate without the

photosensitizer present in the material, and yet provide similar refractive structures in terms of the observed change in refractive index of the material in the irradiated region. Alternatively, the photosensitizer in the polymeric material permits one to set an average laser power to a value that is at least two times less, preferably four times less, than an average laser power without the photosensitizer in the material, yet provide similar refractive structures. Simply stated, it is believed that a photosensitizer having a greater multi-photon absorption cross section captures the light radiation (photons) with greater efficiency and then transfers that energy to the optical, polymeric material within the focal volume. The transferred energy then leads to the formation of the refractive structures and the observed change in the refractive index of the material in the irradiated region (i.e., in the focal volume).

The refractive structures can be designed to enhance the depth of field of the lens or create select regions of variable power to custom fit the lens to the needs of a particular patient. Alternatively, the refractive structures can be designed to create a multifocal lens.

To date, we have used a 60X 0.70NA Olympus LUCPlanFLN long-working-distance microscope objective with variable spherical aberration compensation. As indicated by the following equation

$$\Delta T(r,z,t=0) = \frac{\beta\tau_p[I(0,0)]^2 \exp[-4(\frac{r^2}{a^2}+\frac{z^2}{b^2})]}{c_p\rho}$$

the localized instantaneous temperature depends on both the pulse intensity and the magnitude of the TPA coefficient. In order to produce an optical modification of a material that is of purely refractive character, i.e. not absorbing or scattering, then it is imperative to avoid optical damage, i.e., observed burning (scorching) or carbonization of the polymeric material. Such material or optical damage can be caused by excitation intensities exceeding a critical free-electron density.

For hydrogel polymers containing a fair amount of water, the optical breakdown threshold is much lower than that in silica glasses. This breakdown threshold limits the pulse energy (in many cases, to approximately 0.1 nJ to 10 nJ) that the hydrogel polymers can tolerate, and yet provide the observed changes in the refractive index within the focal volume. The irradiation process and conditions described herein are very different from what has been reported in femtosecond laser micromachining studies in

silica in which much larger pulse energies and much larger temperature increase (several thousand Kelvin) have been observed. See, S.M. Eaton et al. in *"Heat accumulation effects in femtosecond laser-written waveguides with variable repetition rate,"* Opt. Express 2005, 13, 4708-16. Also, the specific heat constant C_p of water is much larger than that of silica glass (C_P=840 $JK^{-1}kg^{-1}$), and therefore the presence of water in the hydrogel polymeric material is believed to moderate the temperature increase in the focal volume.

Likewise, optical polymeric materials prepared with hydrophobic monomers or silicone monomers/macromers, that is, optical materials that do not absorb appreciable amounts of water in an aqueous environment, can undergo a similar thermal process in the presence of an organic solvent, e.g., an alcohol or C_6-C_{18} alkane. In this case, the polymeric material absorbs sufficient amount of the solvent within the predetermined regions to moderate the temperature increase in the focal volume.

The term "solvated" refers to an optical polymeric material that is swelled by inclusion of a solvent in at least the predetermined regions of the polymeric material that is to be irradiated with the laser. In many instances, the polymeric materials will absorb sufficient solvent to provide a solvent content of 10 wt.% to 40 wt.%, based on the dry weight of the material.

Another way to increase energy absorption at a given intensity level is to increase the nonlinear absorption coefficient β by doping the optical, polymeric material with a photosensitizer and tuning the short pulse laser near a two-photon transition of the photosensitizer.

In this regard, we have prepared optical, materials doped with a non-polymerizable photosensitizer or a polymerizable photosensitizer. In the former case of a nonpolymerizble photosensitizer, we prepared solutions containing the photosensitizer and allowed the optical, polymeric materials to come in contact with such solutions such that the photosensitizer is incorporated into the polymeric matrix of the polymer. The photosensitizer will likely have a two-photon cross-section of at least 10 GM. In the later case of a polymerizble photosensitizer, we used monomers containing a photofunctional group (chromophore), e.g., a fluorescein-based monomer, in the monomer mixture such that the chromophore becomes part of the polymeric matrix. Similarly, the polymerizable photosensitizer will likely have a photofunctional group such that the monomer has a two-photon cross-section of at least 10 GM.

Of course, one of ordinary skill would recognize that one could easily use a solution containing a non-polymerizable photosensitizer to dope an optical, polymeric material that had been prepared with a polymerizable photosensitizer. Also, it is to be understood that the chromophoric entities of the two photosensitizers could be the same or different.

Our studies have shown that by doping the optical polymeric material with a photosensitizer either by solution doping or by using a polymerizable photosensitizer the localized temperature increase can reach a transition point of the polymer. The goal being to reach this transition point to provide a desired change in the refraction index, yet maintain a safe margin of intensity below the damage threshold level of the hydrogel material. Due to the high repetition rate pulse sequence we use in the irradiation process, the accumulated focal temperature increase can be much larger than the temperature increase induced by a single laser pulse. The accumulated temperature increases until the absorbed power and the dissipated power are in dynamic balance.

In the case of hydrogel polymers, thermal-induced additional cross-linking within the polymer network can produce a change in the refractive index as the local temperature exceeds a transition temperature. If the temperature increase exceeds a second threshold, a somewhat higher temperature than the transition temperature, the polymer is pyrolytically degraded, and carbonized residue and water bubbles are observed. In other words, the material exhibits visible optical damage (scorching) –like scorching or burning holes in a piece of paper with a magnifying glass on a sunny day.

As a result from our investigations described herein, each of the following experimental parameters such as laser repetition-rate, laser wavelength and pulse energy, TPA coefficient and percent solvation, e.g., percent water content if a hydrogel material, of the materials should be considered so that a desired change in the refractive index can be induced in the solvated polymers without optical damage.

The pulse energy and the average power of the laser, and the rate at which the irradiated regions are scanned, will in-part depend on the type of polymeric material that is being irradiated, how much of a change in refractive index is desired and the type of refractive structures one wants to formwithin the material. The selected pulse energy will also depend upon the scan rate and the average power of the laser at which the

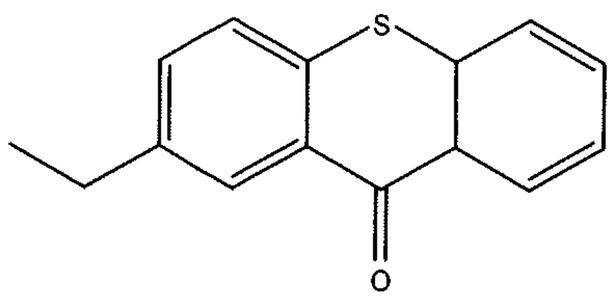
structures are written into the material. Typically, greater pulse energies will be needed for greater scan rates and lower laser power. For example, some materials will call for a pulse energy from 0.05 nJ to 100 nJ, 0.05 nJ to 50 nJ or from 0.2 nJ to 10 nJ.

Within the stated pulse energies above, optical, polymeric materials can be irradiated at a scan rate of at least 0.1 mm/s, from 0.1 mm/s to 10 mm/s or from 0.4 mm/s to 4 mm/s.

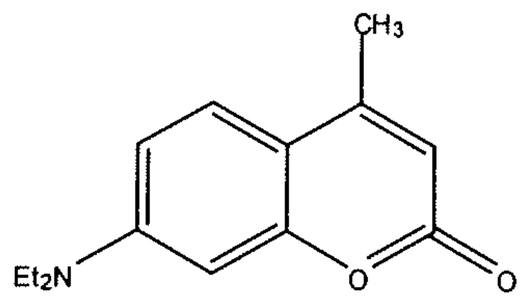
Within the stated pulse energies and scan rates above, the average laser power used in the irradiation process is from 10 mW to 400 mW, 10 mW to 300 mW or from 40 mW to 220 mW.

In one embodiment, the average pulse energy is from 0.2 nJ to 10 nJ and the average laser power is from 40 mW to 220 mW. The laser also operates within a wavelength of 650 nm to 950 nm. Within the stated laser operating powers, the optical, hydrogel polymeric material is irradiated at a scan rate from 0.4 mm/s to 4 mm/s.

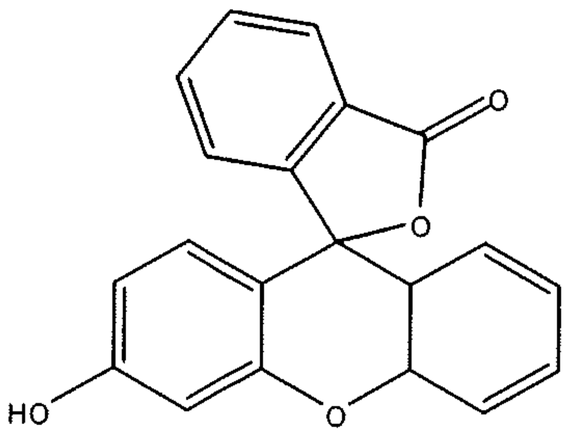
A photosensitizer will include a chromophore in which there is little, if any, intrinsic linear absorption in the spectra range of 600-1000 nm. The photosensitizer is present in the optical, polymeric material to enhance the photoeffiency of the two photon absorption required for the formation of the described refractive structures. Photosensitizers of particular interest include, but are not limited to, the following compounds. The compounds below are merely exemplary.



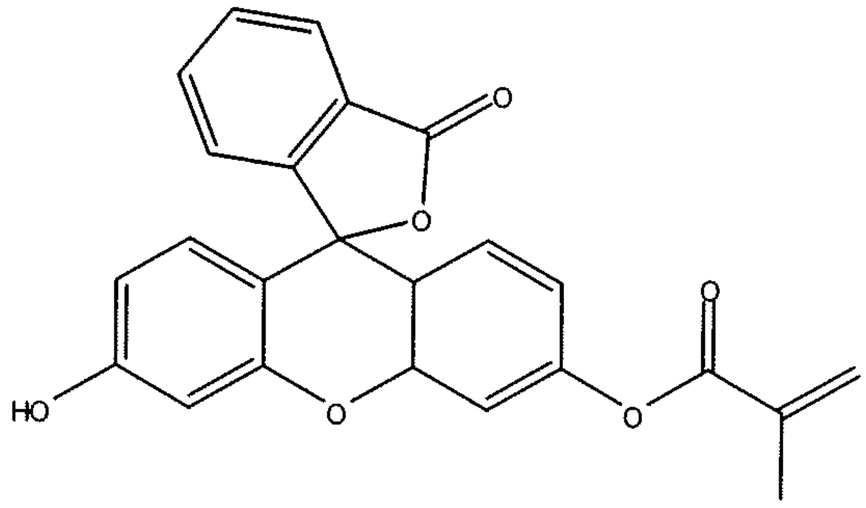
isopropylthioxanthone



coumarin -1



fluoroscein



fluorscein methacrylate

As is described in greater detail in the Example section, a commercial IOL material, Akreos®, presently marketed by Bausch & Lomb, was subjected to laser irradiation according to the processes described herein. The micromachining process was used to form refractive structures in an Akreos® IOL without photosensitizer and an Akreos® IOL doped with a solution containing 17 wt.% cormarin-1. The irradiation experiments were conducted with both dry and solvated materials. The refractive structures formed only in the hydrated materials.

In brief, the magnitude of the measured change in refractive index was at least ten times greater in the Akreos® IOL doped with the coumarin solution at a given scan rate and an average laser power than an Akreos® IOL that was not solution-doped with the coumarin. Surprisingly, an increase in scan rate to 1 mm/s at an average laser power of 160 mW provided refractive structures (a line grating) with a change in refractive index of 0.02 to 0.03. Moreover, reducing the laser power to 60 mW still provided refractive structures with a change in refractive index of about 0.005.

In another embodiment, a balafilcon A silicone hydrogel was prepared by adding fluorescein monomer (0.17% by weight) to the polymer monomer mixture. The balafilcon A doped with polymerizable fluorescein was then subjected to laser light according to the processes described herein. Again, the described irradiation process was conducted in the silicone hydrogel without photosensitizer and the silicone hydrogel doped with 0.17 wt.% fluorescein. Again, experiments were conducted with both dry and solvated (hydrated) materials, and again, the refractive structures formed only in the hydrated materials.

In brief, the magnitude of the measured change in refractive index was at least ten times greater in the balafilcon A silicone hydrogel doped with 0.17 wt.% fluorescein at an average laser power of 60 mW than balafilcon A without the photosensitzer. This 10-fold difference in change in refractive index was observed even with a 10-fold increase in scan rate in the photosensitized material – 0.5 μm/s in the undoped material and 5.0 μm/s in the photosensitized material.

In some cases, the formation of refractive structures as described requires that the pulse width be preserved so that the pulse peak power is strong enough to exceed the nonlinear absorption threshold of the optical, polymeric material. However, the glass of the focusing objective(s) significantly increases the pulse width due to the positive dispersion of the glass. A compensation scheme is used to provide a corresponding

negative dispersion that can compensate for the positive dispersion introduced by the focusing objective(s). Accordingly, a compensation scheme can be used to correct for the positive dispersion introduced by the focusing objective(s). The compensation scheme can include an optical arrangement selected from the group consisting of at least two prisms and at least one mirror, at least two diffraction gratings, a chirped mirror and dispersion compensating mirrors to compensate for the positive dispersion introduced by the focus objective.

In one embodiment, the compensation scheme comprises at least one prism, in many cases at least two prisms, and at least one mirror to compensate for the positive dispersion of the focusing objective. In another embodiment, the compensation scheme comprises at least two gratings to compensate for the positive dispersion of the focusing objective. Any combination of prisms, gratings and/or mirrors can be used for the compensation scheme.

The laser will generate light with a wavelength in the range from visible to near-infrared radiation. In various embodiments, the wavelength of the laser is in the range from from 600 nm to 900 nm. In one particular embodiment, the laser is a pumped Ti:sapphire laser. Such a laser system will generate light with a wavelength of approximately 800 nm. The laser will have a peak intensity at focus of greater than 1013 W/cm^2. At times, it may be advantageous to provide a laser with a peak intensity at focus of greater than 1014 W/cm^2, or greater than 1015 W/cm^2.

The ability to form refractive structures in optical, polymeric materials provides an important opportunity to modify the refractive index of an intraocular lens prior to the surgical implantation of the lens into an eye of a patient. Prior to surgery ocular surgeons determine the required power magnification of an intraocular lens based upon the vision corrective needs of each patient in the hopes that only minor vision correction would be needed following the surgery. Such a positive outcome is, of course, very unlikely because of the present fixed power and spherical design of the optic portion of the lens. For example, the surgeon is not able to correct for astigmatism because custom-fit intraocular lenses are not commercially available. The described irradiation process provides for the custom-fit lens based on the vision correction of each patient.

For example, starting from a base lens of selected power (will vary according to the ocular requirements of the patient), the power of the lens can be adjusted within

predetermined regions. In essence, an intraocular lens would essentially function like contact lenses or glasses to individually correct for the refractive error of a patient's eye.

In addition, the refractive index of an implanted lens can be adjusted by irradiating predetermined regions of the lens. Accordingly, post-operative refractive errors resulting from pre-operative measurement errors, variable lens positioning during implantation and wound healing (aberrations) can also be corrected or fine tuned in-situ.

For instance, cataract surgery typically requires that the natural lens of each eye be replaced with an intraocular lens. Following insertion of the intraocular lens the surgeon can correct for aberrations resulting from the surgery or correct for slight misplacement of the intraocular lens. Following surgery, and after allowing time for the wound to heal, the patient would return to the surgeon to have select regions of the intraocular lens irradiated. These irradiated regions would experience a positive change in refractive index, which would correct for the aberrations as well as the patients needs for vision correction. In some instances, the surgeon would be able to adjust the intraocular lens in one eye for distance and adjust the intraocular lens in the opposite eye for reading.

Typically, the irradiated portions of the optical, hydrogel polymeric material will exhibit a positive change in refractive index of about 0.01 or more. In one embodiment, the refractive index of the region will increase by about 0.03 or more. In fact, applicants have measured a positive change in refractive index in a hydrated, Akreos® IOL material of about 0.06. For example, the described irradiation process can allow for a positive change in refractive index from 0.01 to 0.06.

It is to be understood by one of ordinary skill in the art, that the method described herein modifies the refractive properties of the material not by casting an optical material with nonreacted monomer (refraction modulation composition) followed by laser irradiation to promote additional polymerization chemistry as described in the Calhoun Patent, but rather by a change in the refractive index of an already completely polymerized optical material. The term "completely polymerized" when used to characterize the optical materials used in the method means that the optical materials are 95% or more polymerized. One way to measure the completeness of a polymerized optical material is by near infra-red spectroscopy, which is used to qualitatively determine the vinyl content of the material. Simple gravimetric weight analysis can also be used.

The irradiated regions of the optical, polymeric material can be defined by two- or three-dimensional structures. The two- or three-dimensional structures can comprise an array of discrete cylinders. Alternatively, the two- or three-dimensional structures can comprise a series of lines (a grating) or a combination of an array of cylinders and a series of lines. Moreover, the two- or three-dimensional structures can comprise area or volume filled structures, respectively. These area or volume filled structures are formed by continuously scanning the laser over a select region of the polymeric material.

Nanometer-sized structures can also be formed by the zone-plate-array lithography method describe by R. Menon et al., Proc. SPIE, Vol. 5751, 330-339 (May 2005); Materials Today, p. 26 (February 2005).

In one embodiment, the three-dimensional refractive structure is in the form of positive or negative lens element. To optimize the optical affect of these structures, the positive or negative lens element is disposed in a volume of the lens within 300 μm from the anterior surface of the intraocular lens.

In one embodiment, an irradiated region of an intraocular lens is defined by a series of lines in a two dimensional plane having a width from 0.2 μm to 3 μm, preferably a width from 0.6 μm to 1.5 μm and a height from 0.4 μm to 8 μm, preferably a height from 1.0 μm to 4 μm (height is measured in the z direction of the material, which is parallel to direction of the laser light). For example, one can generate a line grating comprising a plurality of lines with each line of any desired length, about 0.8 μm to about 1.5 μm in width and about 2 μm to 5 μm in height. The lines can be separated by as little as 1.0 μm (0.5 μm spacing), and any number of lines can be incorporated into the material. Moreover, the grating can be positioned at any selected depth (z-direction), and any number of line gratings can be generated at various depths into the material.

Figure 1A is a microscope photograph with contrasting background of a line grating comprising 20 lines written into an optical material. Figure 1B is a schematic representation of the microscope photograph of Figure 1A. Each line is about 100 μm in length, about 1 μm in width with a line separation of about 5 μm. The lines have a height of about 3 μm and were written into the material at a distance of about 100 μm from the top surface of the material. Similar microscope photographs exhibiting line gratings were obtained at a distance of about 200 μm and 400 μm from the top surface of the material, thereby demonstrating that structures can be written into the optical material at any selected depth.

Figure 2A is a microscopic photograph with contrasting background of one line grating written above and orthogonal to another line grating. Figure 2B is a schematic representation of the microscope photograph of Figure 2A. Each of the gratings has a similar dimensional structure to that described for Figure 1 above. One line grating is positioned about 100 μm into the material, and the other line grating is positioned about 110 μm into the material for a center-line, grating separation of about 10 μm. Again, each of these line structures has a height (depth) of about 3 μm.

Figure 3A is a microscopic photograph with contrasting background of an array of cylinders formed into an optical material. Figure 3B is a schematic representation of the microscope photograph of Figure 3A. Each cylinder is about 1 μm in diameter with a height of about 3 μm. The cylinders are separated by about 5 μm. The cylinders were formed into the material at a distance of about 100 μm from the top surface of the material.

Figure 4A is a microscopic photograph with contrasting background of one array of cylinders (20 x 20) formed above and slightly offset to another array of cylinders (20 x 20). Figure 4B is a schematic representation of the microscope photograph of Figure 4A. Each of the cylinders has a similar dimensional structure to that described for Figure 3 above. One array is positioned about 100 μm into the material, and the other array is positioned about 105 μm into the material for a center-line separation of about 5 μm. Each of the cylinders has a height (depth) of about 3 μm.

The area-filled or volume-filled two- or three-dimensional structures can be formed by continuously scanning the laser over predetermined regions of the optical, polymeric material. Refractive-type optical devices can be micro-machined inside the volume of an optical, polymer material by repeatedly scanning a tightly focused beam of femtosecond pulses in an area segment. The area of the segment can be changed correspondingly with the depth of the scan, so as to produce three-dimensionally shaped lenses with spheric, aspheric, toroidal or cylindrical shapes as shown in Figure 5. Although the refractive index change is positive (+0.02 to +0.06), these refractive corrective lenses can be made in various combinations of convex, plano- or concave to yield a positive correction, or negative correction, as shown in Figure 6. The devices can be stacked vertically, written separately in different planes, so as to act as a single lens. Additional corrective layers can be written as desired.

As indicated by the micrographs of the refractive structures described the area-filled or volume-filled two- or three-dimensional structures one can create a pattern of grating lines, cylinders and radial patterns in optical materials, however, it is also possible to create other optical features using the irradiation method described herein. For examples, arrays of dots (e.g., having a dimension in the nanometer range) can be created by directing the laser beam at discrete points or spots within the material. Such an array can be arranged substantially on one plane or several such arrays can be created at different depths within the material. A material thus modified can be advantageously useful when light is not substantially scattered by the dots.

In one embodiment, the refractive structures are formed proximate to the top anterior surface of an intraocular lens. For example, a positive or negative lens element (three-dimensional) is formed within a 300 μm volume, or within a 100 μm volume, from the anterior surface of the lens. The term "anterior surface" is the surface of the lens that faces anterior chamber of a human eye.

A Laser and Optical Configuration For Modifying an Optical Material.

A non-limiting embodiment of a laser system 10 for irradiating an optical, polymeric material with a laser to modify the refractive index of the material in select regions is illustrated in Figure 7. A laser source comprises a Kerr-lens mode-locked Ti:Sapphire laser 12 (Kapteyn-Murnane Labs, Boulder, Colorado) pumped by 4 W of a frequency-doubled Nd:YVO4 laser 14. The laser generates pulses of 300 mW average power, 30 fs pulse width and 93 MHz repetition rate at wavelength of 800 nm. Because there is a reflective power loss from the mirrors and prisms in the optical path, and in particular, from the power loss of the objective 20, the measured average laser power at the objective focus on the material is about 120mW, which indicates the pulse energy for the femtosecond laser is about 1.3 nJ.

Due to the limited laser pulse energy at the objective focus, the pulse width must be preserved so that the pulse peak power is strong enough to exceed the nonlinear absorption threshold of the materials. Because a large amount of glass inside the focusing objective significantly increases the pulse width due to the positive dispersion inside of the glass, an extra-cavity, compensation scheme is used to provide the negative dispersion that compensates for the positive dispersion introduced by the focusing objective. Two SF10 prisms 24 and 28 and one ending mirror 32 form a two-pass one-prism-pair configuration. We used a 37.5 cm separation distance between the prisms to

compensate the dispersion of the microscope objective and other optics within the optical path.

A collinear autocorrelator 40 using third-order harmonic generation is used to measure the pulse width at the objective focus. Both 2nd and 3rd harmonic generation have been used in autocorrelation measurements for low NA or high NA objectives. We selected third order surface harmonic generation (THG) autocorrelation to characterize the pulse width at the focus of the high-numerical-aperture objectives because of its simplicity, high signal to noise ratio and lack of material dispersion that second harmonic generation (SHG) crystals usually introduce. The THG signal is generated at the interface of air and an ordinary cover slip 42 (Corning No. 0211 Zinc Titania glass), and measured with a photomultiplier 44 and a lock-in amplifier 46. After using a set of different high-numerical-aperture objectives and carefully adjusting the separation distance between the two prisms and the amount of glass inserted, we selected a transform-limited 27-fs duration pulse, which is focused by a 60X 0.70NA Olympus LUCPlanFLN long-working-distance objective 48.

Because the laser beam will spatially diverge after it comes out of the laser cavity, a concave mirror pair 50 and 52 is added into the optical path in order to adjust the dimension of the laser beam so that the laser beam can optimally fills the objective aperture. A 3D 100nm resolution DC servo motor stage 54 (Newport VP-25XA linear stage) and a 2D 0.7 nm resolution piezo nanopositioning stage (PI P-622.2CD piezo stage) are controlled and programmed by a computer 56 as a scanning platform to support and locate the samples. The servo stages have a DC servo-motor so they can move smoothly between adjacent steps. An optical shutter controlled by the computer with 1 ms time resolution is installed in the system to precisely control the laser exposure time. With customized computer programs, the optical shutter could be operated with the scanning stages to micro-machine different patterns in the materials with different scanning speed at different position and depth and different laser exposure time. In addition, a CCD camera 58 along with a monitor 62 is used beside the objective 20 to monitor the process in real time.

The method and optical apparatus described above can be used to modify the refractive index of an intraocular lens following the surgical implantation of the intraocular lens in a human eye.

Accordingly, the invention is directed to a method comprising identifying and measuring the aberrations resulting from the surgical procedure. Once the aberrations are identified and quantified using methods well known in the art of ophthalmology, this information is processed by a computer. Of course, information related to the requisite vision correction for each patient can also be identified and determined, and this information can also be processed by a computer. There are a number of commercially available diagnostic systems that are used to measure the aberrations. For example, common wavefront sensors used today are based on the Schemer disk, the Shack Hartmann wavefront sensor, the Hartmann screen, and the Fizeau and Twymann-Green interferometers. The Shack-Hartmann wavefront measurement system is known in the art and is described in-part by U.S. Patent Nos.: 5,849,006; 6,261,220; 6,271,914 and 6,270,221. Such systems operate by illuminating a retina of the eye and measuring the reflected wavefront.

Once the aberrations are identified and quantified, the computer programs determine the position and shape of the optical structures to be written into the lens material to correct for those aberrations or to provide vision correction to the patient. These computer programs are well known to those of ordinary skill in the art. The computer than communicates with the laser-optical system and select regions of the lens are irradiated with a laser having a pulse energy from 0.05 nJ to 1000 nJ.

The Optical Polymeric Materials

The optical polymeric materials that can be irradiated with a laser according to the methods described in this application can be any optical polymeric material known to those of ordinary skill in the polymeric lens art, particularly those in the art familiar with optical polymeric materials used to make intraocular lenses. Non-limiting examples of such materials include those used in the manufacture of optical polymeric materials, such as siloxy-containing polymers, acrylic, hydrophilic or hydrophobic polymers or copolymers thereof.

The forming of the refractive structures is particularly suited for modifying the refractive index in select and distinct regions of a polymeric, optical silicone hydrogel, or a polymeric, optical non-silicone hydrogel. The term "hydrogel" refers to an optical, polymeric material that can absorb greater than 10% by weight water based on the total hydrated weight. In fact, many of the optical, hydrogel polymeric materials will have a water content greater than 15% or greater than 20%. For example, many of the optical,

hydrogel polymeric materials will have a water content from 15% to 60% or from 15% to 40%.

The optical polymeric materials are of sufficient optical clarity, and will have a relatively high refractive index of approximately 1.40 or greater, preferably 1.48 or greater. Many of these materials are also characterized by a relatively high elongation of approximately 80 percent or greater.

In one embodiment, the optical polymeric materials are prepared as a copolymer from at least three monomeric components. The first monomeric component is present in the copolymer in an amount of at least 60% by weight, and its homopolymer will have a refractive index of at least 1.50, preferably at least 1.52 or at least 1.54. The second monomeric component is present in the copolymer in an amount from 3% to 20% or from 3% to 10%, by weight. The first and second monomeric components together represent at least 70% by weight of the copolymer. The term "homopolymer" refers to a polymer that is derived substantially completely from the respective monomeric component. Minor amounts of catalysts, initiators and the like can be included, as is conventionally the case, in order to facilitate the formation of the homopolymer.

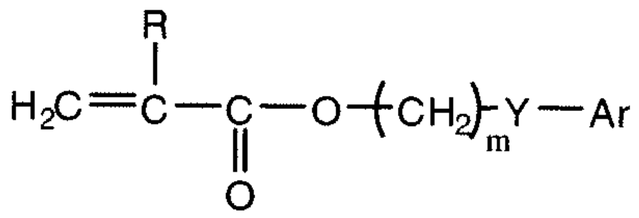
Particularly useful first monomeric components include styrene, vinyl carbazole, vinyl naphthalene, benzyl(meth)acrylate, phenyl(meth)acrylate, naphthyl(meth)acrylate, 2-phenoxyethyl(meth)acrylate, 2,3-dibromopropyl- (meth)acrylate and any one mixture thereof. Particularly useful second monomeric components include n-butyl(meth)acrylate, n-hexyl(meth)acrylate, 2-ethylhexyl-(meth)acrylate, 2-ethoxyethyl(meth)acrylate, 2,3-dibromopropyl(meth)acrylate, 1,1-dihydroperfluorobutyl(meth)acrylate and any one mixture thereof.

The copolymer can further include a fourth monomeric component derived from a hydrophilic monomeric component. The hydrophilic component is present in an amount, from 2% to 30% by weight of the copolymer. The hydrophilic component is preferably present in an amount of less than about 20% by weight of the copolymer. Copolymers which include about 10% by weight or more of a hydrophilic monomeric component tend to form hydrogels if placed in an aqueous environment. The term "hydrophilic monomeric component" refers to compounds which produce hydrogel-forming homopolymers, that is homopolymers which become associated with at least 25% of water, based on the weight of the homopolymer, if placed in contact with an aqueous solution.

Specific examples of useful hydrophilic monomeric components include N-vinyl pyrrolidone; hydroxyalkyl (meth)acrylates such as 2-hydroxyethyl (meth)acrylate, 3-hydroxypropyl (meth)acrylate, 3-hydroxypropyl (meth)acrylate, 4-hydroxybutyl (meth)acrylate, 2,3-dihydroxypropyl (meth)acrylate and the like; acrylamide; N-alkyl acrylamides such as N-methyl acrylamide, N-ethyl acrylamide, N-propyl acrylamide, N-butyl acrylamide and the like; acrylic acid; methacrylic acid; and the like and any one mixture thereof.

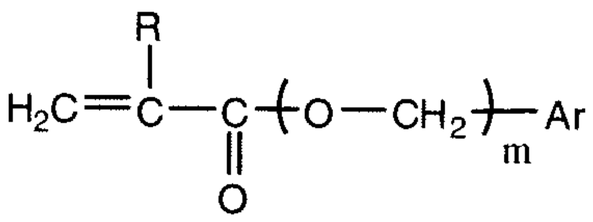
The polymeric optical materials will likely include a cross-linking component that can form crosslinks with at least the first or the second monomeric components. Preferably, the crosslinking component is multi-functional and can chemically react with both the first and second monomeric components. The crosslinking component is often present in a minor amount relative to the amounts of the first and second monomeric components. Preferably, the crosslink component is present in the copolymer in an amount of less than about 1% by weight of the copolymer. Examples of useful crosslinking components include ethylene glycol dimethacrylate, propylene glycol dimethacrylate, ethylene glycol diacrylate and the like and mixtures thereof.

In one embodiment, the optical, polymeric materials can be prepared from one or more aromatic (meth)acrylate monomers having the formula:



wherein: R is H or CH_3; m is an integer selected from 0 to10;
Y is nothing, 0, S, or NR wherein R is H, CH_3, C_2-C_6alkyl, iso-OC_3H_7, phenyl or benzyl;
Ar is any aromatic ring, e.g., phenyl, which can be unsubstituted or substituted with H, CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, OCH_3, C_6H_{11}, Cl, Br, phenyl or benzyl; and
a crosslinking component.

In another embodiment, the optical, polymeric materials can be prepared from one or more aromatic (meth)acrylate monomers having the formula:



wherein: R is H or CH_3; m is an integer selected from 0 to 6;

Ar is any aromatic ring, e.g., phenyl, which can be unsubstituted or substituted with H, CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, OCH_3, OH, C(O)OH; and a crosslinking component.

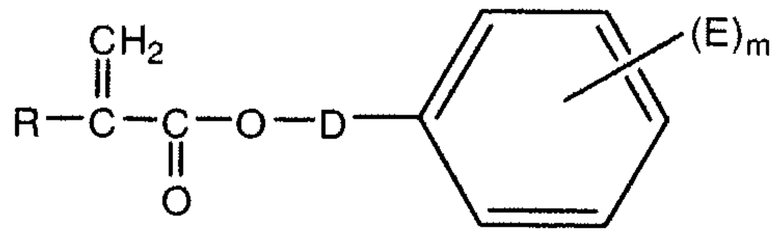
Exemplary aromatic (meth)acrylate monomers include, but are not limited to: 2-ethylphenoxy (meth)acrylate, 2-ethylthiophenyl (meth)acrylate, 2-ethylaminophenyl (meth)acrylate, phenyl-(meth)acrylate, benzyl (meth)acrylate, 2-phenylethyl (meth)acrylate, 3-phenylpropyl- (meth)acrylate, 4-phenylbutyl (meth)acrylate, 4-methylphenyl (meth)acrylate, 4-methylbenzyl (meth)acrylate, 2-2-methylphenylethyl (meth)acrylate, 2-3-methylphenylethyl (meth)acrylate, 2-4-methylphenylethyl (meth)acrylate, 2-(4-propylphenyl)ethyl (meth)acrylate, 2-(4-(1-methylethyl)phenyl) ethyl methacrylate, 2-(4-methoxyphenyl)ethyl methacrylate and the like. The term "(meth)acrylate" refers to a monomer having either an acrylate or methacryalate polymerizable functional group.

Generally, if the optical, polymeric material is prepared with both an aromatic acrylate and an aromatic methacrylate as defined by the formula above, the materials will generally comprise a greater mole percent of aryl acrylate ester residues than of aryl methacrylate ester residues. It is preferred that the aryl acrylate monomers constitute from about 60 mole percent to about 90 mole percent of the polymer, while the aryl methacrylate monomers constitute from about 5 mole percent to about 40 mole percent of the polymer. Most preferred is a polymer comprising about 60-70 mole percent 2-phenylethyl acrylate and about 30-40 mole percent 2-phenylethyl methacrylate.

In another embodiment, the optical, polymeric materials will have a fully hydrated (equilibrium) water content from 5% to 15% by weight, which also helps to minimize the degree of hazing following thermal stress as described as well as minimize the formation of water vacuoles in vivo. To achieve the desired water content applicants have discovered that one could include a hydrophilic, aromatic monomer having a formula,

G-D-Ar, wherein Ar is a C_6-C_{14} aromatic group having a hydrophilic substituent, in the polymerizable compositions. D is a divalent linking group, and G is a polymerizable ethylenic site,

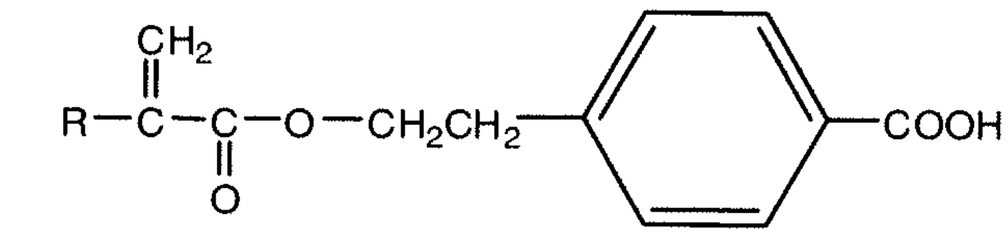
One particular hydrophilic aromatic monomer is represented by formula

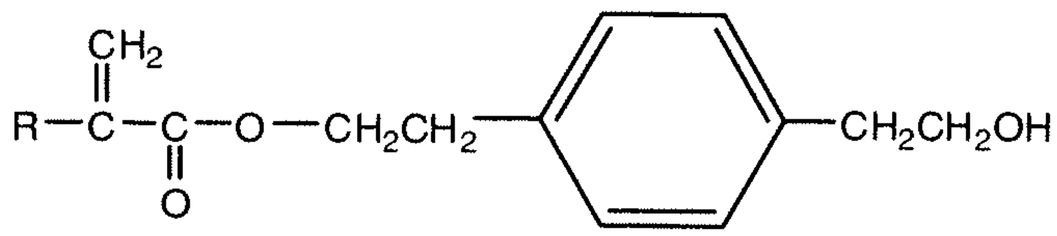


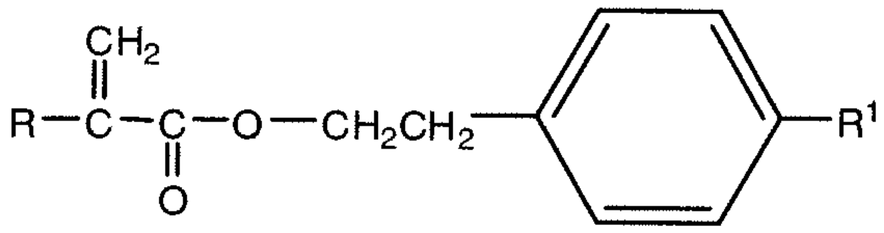
wherein R is hydrogen or CH_3; D is a divalent group selected from the group consisting of straight or branched C_1-C_{10} hydrocarbons, and E is selected from the group consisting of carboxy, carboxamide, and monohydric and polyhydric alcohol substituents.

Exemplary hydrophilic substituents include, but are not limited to, -COOH, -CH_2-CH_2OH, -$(CHOH)_2CH_2OH$, -CH_2-CHOH-CH_2OH, poly(alkylene glycol), -C(O)O-NH_2 and -C(O)-$N(CH_3)_2$.

Exemplary hydrophilic, aromatic monomers are represented by the following







wherein R is hydrogen or CH_3 and R^1 is –C(O)O-NH_2 or –C(O)-$N(CH_3)_2$.

In another embodiment, the optical, polymeric material is prepared from a first aryl monomeric component, which is present in 5-25% by weight, the second monomeric component is 2-hydroxyethyl (meth)acrylate, which is present from 30 to 70% by weight; and 5 to 45% by weight of a another alkyl (meth)acrylate selected from the group consisting of methyl (meth)acrylate, ethyl (meth)acrylate, propyl (meth)acrylate, butyl (meth)acrylate, pentyl (meth)acrylate, hexyl meth)acrylate, heptyl (meth)acrylate, nonyl (meth)acrylate, stearyl meth)acrylate, octyl (meth)acrylate, decyl (meth)acrylate, lauryl (meth)acrylate, pentadecyl (meth)acrylate and 2-ethylhexyl (meth)acrylate. Among the alkyl (meth)acrylates those containing 1 to 3 carbon atoms of alkyl group are preferred.

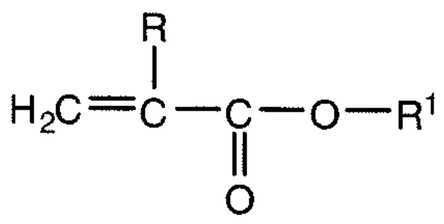
Exemplary aryl monomeric components include ethylene glycol phenyl ether acrylate (EGPEA), poly(ethylene glycol phenyl ether acrylate) (polyEGPEA), phenyl

methacrylate, 2-ethylphenoxy methacrylate, 2-ethylphenoxy acrylate, hexylphenoxy methacrylate, hexylphenoxy acrylate, benzyl methacrylate, 2-phenylethyl methacrylate, 4-methylphenyl methacrylate, 4-methylbenzyl methacrylate, 2-2-methyphenylethyl methacrylate, 2-3-methylphenylethyl methacrylate, 2-4-methylphenylethyl methacrylate, 2-(4-propylphenyl)ethyl methacrylate, 2-(4-(1-methylethyl)pheny)ethyl methacrylate, 2-(4-methoxyphenyl)ethylmethacrylate, 2-(4-cyclohexylpheny)ethyl methacrylate, 2-(2-chlorophenyl)ethyl methacrylate, 2-(3-chlorophenyl)ethyl methacrylate, 2-(4-chlorophenyl)ethyl methacrylate, 2-(4-bromophenyl)ethyl methacrylate, 2-(3-phenylphenyl)ethyl methacrylate, 2-(4-phenylphenyl)ethyl methacrylate), 2-(4-benzylphenyl)ethyl methacrylate, and the like, including the corresponding methacrylates and acrylates, and including mixtures thereof. EGPEA and polyEGPEA are two of the more preferred first monomeric components.

In another embodiment, the optical, polymeric material is prepared from a hydrophilic acrylic that comprises about 90% (by weight) N-vinylpyrrolidone (NVP) and about 10% (by weight) 4-t-butyl-2-hydroxycyclohexyl methacrylate. This methacrylate hydrogel can absorb about 80% (by weight) water because of the high percentage of NVP. Its refractive index when hydrated is very close to the index of water. Another hydrophilic acrylic of interest is referred to as HEMA B, which is a poly(2-hydroxyethyl methacrylate) cross-linked with about 0.9% (by weight) of ethylene glycol dimethacrylate ("EGDMA"). This HEMA-hydrogel can absorb about 37% (by weight) water.

One particular hydrophilic, acrylic material of interest is based upon a commercially available IOL sold in the market by Bausch & Lomb under the tradename Akreos®. This acrylic material comprises about 80% by weight HEMA and 20 wt% MMA.

The optical, polymeric material can also be prepared by copolymerizing a specific monomer mixture comprising perfluorooctylethyloxypropylene (meth)acrylate, 2-phenylethyl (meth)acrylate, an alkyl (meth)acrylate monomer having the following general formula,



wherein R is hydrogen or methyl and R^1 is a linear or branched C_4-C_{12} alkyl group, and a crosslinking monomer. An examplary list of alkyl (meth)acrylate monomer include n-butyl acrylate, isobutyl acrylate, isoamyl acrylate, hexyl acrylate, 2-ethylhexyl acrylate, octyl acrylate, isooctyl acrylate, decyl acrylate, isodecyl acrylate, and the like.

The perfluorooctylethyloxypropylene (meth)acrylate is present from 5%to 20% by weight, the 2-phenylethyl (meth)acrylate is present from 40%to 60% by weight, the alkyl (meth)acrylate monomer is present from 30% to 50% by weight and the crosslinking agent is present from 0.5% to 4% by weight.

The optical, polymeric materials can also be prepared from a reinforced cross-linked silicone elastomer which includes a polymer containing 12 to 18 mol percent of aryl substituted siloxane units of the formula R^4R^5-SiO. In the formula, R^4 and R^5 are the same or different and represent phenyl, mono- lower alkyl substituted phenyl groups, or di- lower alkyl substituted phenyl groups. Preferably both R^4 and R^5 are phenyl.

The polymer has end blockers containing siloxane units of the formula $R^1R^2R^3$-SiO_5 wherein R^1 and R^2 are alkyl, aryl or substituted alkyl or substituted aryl groups, and R^1 and R^2 can be the same or different. The R^3 group of the end blocking siloxane units is an alkenyl group. Preferably, the end blocker is a dimethylvinyl siloxane unit.

The balance of the polymer consists of dialkyl siloxane units of the formula R^6R^7-SiO wherein R^6 and R^7 are the same or different from and are methyl or ethyl groups, and the polymer has a degree of polymerization from 100 to 2000. Preferably, R^6 and R^7 are both methyl, and the degree of polymerization is approximately 250.

A trimethyl silyl treated silica reinforcer is finely dispersed in the polymer, in a weight ratio of approximately 15 to 45 parts of the reinforcer to 100 parts of the polymer. Preferably, there is approximately 27 parts of reinforcer to 100 parts of the copolymer.

The optical, polymeric component will likely include a crosslinking agent. The copolymerizable crosslinking agent(s) useful in forming the copolymeric material of the invention include any terminally ethylenically unsaturated compound having more than one unsaturated group. Preferably, the crosslinking agent includes a diacrylate or a dimethacrylate. The crosslinking agent may also include compounds having at least two (meth)acrylate and/or vinyl groups. Particularly preferred crosslinking agents include diacrylate compounds

The optical, polymeric materials are prepared by generally conventional polymerization methods from the respective monomeric components. A polymerization mixture of the monomers in the selected amounts is prespared and a conventional thermal free-radical initiator is added. The mixture is introduced into a mold of suitable shape to form the optical material and the polymerization initiated by gentle heating. Typical thermal, free radical initiators include peroxides, such as benzophenone peroxide, peroxycarbonates, such as bis-(4-t-butulcyclohexyl) peroxydicarbonate, azonitriles, such as azobisisobytyronitrile, and the like. A preferred initiator is bis-(4-t-butylcyclohexyl) peroxydicarbonate (PERK). Alternatively, the monomers can be photopolymerized by using a mold which is transparent to actinic radiation of a wavelength capable of initiating polymerization of these acrylic monomers by itself. Conventional photoinitiator compounds, e.g., a benzophenone-type photoinitiator, can also be introduced to facilitate the polymerization.

While specific embodiments of the present invention have been described in the foregoing, it will be appreciated by those skilled in the art that many equivalents, modifications, substitutions, and variations may be made thereto without departing from the spirit and scope of the invention as defined in the claims.

Examples

Example 1. Preparation of Akreos® IOL with 17% coumarin-1.

Coumarin 1 dye (2.5 g) is dissolved in an ethanol-water mixture containing 10 mL ethanol and 5 mL water. Dry weight of the Akreos sample is recorded. The samples are hydrated in pure water and the mass is recorded. Following the hydration step, the samples are soaked in the ethanol-water mixture containing the coumarin 1 dye until a constant mass is attained. The mass after soaking in the dye solution is recorded. Mass of the dye doped is calculated as the difference between the mass after soaking in the solution, and the dry mass multiplied by the mass concentration of the dye in the ethanol-water solution. Percentage of the dye doped is calculated as the ratio of mass of coumarin 1 dye doped over the dry mass multiplied by 100.

Example 2. Forming Structures In Akreos® IOL Materials.

The optical system described was used to form line structures in select regions of optical materials. Experiments were conducted with Akreos® IOL materials with and without photosensitizer. Akreos® IOL materials comprise about 80 wt% HEMA and 20

wt% MMA with a water content of about 26% using similar process conditions described above.

The hydrated sample was mounted horizontally on the scanning platform, and the femtosecond laser beam was directed vertically downward through the high-numerical-aperture objective and was focused inside the bulk material, as shown in Figure 7, at a depth of about 100 μm from the upper surface of the sample. Periodic gratings structures were created with a scanning speed of 0.4 μm/sec in an X-Y plane perpendicular to the laser beam. An Olympus BX51 Model microscope was used to observe the gratings that were created inside these three materials.

The microscope images showed periodically parallel gratings inside the samples with 5-μm spacing. The gratings were difficult to see in bright-field microscope, indicating that these gratings exhibit low scattering. The width of the gratings was about 1 μm, which was significantly smaller than the laser focus diameter of 2.5 μm that was measured using a knife-edge method. Therefore, the modified region is still within the laser irradiation focus volume although there would be heat accumulation generated in the process.

A cross section of the irradiated materials revealed that the cross section of the gratings was elliptical with the longer axis oriented in the direction of the laser beam, indicating that there was a larger laser intensity distribution in this direction. By carefully adjusting the cover-slip correction of the objective, this spherical aberration could be minimized.

As indicated in Figures 8A and 8B, the incorporation of coumarin-1 into an Akreos® IOL provided a red shift in the transmission spectrum of an Akreos® IOL material of about 50 nm. The Akreos® IOL material with coumarin-1 has a relatively significant absorption profile at 400 nm and to about 425 nm, whereas an Akreos® IOL material without photosensitizer is essentially transparent at these wavelengths.

Figures 9A and 9B are phase contrast photographs of Akreos® IOL materials with refractive structures micromachined within the materials at a depth of about 200 μm from the top irradiated surface. The irradiation process was conducted at 160 mW average power and a scan rate of 50 μm/s. As indicated in Figure 9A, the refractive structures micromachined in the Akreos® IOL material without photosensitizer provide little, if any, change in refractive index, $\Delta RI << 0.005$ (visible detection limit of the

structures). In fact, it is very difficult to see the refractive structures in the material even with phase contrast enhancement. In contrast, as indicated in Figure 9B, the refractive structures micromachined in the Akreos® IOL material with 17% coumarin-1 at the identical power and scan rate provide a very significant change in refractive index, $\Delta RI > 0.06$. The refractive structures are clearly visible with phase contrast enhancement.

Figures 10A and 10B indicate how differences in the refractive power of the micromachined structures (the magnitude of change in refractive index) can be varied based on the scan rate and laser power. More importantly, Figure 10A shows that one can form refractive structures in Akreos® IOL materials with 17% coumarin-1 at a scan rate of 1 mm/s, and with a ΔRI of about 0.02 to 0.3. A very surprising and exciting result since one would have to scan at about 10 μm/s to generate a similar refractive structure in an Akreos® IOL material without photosensitizer. The presence of the coumarin-1 allows one to increase the scan rate nearly 100-fold. Moreover, even with a relatively low laser power, i.e., 60 mW, one can still generate refractive structures with a ΔRI of about 0.005.

Example 3. Preparation of Pure Vision® silicone hydrogel with 0.07 wt.% fluorescein.

Fluorescein (0.25 g) dye is dissolved in an ethanol-water mixture containing 50 mL ethanol and 50 mL water. Dry weight of the Pure Vision sample is recorded. The samples are hydrated in pure water and the mass is recorded. Following the hydration step, the samples are soaked in the ethanol-water mixture containing fluorescein dye until a constant mass is attained. The mass after soaking in the dye solution is recorded. Mass of the dye doped is calculated as the difference between the mass after soaking in the solution, and the dry mass multiplied by the mass concentration of the dye in the ethanol-water solution. Percentage of the dye doped is calculated as the ratio of mass of Fluorescein dye doped over the dry mass multiplied by 100.

Example 4. Forming structures in Balafilcon A silicone hydrogel.

The optical system as described in Example 2 was used to form line structures in select regions of hydrated balafilcon A (PureVision®) silicone hydrogel materials. Experiments were conducted with and without the photosensitizer, fluorescein..

As indicated in Figures 11A and 11B, the incorporation of fluorescein into a balafilcon A silicone hydrogel provided a red shift in the transmission spectrum of at least 150 nm. The balafilcon A silicone hydrogel with fluorescein has a relatively

significant absorption profile at 500 nm, Figure 12B whereas a silicone hydrogel without photosensitizer is essentially transparent at these wavelengths, Figure 12A.

Figure 12A is phase contrast photograph of a balafilcon A silicone hydrogel that was micromachined at a depth of about 200 μm from the top irradiated surface. The irradiation process was conducted at 60 mW, and a scan rate of 0.5 μm/s. As indicated in Figure 12A, the refractive structures micromachined in the balafilcon A silicone hydrogel without photosensitizer provide little, if any, change in refractive index, $\Delta RI << 0.005$ (visible detection limit of the structures). In fact, it is very difficult to see the refractive structures in the material even with phase contrast enhancement. In contrast, as indicated in Figure 12B, the refractive structures micromachined in the balafilcon A silicone hydrogel with 0.17 wt.% fluorescein at the identical power and at a scan rate of 5.0 μm/s (a ten-fold increase over the undoped balafilcon A) provide a very significant change in refractive index, ΔRI of about 0.02 to 0.03. The refractive structures are clearly visible with phase contrast enhancement. Moreover, even with a relatively low laser power, i.e., 60 mW, one can still generate refractive structures with a ΔRI of about 0.01 with a scan rate of 1mm/s.

A plot showing the change in refractive index vs. scan rate in balafilcon A materials; undoped or doped with fluorescein or coumarin-1. The plot demonstrates the significant enhancement of the photo-adjusting affect in the hydrogel material doped with a photosensitzer. The doping of the material permits one to increase the scan rate of the laser through the material, i.e., form refractive structures in the material, by nearly 100-fold to achieve a comparable modification of the refractive index in the material.

In Examples 2 and 4, the refractive structures (line gratings) were investigated by focusing an unpolarized He-Ne laser beam with a wavelength of 632.8 nm on these gratings and monitoring the diffraction pattern. The diffraction angles showed good agreement with the diffraction equation

$$m\lambda = d\sin\theta \qquad (1)$$

where m is the diffraction order, λ is the wavelength of the incident laser beam which here is 632.8 nm, and d is the grating period.

The diffraction efficiency of the grating can be measured, and since the efficiency is a function of the refractive index change, it may be used to calculate the

refractive index change in the laser irradiation region. Consider the grating as a phase grating, its transmittance function could be written as

$$t(x_0, y_0) = (e^{i\phi_2} - e^{i\phi_1}) rect\left(\frac{x_0}{a}\right) * \frac{1}{d} comb\left(\frac{x_0}{d}\right) + e^{i\phi_1} \qquad (2)$$

where a is the grating line width, d is the groove spacing, ϕ_2 and ϕ_1 are the phase delays through the lines and ambient region respectively, $\phi_2 = 2\pi \times \frac{(n+\Delta n)\times b}{\lambda}$ and $\phi_1 = 2\pi \times \frac{n \times b}{\lambda}$, b is the thickness of the grating line, n is the average refractive index of the material, Δn is the average refractive index change in the grating lines, and λ is the incident light wavelength of the measurement (632.8nm). Here, the grating line width is 1 μm and the thickness is 3 μm. The index change within the laser effect region can be approximated to be uniform. The convolution theorem can be used to calculate the spectrum of the grating such as

$$T(f_x, f_y) = F\{t(x_0, y_0)\} = (e^{i\phi_2} - e^{i\phi_1}) a \sin c(af_x) comb(df_x)\delta(f_y) + e^{i\phi_1}\delta(f_x, f_y) \quad (3)$$

Then, the intensity distribution of the grating diffraction pattern is:

$$I(x, y) = \left(\frac{1}{\lambda z}\right)^2 \times \left[\left(e^{i\phi_2} - e^{i\phi_1}\right)\frac{a}{d}\sum_{n=-\infty}^{\infty} \sin c\left(\frac{an}{d}\right)\delta\left(\frac{x}{\lambda z} - \frac{n}{d}, \frac{y}{\lambda z}\right) + e^{i\phi_1}\delta\left(\frac{x}{\lambda z}, \frac{y}{\lambda z}\right)\right]^2 \qquad (4)$$

From this formula, the intensity of the 0th (I0), 1st (I1), and 2nd (I2) order diffraction light is

$$I_0 = \left(\frac{1}{\lambda z}\right)^2 \times \left[\left(e^{i2\pi \times \frac{(n+\Delta n)\times b}{\lambda}} - e^{i2\pi \times \frac{n\times b}{\lambda}}\right)\frac{a}{d} + e^{i2\pi \times \frac{n\times b}{\lambda}}\right]^2 \qquad (5)$$

$$I_1 = \left(\frac{1}{\lambda z}\right)^2 \times \left[\left(e^{i2\pi \times \frac{(n+\Delta n)\times b}{\lambda}} - e^{i2\pi \times \frac{n\times b}{\lambda}}\right)\frac{a}{d} \sin c\left(\frac{a}{d}\right)\right]^2 \qquad (6)$$

and

$$I_2 = \left(\frac{1}{\lambda z}\right)^2 \times \left[\left(e^{i2\pi \times \frac{(n+\Delta n)\times b}{\lambda}} - e^{i2\pi \times \frac{n\times b}{\lambda}}\right)\frac{a}{d} \sin c\left(\frac{2a}{d}\right)\right]^2 \qquad (7)$$

By comparing the light intensities of 1st, 2nd and 0th diffraction orders, the refractive index change within the grating lines can be determined. Figure 3 shows the ratio of intensity of the 1st and 2nd diffraction order to 0th order of the grating in PV2526-164 is 0.1374 and 0.0842 respectively, and the corresponding refractive index change

determined by the analysis is about 0.06. Using the same method, we determined the average refractive index change in RD1817 and HEMA B to be 0.05 ± 0.0005 and 0.03 ± 0.0005. Thus, it was demonstrated that the refractive index of a material can be modified by applying an ultrafast laser thereto.

Example 5.

A femtosecond laser oscillator with a Kerr-lens mode-locked Ti:Sapphire laser (MaiTai HP from Newport), generating pulses of 100fs pulsewidth and 80 MHz repetition rate at a tunable wavelength range from 690nm to1040 nm was used in the following Examples. In the experiments, the average laser power at the focus of the objective was attenuated and adjusted by a variable attenuator, and was set below 160 mW (2 *nJ* pulse energy) to avoid gross optical damage in the hydrogel polymers. Three Newport VP-25XA linear servo stages with 100 nm resolution formed a 3D smooth scanning platform which was controlled and programmed by a computer. The focusing objective was a 60X 0.70NA Olympus LUCPlanFLN long-working-distance objective which could precisely correct the spherical aberration and create nearly diffraction-limited laser focal spot at different depths below the material surface.

During the laser pulse irradiation sequence, the optical, hydrogel polymeric materials were maintained within an aqueous environment in a sandwich structure between two coverslips, and mounted horizontally on the scanning platform. The femtosecond laser pulses were focused vertically inside the hydrogel samples through the focusing objective. Different horizontal scanning speeds from 0.4μm/s to 4mm/s were used with different polymeric hydrogels and different average laser power. A CCD camera was used to monitor the irradiation process and detect plasma illumination, which indicated the onset of laser-induced material breakdown. After laser irradiation, the materials were removed and observed under a calibrated Olympus BX51 microscope with different modes. The change in refractive index of the irradiated regions were measured either by grating experiments as described in L. Ding et al., in *"Large refractive index change in silicone-based and non-silicone-based hydrogel polymers induced by femtosecond laser micro-machining,"* Opt. Express 2006, 14, 11901-11909, or by a calibrated differential interference contrast (DIC) mode microscope.

Example 5A to 5D.

Optical, hydrogel polymeric materials comprising hydroxyethyl methacrylate (HEMA), methylmethacrylate (MMA), ethylene glycol dimethacrylate (EGDMA) and variable concentrations of fluorescein-methacrylate (Fluo-MA), were prepared and are summarized in Table 1. A master monomer batch containing HEMA (83.7 wt.%), MMA (13.7 wt.%), EGDMA (0.51 wt.%) and AIBN (0.1 wt.%) initiator was prepared. An appropriate amount of Fluor-MA was added to separate monomer preparations to provide monomer mixture with the stated wt.% of Fluor-MA listed in Table 1. The monomer mixtures were polymerized according to well known methods in the art and cured in the form of 700μm-thick flat films.

The HEMA-based hydrogel polymers have a water content of about 28% by weight and an average refractive index of 1.44. An Ocean Optics HR4000 spectrometer was usually used to measure their transmission spectra.

Table 1.

Ex. No.	5A	5B	5C	5D	5E
Fluor-MA	-	0.0625	0.125	0.25	0.5

Figure 14 shows the transmission spectra of the non-photosensitized hydrogel material as well as the near identical hydrogel materials doped with different concentrations of Fluor-MA. As shown, the absorption peaks centered at about 350nm to about 450nm increased with an increase in the Fluor-MA concentration. Each of the Fluor-MA doped hydrogel materials remained transparent in the near infrared region though some scattering loss was observed at higher doping concentrations.

Each of the HEMA-based hydrogel materials were micromachined (irradiated) with femtosecond pulse sequence at 800nm and 120mW average power. Horizontal periodic gratings were typically written ~100-150 μm beneath the top surface of the materials at different scanning speeds. The changes in refractive index with different scanning speeds were measured for each material and are shown in FIG. 15. The degree of change in refractive index decreased as the scanning speed increased. For example, the largest refractive index change in the non-doped material was about 0.03±0.005 at a scan speed of 3μm/s. Carbon damage spots were observed in the non-doped material if the scanning speed was less than 2μm/s. Also, the degree of change in refractive index decreased very quickly as the scanning speed increased. At a scanning speed greater

than 10μm/s, the changes in refractive index were too small to be measured in our experiments (<0.005).

In contrast, with the doped hydrogel materials, we needed to significantly increase the scanning speed to avoid optical damage (carbonization) of the materials, which we believe are induced by accumulated heat. For Example 5B with 0.0625% Fluo-MA, a scanning speed of at least 40μm/s was required to avoid carbonized damage to the material. For Example 5E with 0.5% Fluo-MA one would observe small spot evidence of damage within the material even at a scanning speed of 500μm/s. Also, trradiation of the Example 5E at a scanning speed of 600μm/s, we measured a change in the refractive index of 0.085±0.005.

In general, the degree of change in the refractive index decreased as the Fluor-MA doping concentration decreased with a constant scan speed. For example, with a scanning speed of 1mm/s, the measured change in refractive index for the 0.5% and 0.0625% Fluor-doped materials was 0.065±0.005 and 0.005±0.002, respectively. In fact, for the 0.5% Fluo-MA material, a change of refractive index of 0.025±0.005 was obtained at a scanning speed of 4mm/s. These results indicate that nonlinear absorption within the hydrogel polymers could be greatly increased if Fluo-MA is copolymerized into the polymer network.

Large changes in refractive index could be observed at scanning speeds that are 1000x faster than the non-doped material. If the Fluor-MA concentration in the hydrogel materials of Example 5 was too high, i.e., greater than 3 wt%, we began to see aggregates (scattering centers) form within the hydrogel polymer network. Accordingly, for the HEMA-based materials of Example 5, the Fluor-MA concentration is from about 0.05 wt.% to about 2 wt.%, or from 0.1 wt.% to about 1.5 wt.%. To summarize, we have shown that as the concentration of the photosensitizer monomer, Fluor-MA, in the polymeric hydrogels increased, we observed a corresponding increase in the degree of change in refractive index within the focal volume even at significantly greater scan rates (Figure 15).

Figures 16A and 16B summarizes our experimental investigations with Example 5A (non-doped) and Example 5E (0.5% Fluo-MA) using two different pulse energies: (a) 1.5 nJ (120 mW average power); and (b) 2 nJ (160 mW average power). For both hydrogel materials, the degree of change in refractive index decreased as the femtosecond laser was tuned to operate at a longer wavelength at a constant scan rate.

For Example 5A, the degree of change in refractive index was less than 0.01 for all laser wavelengths. An attempt to increase the pulse energy or decrease the scan rate resulted only in optical damage. For all wavelengths longer than 850nm, no change in refractive index was observed in Example 5A at either pulse energy even if the scan rate was greater than 100μm/s. Higher pulse energies and slower scan rates were also tested in this wavelength region, but only optical damage with no change in refractive index was observed. In contrast, significantly large changes in refractive index was measured in Example 5E. In addition, because of the nonlinear absorption enhancement provided by the photosensitized material, material damage was observed at the shorter wavelengths. For example, even with a scan rate of 2mm/s and a pulse energy of 1.5 nJ, some optical damage is observed at wavelengths less than 775nm.

The irradiation of Example 5E at longer wavelengths (greater than 800nm) did result in relatively large changes in refractive index within the focal volume of the material. Figure 16A shows that one could achieve a change in refractive index of 0.06 in the focal volume of the material with a scan rate of 0.5mm/s at a wavelength of 900nm. Also, by increasing the average laser pulse energy from 1.5 nJ to 2.0 nJ one could achieve even greater changes in refractive index, but some optical damage was observed. A comparison of the data and plots of Figure 16A and Figure 16B, indicates that an increase in pulse energy from 1.5nJ to 2nJ results in optical damage at a wavelength of 900 nm and the scan rate of 0.5mm/s. Also, if the scan rate is increased to 1mm/s, we observed very small changes in refractive index (on the order of about 0.005) was observed.

To further investigate the wavelength dependence with respect to changes in refractive index within the focal volume, Examples 5A to 5E were irradiated over a wavelength range from 700nm to 1000nm at variable scan rates and an average pulse energy of 1.5 nJ. For each hydrogel material, the degree of change in refractive index decreased with laser wavelength and increased with the Fluor-MA concentration. Figure 17 shows the data and plots of Example 5E at a scan rate of 1mm/s. The data of Figure 17 is very helpful because it suggests a window of operating parameters in which one can form the refractive structures in the hydrogel materials, and yet, remain a safe working distance from forming any significant optical damage (scattering features) in the materials. For Example 5D and 5E, irradiation at 850nm to 900nm provides a safe working distance from optical damage, and yet provides a significant appreciable change

in refractive index, i.e., from 0.01 to 0.04, respectively, at the given scan rate and average laser power – one can even see an appreciable change in refractive index at 950nm for Example 5E.

As already stated, we believe that the presence of water within the polymer matrix, as in the case of a hydrated hydrogel material, plays a critical part in forming the observed changes in refractive index within the focal volume. Accordingly, we investigated the effect of water concentration on the degree of change in refractive index in the hydrogel materials of Examples 5B to 5E as well as those of similar composition, but with reduced water content. A master monomer batch containing HEMA (68.6 wt.%), MMA (28.9 wt.%), EGDMA (0.51 wt.%) and AIBN (0.1 wt.%) initiator was prepared. An appropriate amount of Fluor-MA was added to separate monomer preparations to provide monomer mixture with the stated wt.% of Fluor-MA listed in Table 2. The monomer mixtures were polymerized according to well known methods in the art and cured in the form of 700μm-thick flat films. The hydrogel polymers of Example 6 have a 21% water content.

Likewise, the hydrogel materials of Example 7 were prepared from a master monomer batch containing HEMA (49.0 wt.%), MMA (48.4 wt.%), EGDMA (0.51 wt.%) and AIBN (0.1 wt.%) initiator was prepared. An appropriate amount of Fluor-MA was added to separate monomer preparations to provide monomer mixture with the stated wt.% of Fluor-MA listed in Table 2. The monomer mixtures were polymerized according to well known methods in the art and cured in the form of 700μm-thick flat films. The hydrogel polymers of Example 7 have a 12% water content.

Table 2.

Ex. No.	6A	6B	6C	6D
Fluor-MA	0.0625	0.125	0.25	0.5

Table 3.

Ex. No.	7A	7B	7C	7D
Fluor-MA	0.0625	0.125	0.25	0.5

As indicated, each set of materials of Examples 5 to 7 have varying concentrations of the photosensitizer, Fluo-MA. Figure 18 shows the resulting change in refractive index in these hydrogel materials at an irradiation wavelength of 800nm, 1.5nJ

average pulse energy and a scan rate of 1mm/s. Again, the data and plots provide very important information. As shown, the degree of change in refractive index decreased as the water concentration decreased in all the photosensitized hydrogel materials. We believe the localized water concentration of the hydrogel affects the thermodynamic properties such as specific heat, heat capacity, etc. as well as the material density of the materials. The largest change in refractive index is obtained in the hydrogels of Example 5, which have largest water content of about 28%. More importantly, the hydrogels with relatively larger water content provide the largest safe working distance to form the refractive structures without optical damage to the material.

We also investigated the wavelength dependence of the hydrogel materials of Example 5E, Example 6D and Example 7D, each with 0.5% Fluor-MA, but with the different water contents, see Figure 19. Interestingly, a relatively large change in refractive index (greater than 0.02) without any optical damage was observed only in Example 5E at an average pulse energy of 1.5 nJ. One must note, however that we also used a relatively fast scan rate of 1mm/s in this investigation. As indicated, if the laser wavelength was less than about 750nm, we observed only optical damage. If the laser pulses were operating at a wavelength greater than 800nm, no change in refractive index is observed and optical damage is observed in the hydrogel materials of Example 7 (12% water content). For the hydrogel materials of Example 6 (21% water content), a change in refractive index of 0.01 is observed without optical damage if the irradiation wavelength is about 875nm.

Collectively, our investigation suggests the optimal irradiation conditions for forming the described refractive structure in optical, polymeric materials.

The embodiments of the present invention for which an exclusive property or privilege is claimed are defined as follows:

1. A method for modifying the refractive index of an intraocular lens prior to the surgical insertion of the lens, the method comprising irradiating a solvated intraocular lens at predetermined regions with light from a laser, the light having a wavelength from 600 nm to 900 nm to form refractive structures characterized by a change in the refractive index within the irradiated regions of the lens with little or no scattering loss,

the intraocular lens comprising a polymeric, optical material that includes a photosensitizer.

2. The method of claim 1 wherein the polymeric, optical material is prepared from at least one monomer having a photofunctional group, the monomer having a two-photon cross-section of at least 10 GM.

3. The method of claims 1 or 2 wherein the polymeric, optical material is solution-doped with a photosensitizer having a two-photon cross-section of at least 10 GM.

4. The method of any one of claims 1 to 3 wherein the irradiation is conducted with a laser having a pulse width of 4 fs to 100 fs and a pulse energy from 0.05 nJ to 50 nJ.

5. The method of any one of claims 1 to 4 wherein the laser operates with an average laser power from 10 mW to 300 mW.

6. The method of any one of claims 1 to 5 wherein the laser is focused with a compensation scheme to compensate for the positive dispersion introduced by the focus objective.

7. The method of any one of claims 1 to 6 wherein the optical polymeric material is prepared from one or more (meth)acrylate monomers selected from the group consisting of 2-hydroxymethyl (meth)acrylate, 2-phenylethyl (meth)acrylate, methyl (meth)acrylate and 3-phenylpropyl (meth)acrylate.

8. The method of any one of claims 1 to 7 wherein the change is refractive index is a positive change from 0.01 to 0.06.

9. The method of any one of claims 1 to 8 wherein the irradiated region is defined by a three-dimensional refractive structure in the form of positive or negative lens element.

10. The method of claim 9 wherein the positive or negative lens element is disposed in a volume of the lens within 300 μm from the anterior surface of the intraocular lens.

11. An intraocular lens comprising an optical, polymeric material, wherein said optical, polymeric material includes a photosensitizer that enhances the photoefficiency when irradiated with light from a laser, the light having a wavelength from 600 nm to 900 nm to form refractive structures characterized by a change in refractive index.

12. The intraocular lens of claim 11, wherein the polymeric, optical material is prepared from at least one monomer having a photofunctional group, the monomer having a two-photon cross-section of at least 10 GM.

13. The intraocular lens of claim 11 or 12 wherein the change in refractive index is a positive change in refractive index from 0.01 to 0.06.

14. The intraocular lens of any one of claims 11 to 13 wherein the irradiated region is defined by a three-dimensional refractive structure in the form of a positive or negative lens element.

15. The intraocular lens of claim 14 wherein the positive or negative lens element is disposed in a volume of the lens within 300 μm from the anterior surface of the intraocular lens.

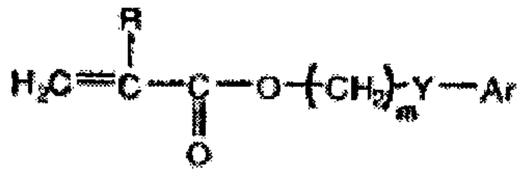
16. The intraocular lens of any one of claims 11 to 15, wherein the optical, polymeric material is an optical, polymeric silicone hydrogel, or an optical, polymeric non-silicone hydrogel.

17. The intraocular lens of any one of claims 11 to 16 wherein the optical polymeric material is prepared from one or more (meth)acrylate monomers selected from the group consisting of 2-hydroxymethyl (meth)acrylate, 2-phenylethyl (meth)acrylate, methyl (meth)acrylate and 3-phenylpropyl (meth)acrylate.

18. The intraocular lens of any one of claims 11 to 16 wherein the optical polymeric material is prepared with poly(2-hydroxyethyl methacrylate).

19. The intraocular lens of any one of claims 11 to 16 wherein the optical polymeric material is prepared with a cross-linked silicone elastomer.

20. The intraocular lens of any one of claims 11 to 16, wherein the optical, polymeric material is prepared from one or more aromatic (meth)acrylate monomers having the formula:



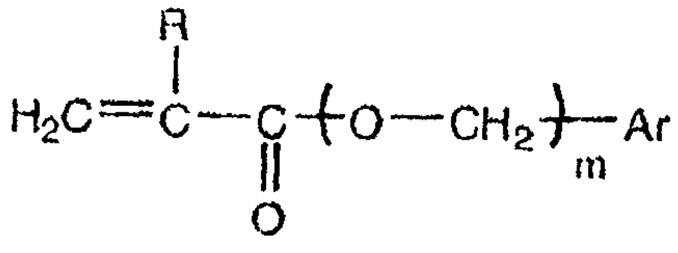
wherein:

R is H or CH_3;

m is an integer selected from 0 to 10;

Y is nothing, O, S, or NR, wherein R is H, CH_3, C_2-C_6alkyl, iso-OC_3H_7, phenyl or benzyl; Ar is any aromatic ring, preferably phenyl, which can be unsubstituted or substituted with H, CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, OCH_3, C_6H_{11}, Cl, Br, phenyl or benzyl.

21. The intraocular lens of any one of claims 11 to 16, wherein the optical, polymeric material is prepared from one or more aromatic (meth)arcrylate monomers having the formula:



wherein:

R is H or CH_3;

m is an integer selected from 0 to 6;

Ar is any aromatic ring, preferably phenyl, which can be unsubstituted or substituted with H, CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, OCH_3, OH, or C(O)OH.

22. The intraocular lens of any one of claims 11 to 16, wherein the optical, polymeric material is prepared as a copolymer from at least three monomeric components,

the first monomer component being present in the copolymer is an amount of at least 60% by weight, and its homopolymer will have a refractive index of at least 1.5;

the second monomeric component being present in the copolymer in an amount from 3% to 20%;

the first and second monomeric components together representing at least 70% by weight of the copolymer; and

optionally a fourth monomeric component derived from a hydrophilic monomeric component, the hydrophilic component being present in an amount from 2% to 30% by weight of the copolymer.

23. The intraocular lens of any one of claims 11 to 22, wherein the change in refractive index is variable within the irradiated region to provide an extended depth of field to the lens relative to a base lens without irradiated regions.

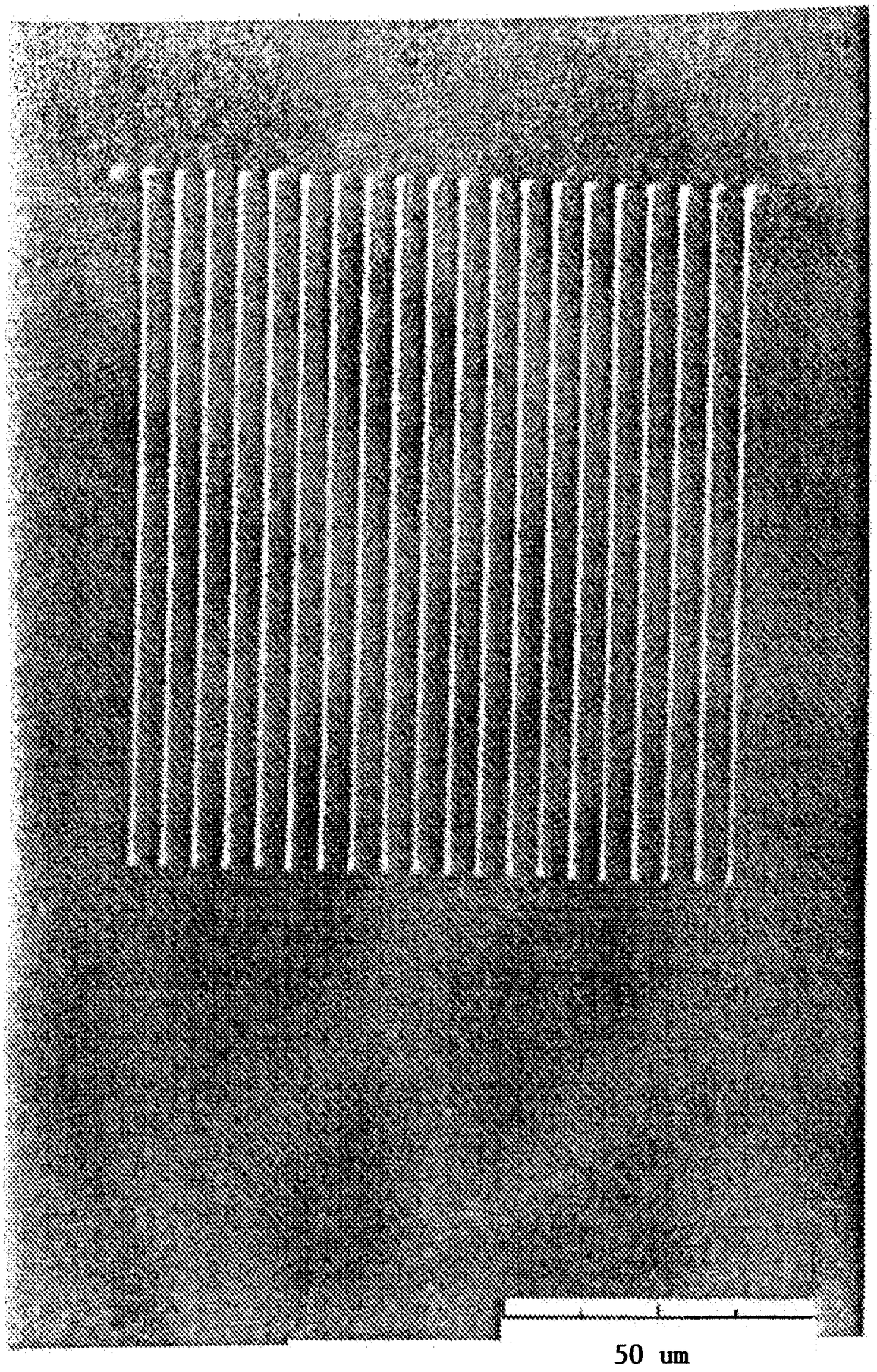


Figure 1A

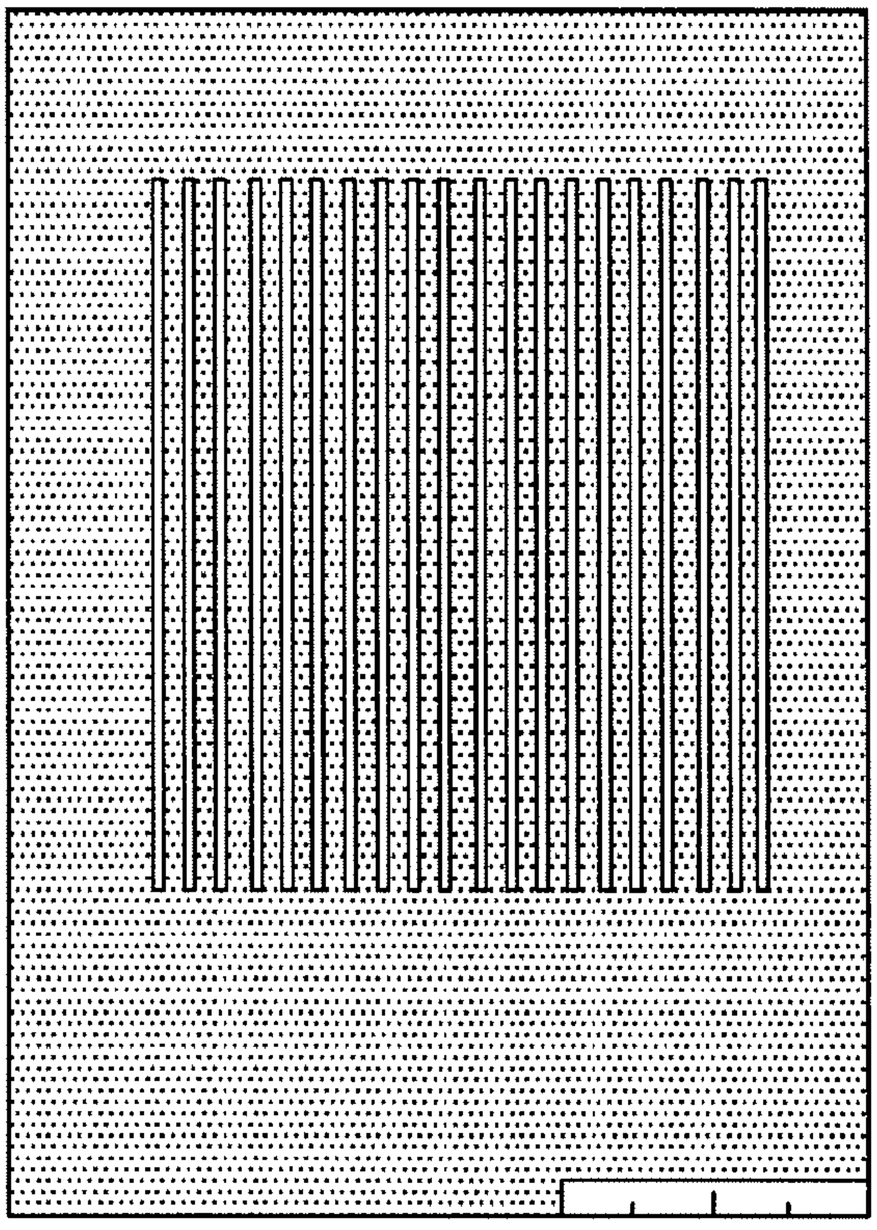


FIG. 1B

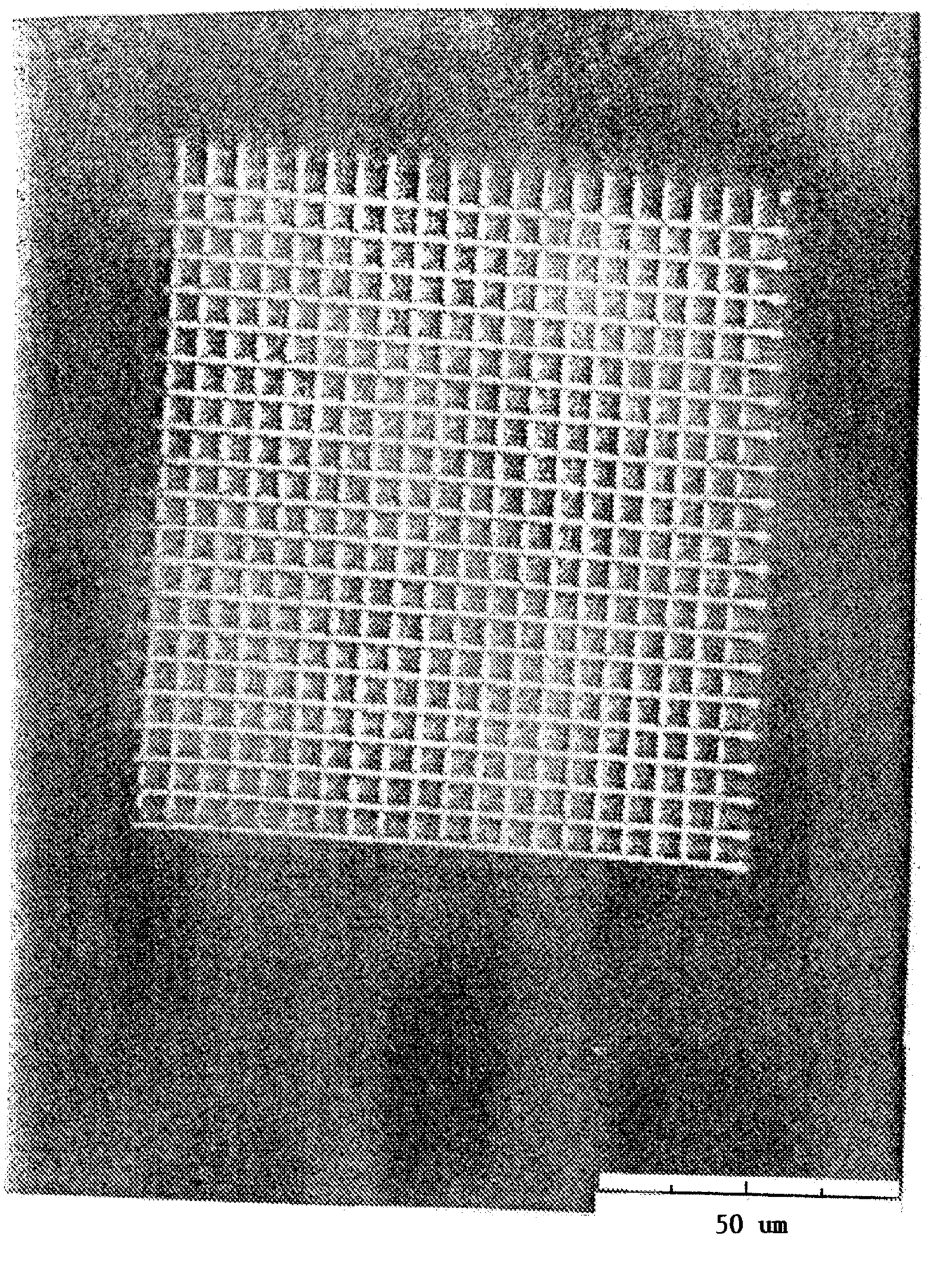


Figure 2A

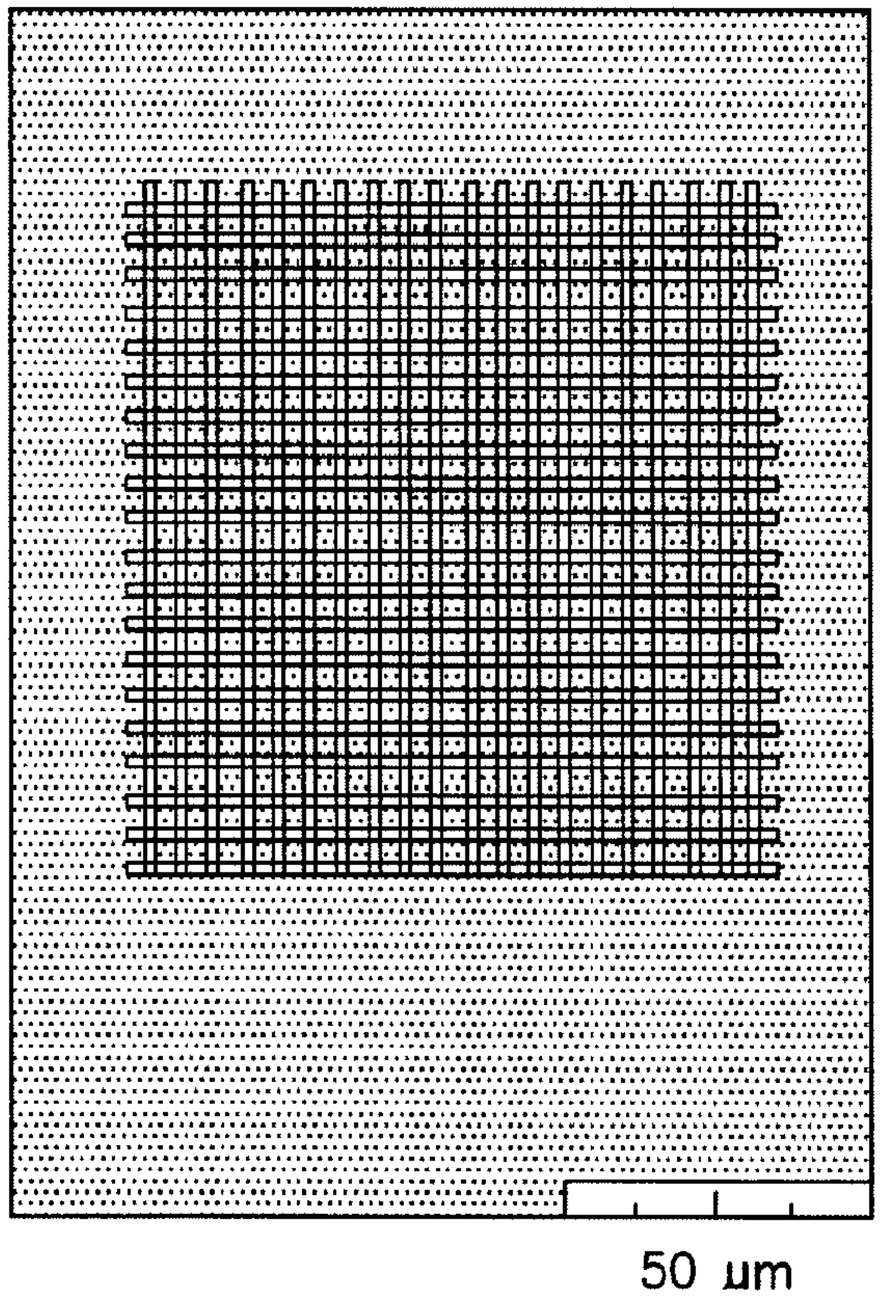


FIG. 2B

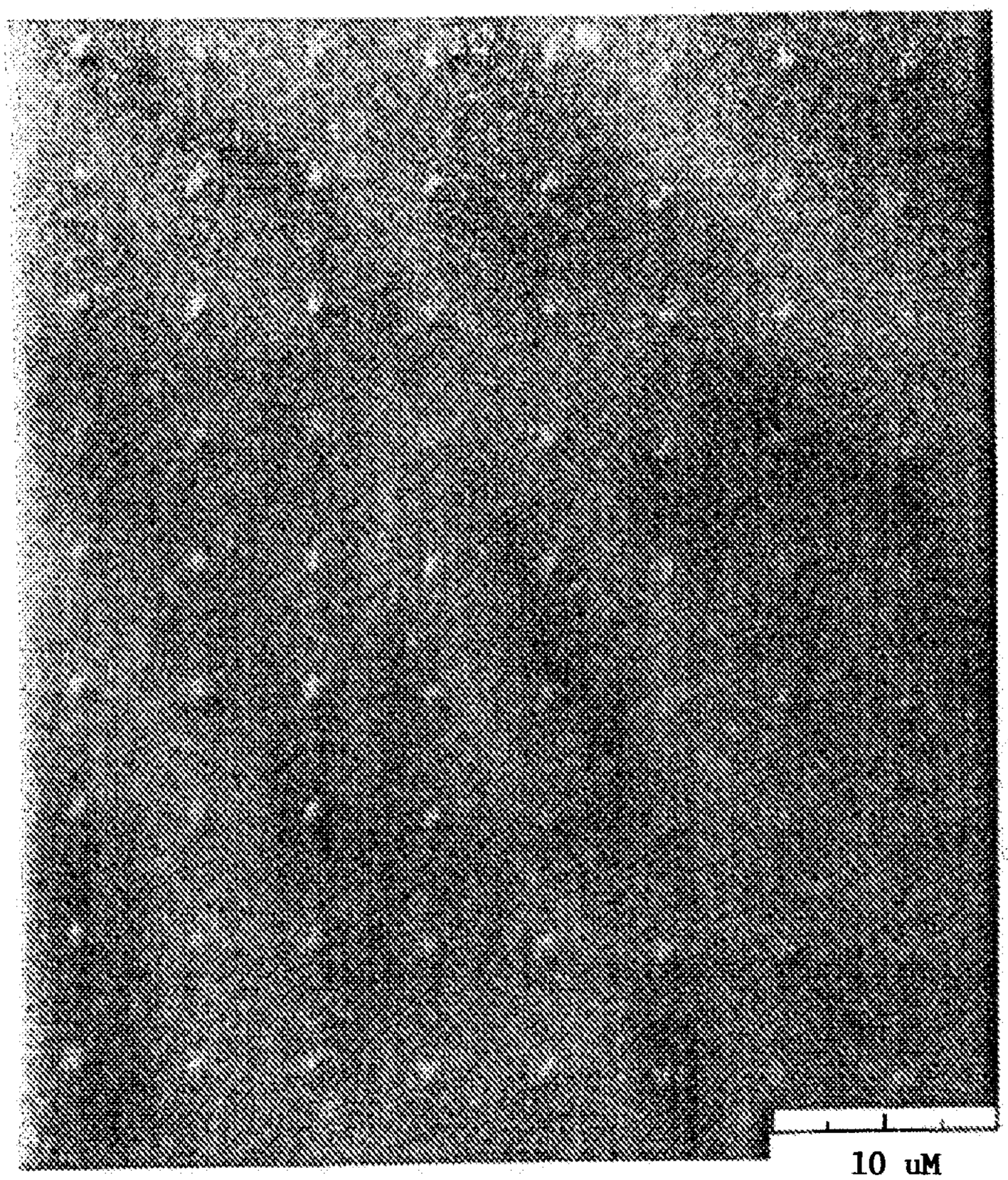


Figure 3A

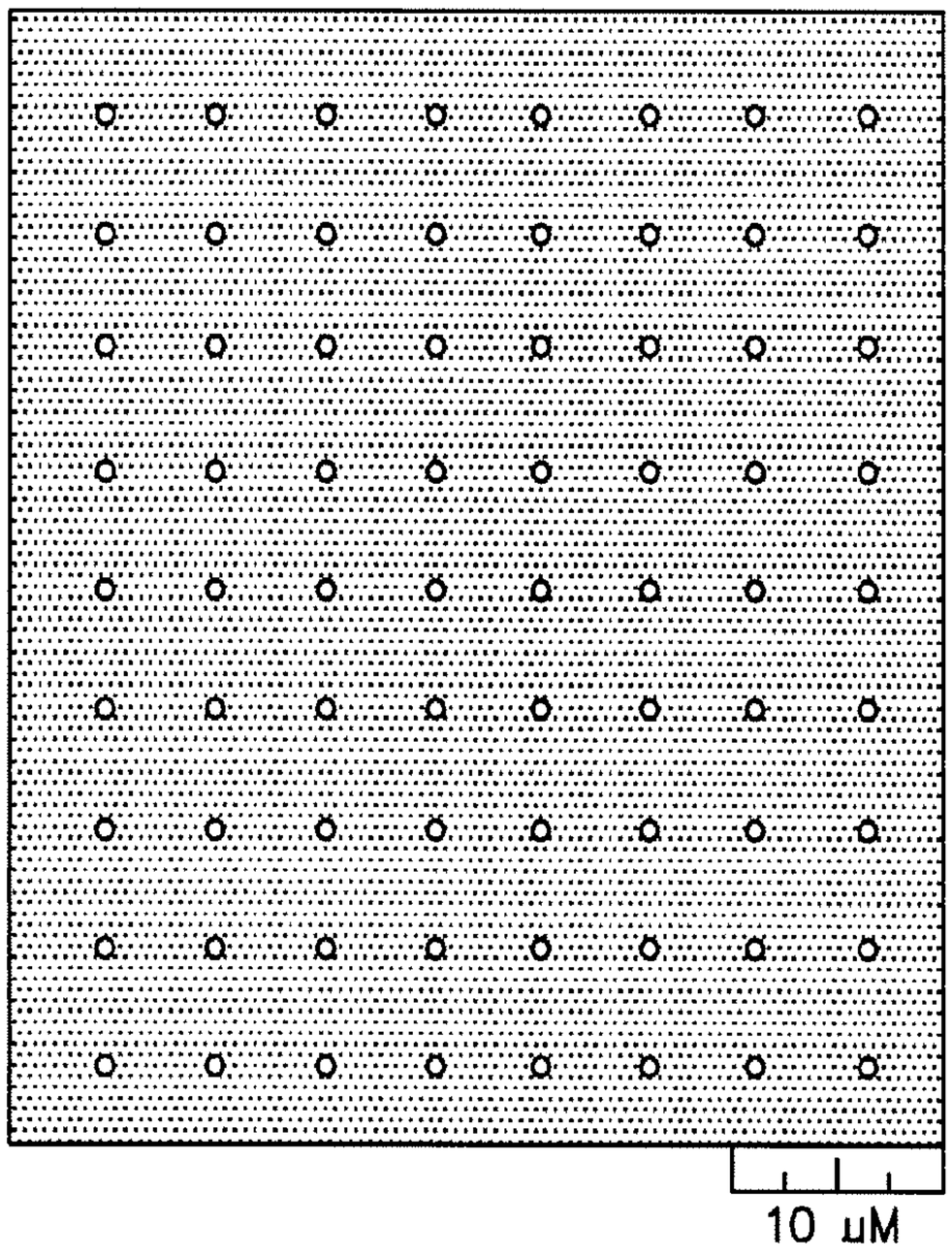


FIG. 3B

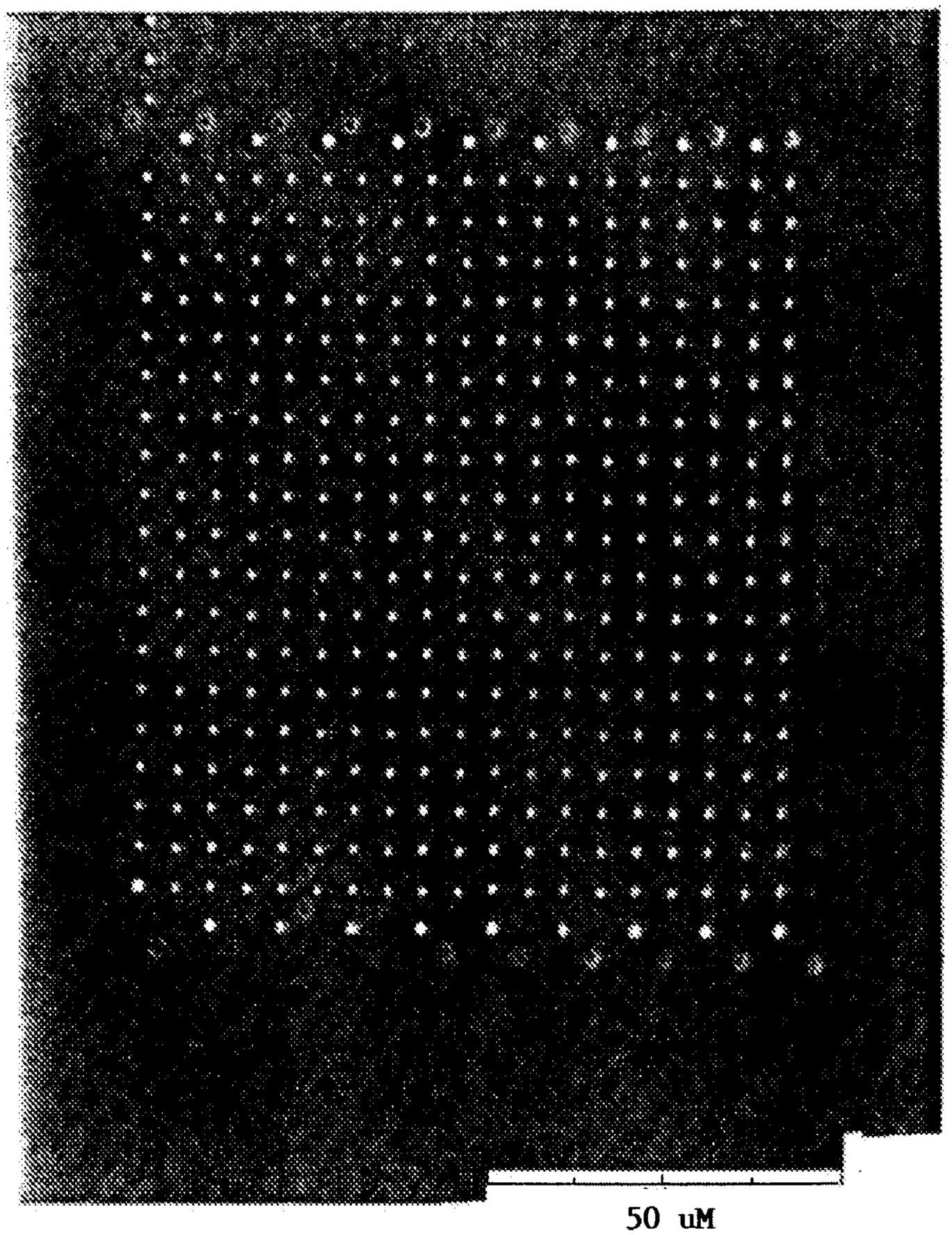


Figure 4A

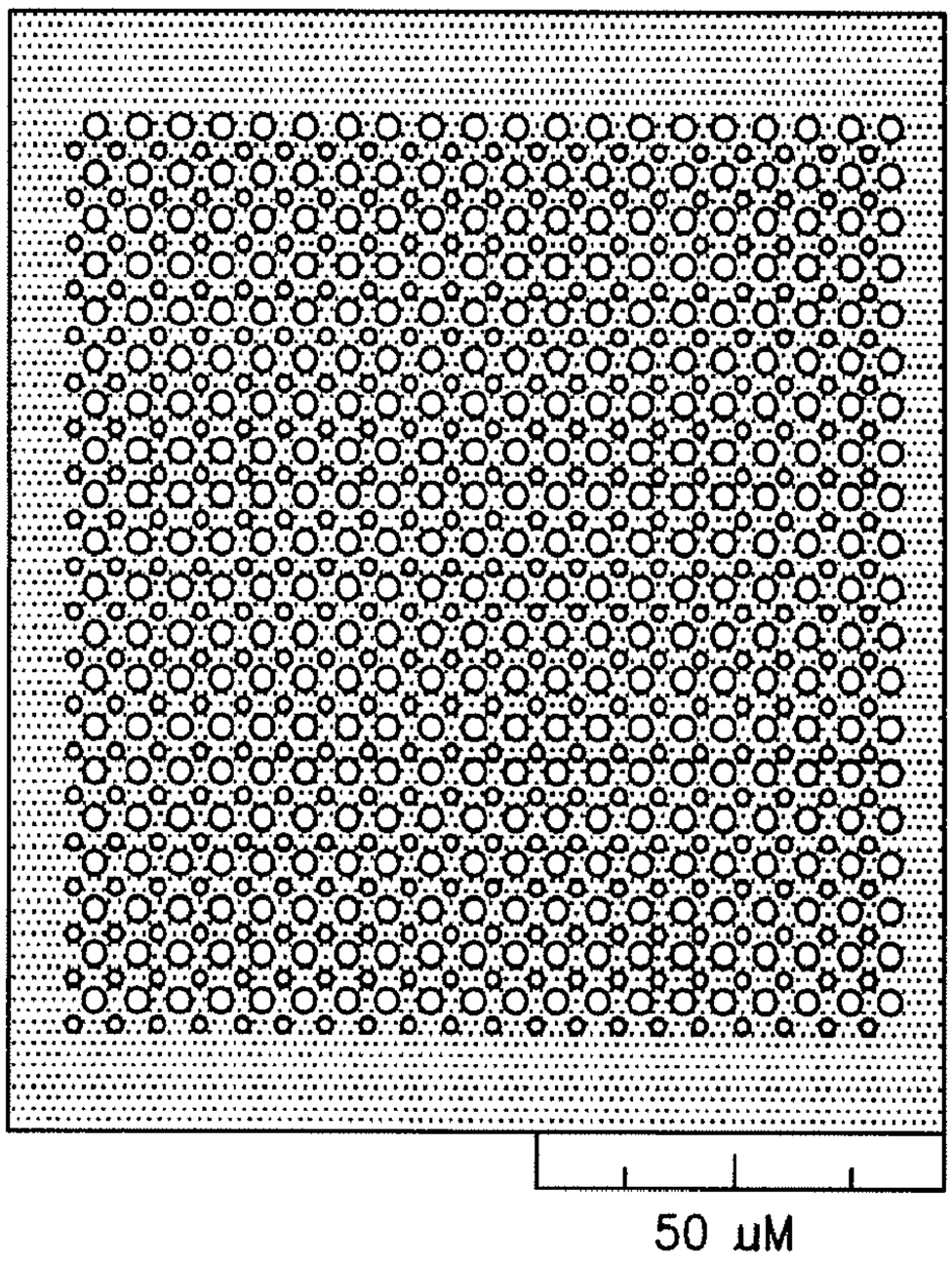


FIG. 4B

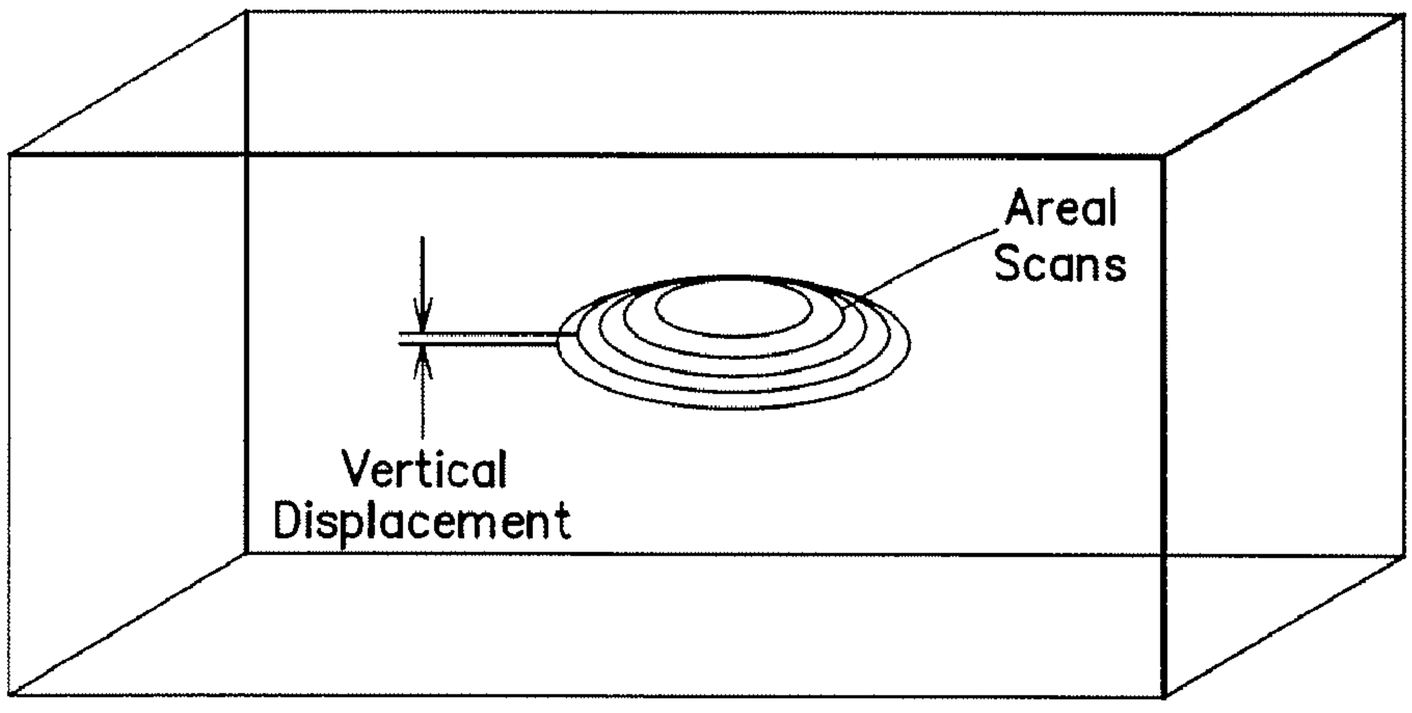

Areal
Scans
Vertical
Displacement

FIG. 5

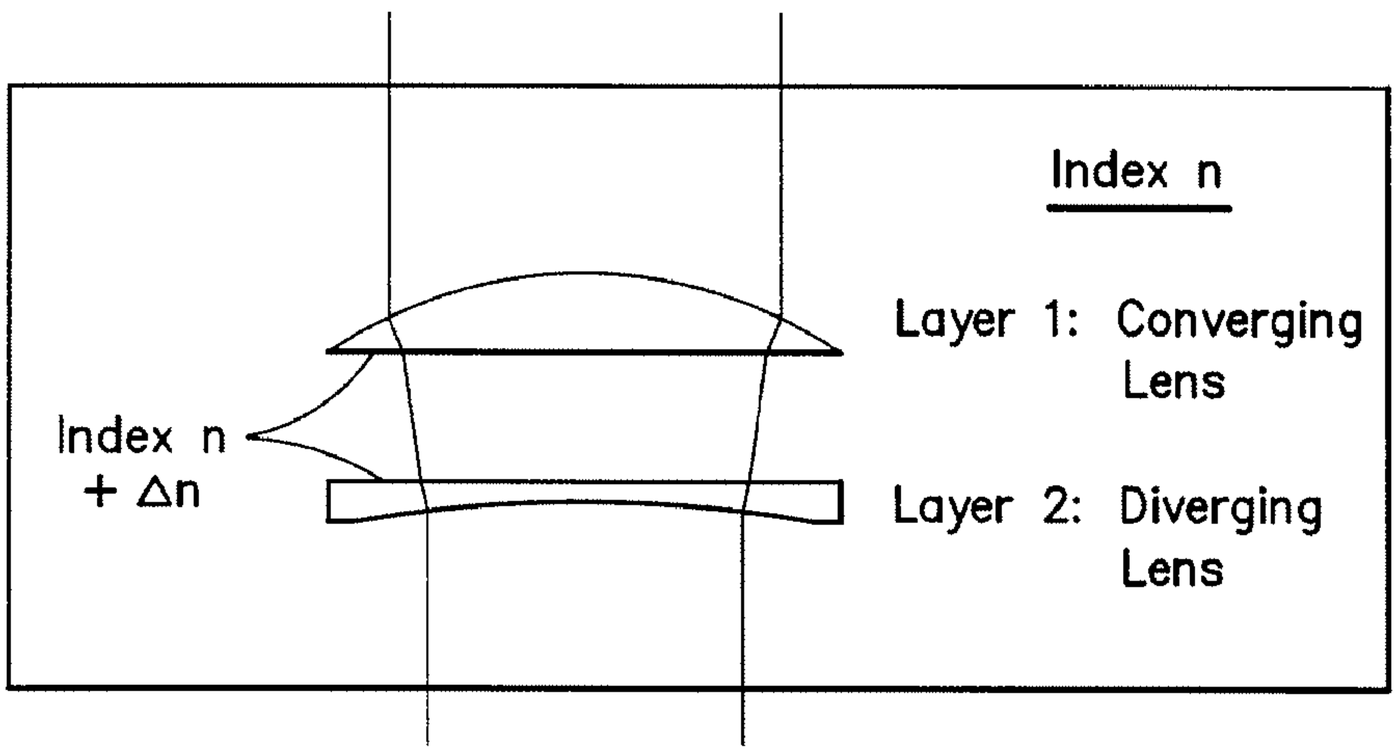

Index n
Layer 1: Converging
Lens
Index n
+ Δn
Layer 2: Diverging
Lens

FIG. 6

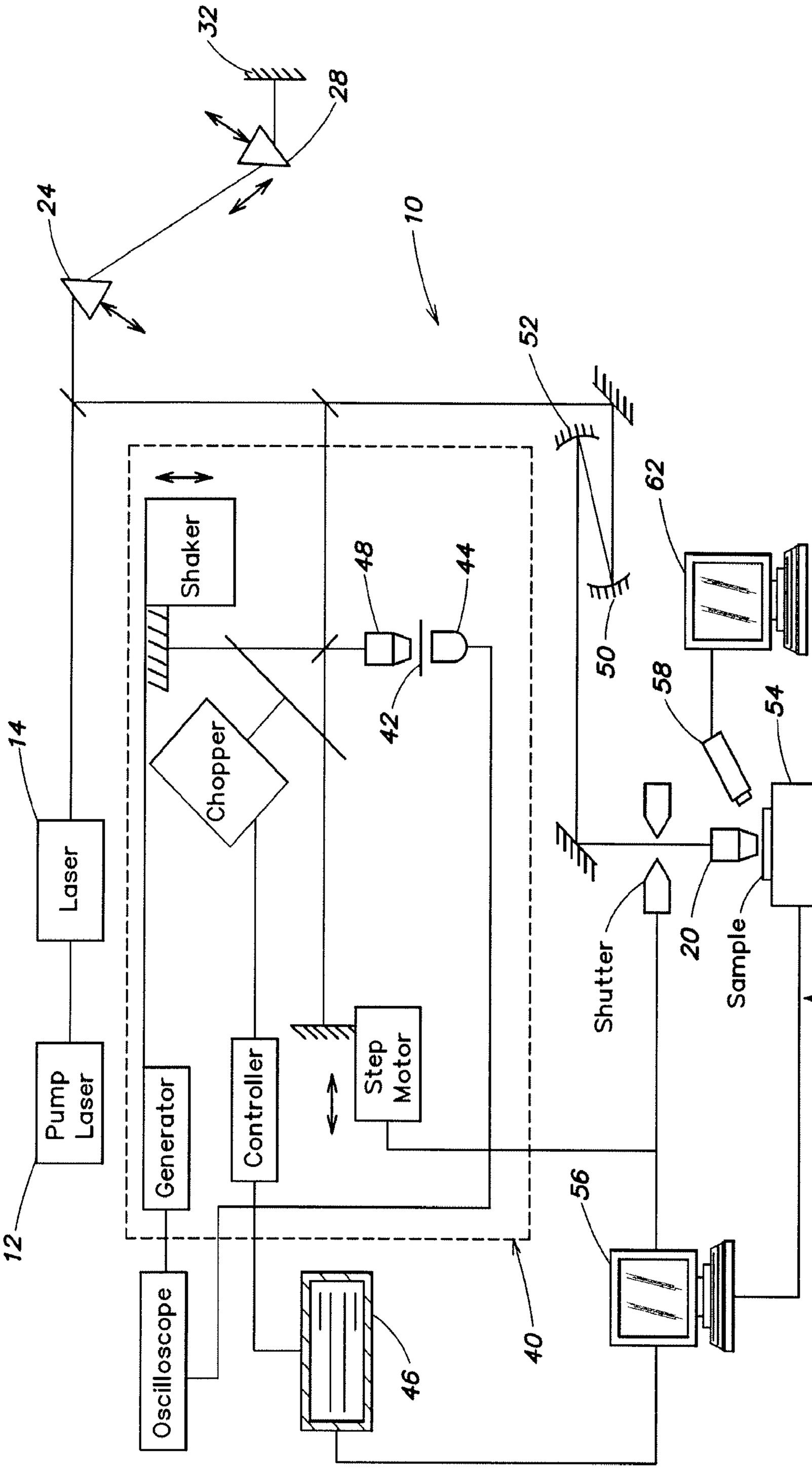

32
28
24
10
52
62
Shaker
48
44
Chopper
42
14
Laser
Pump Laser
12
Generator
Controller
Step Motor
50
58
54
Shutter
20
Sample
56
Oscilloscope
46
40

FIG. 7

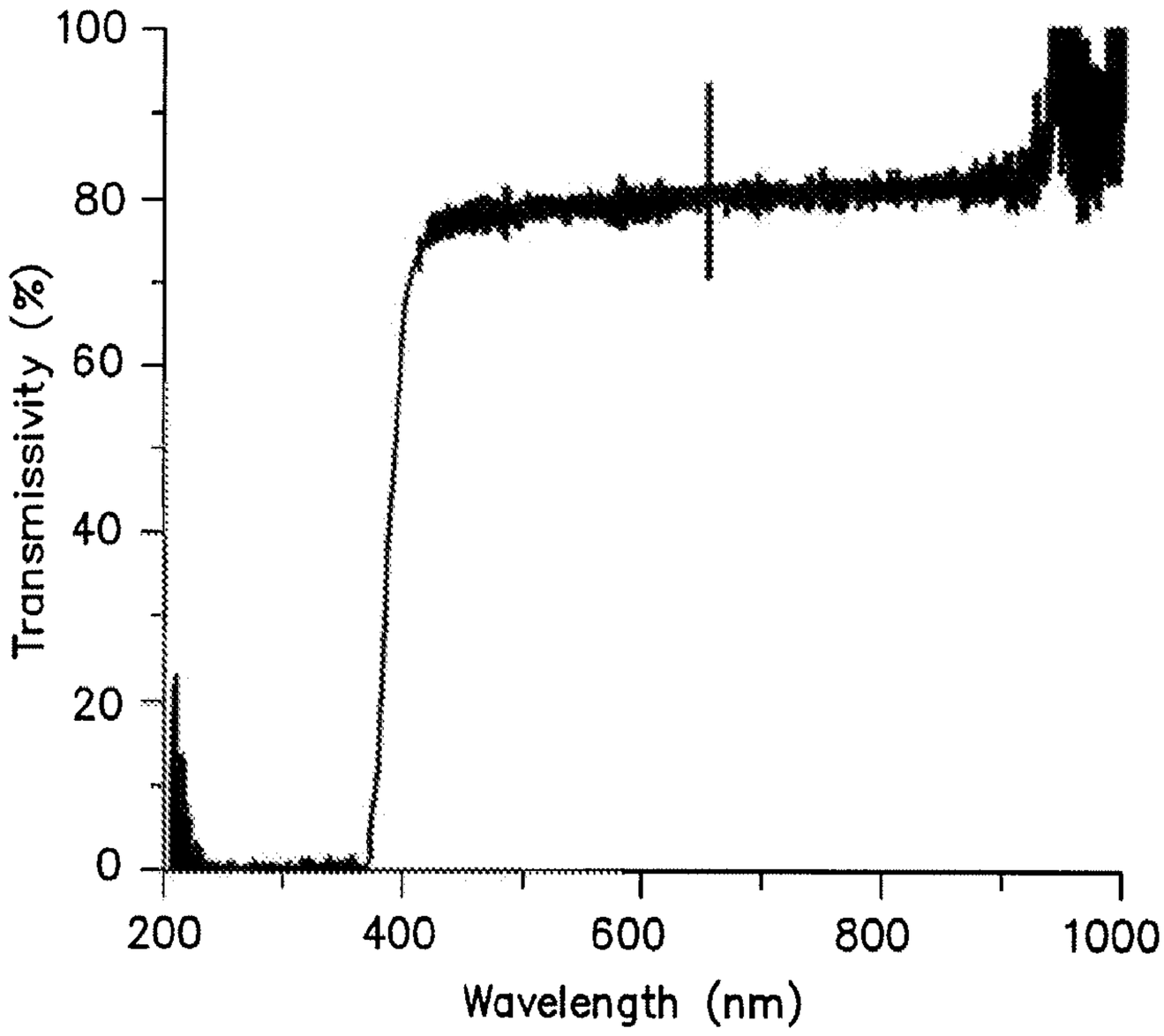

100
80
60
40
20
0
Transmissivity (%)
200
400
600
800
1000
Wavelength (nm)

FIG. 8A

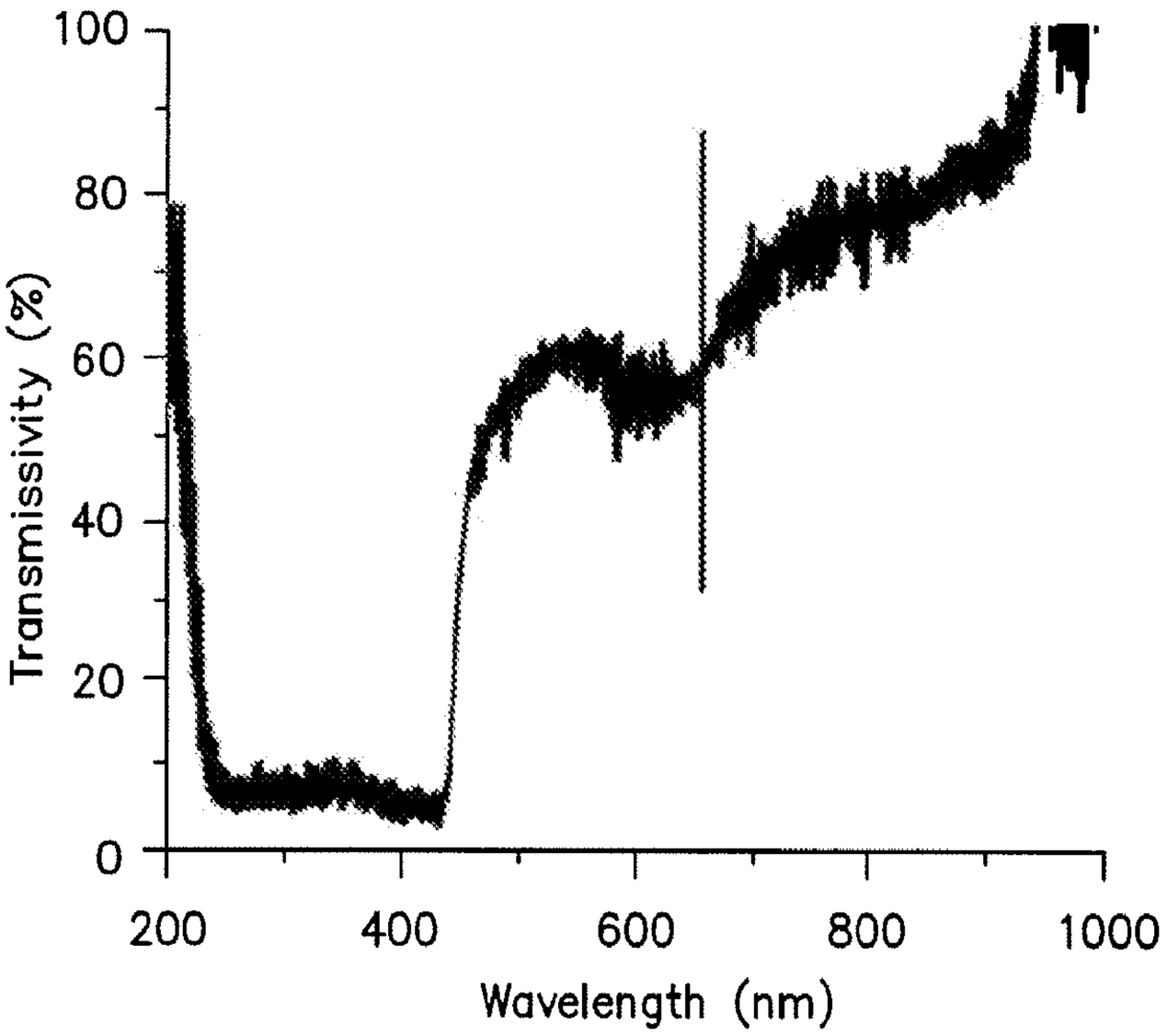

100
80
60
40
20
0
Transmissivity (%)
200
400
600
800
1000
Wavelength (nm)

FIG. 8B

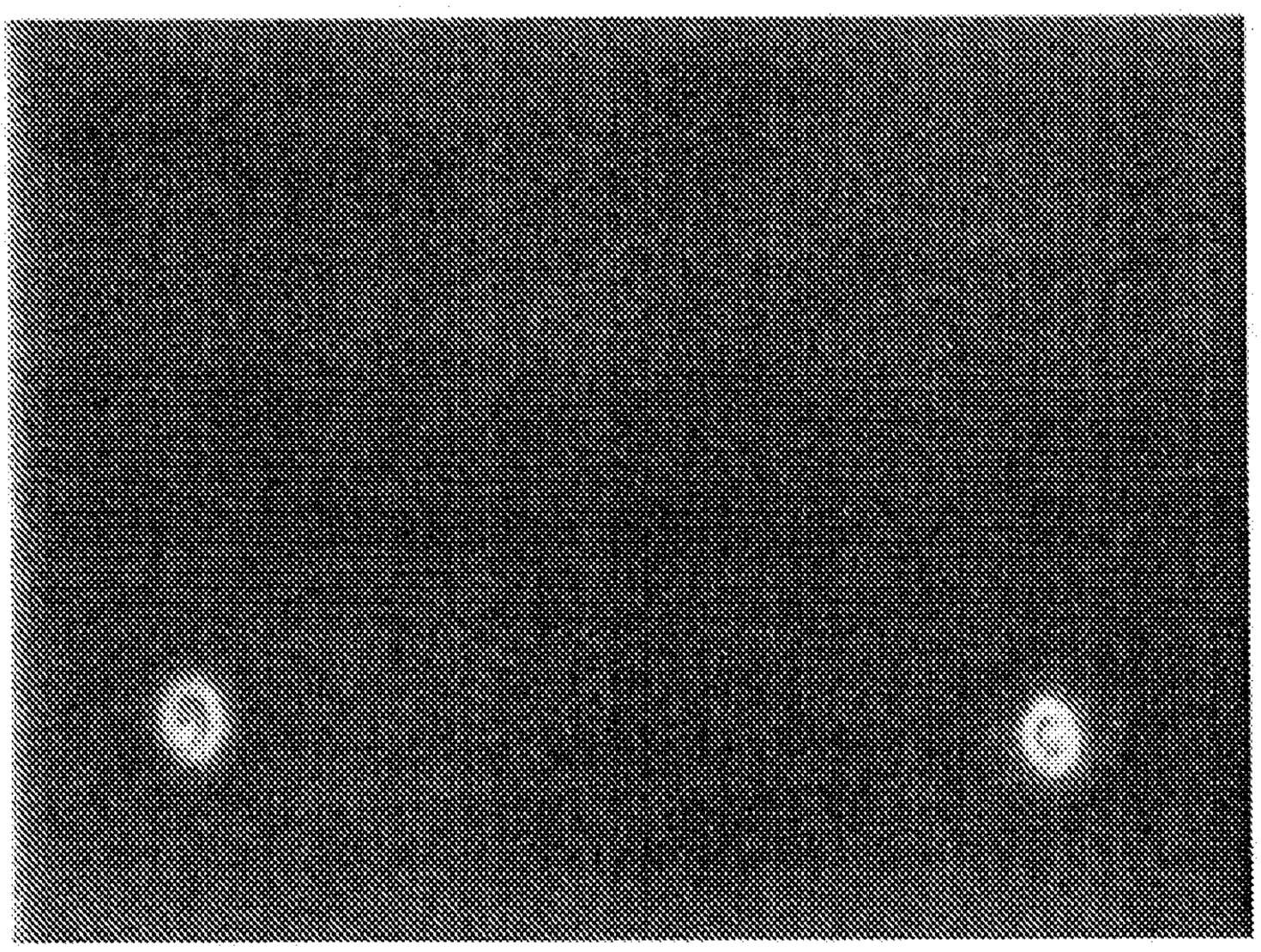


Figure 9A

Figure 9B

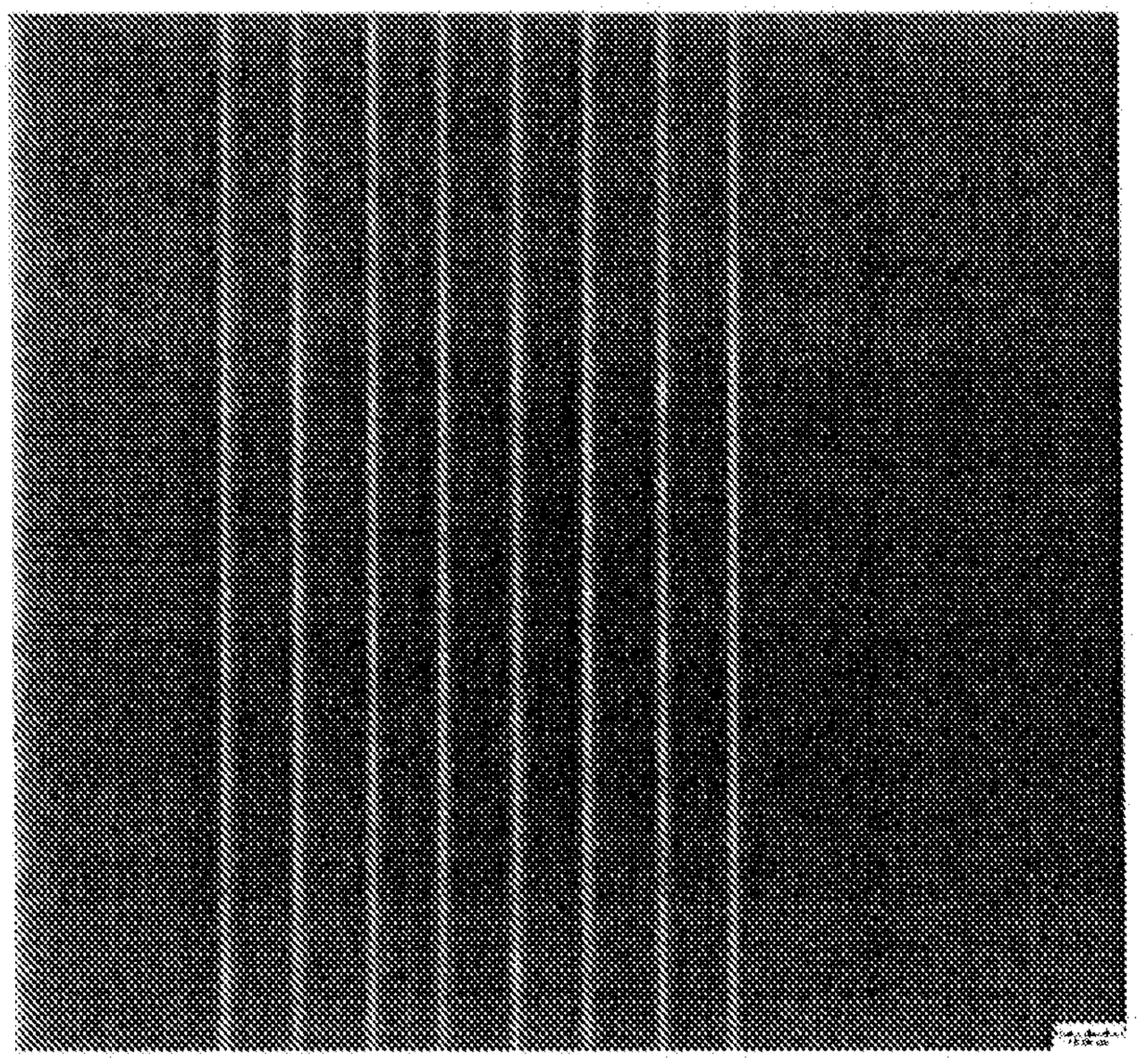


Figure 10A

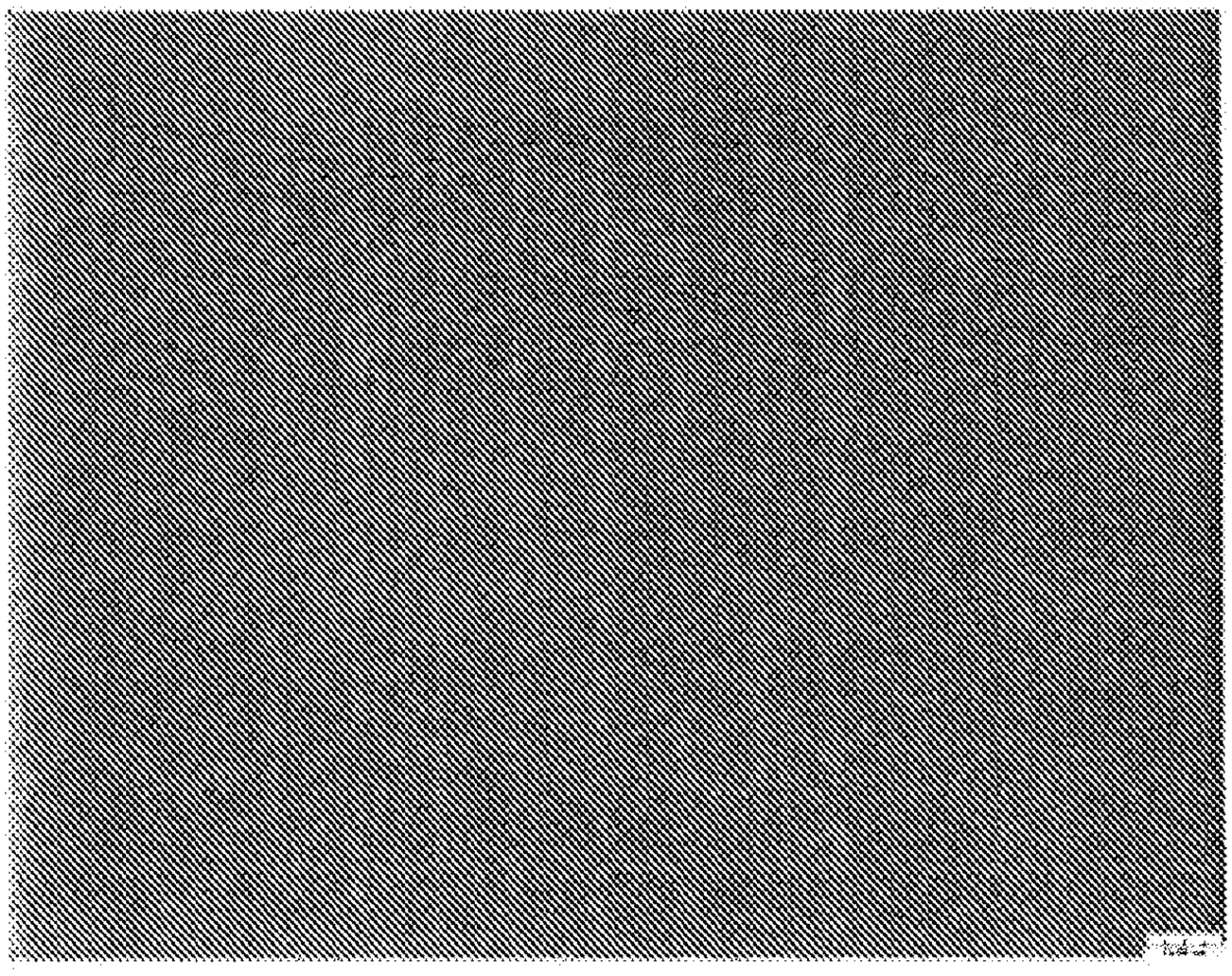


Figure 10B

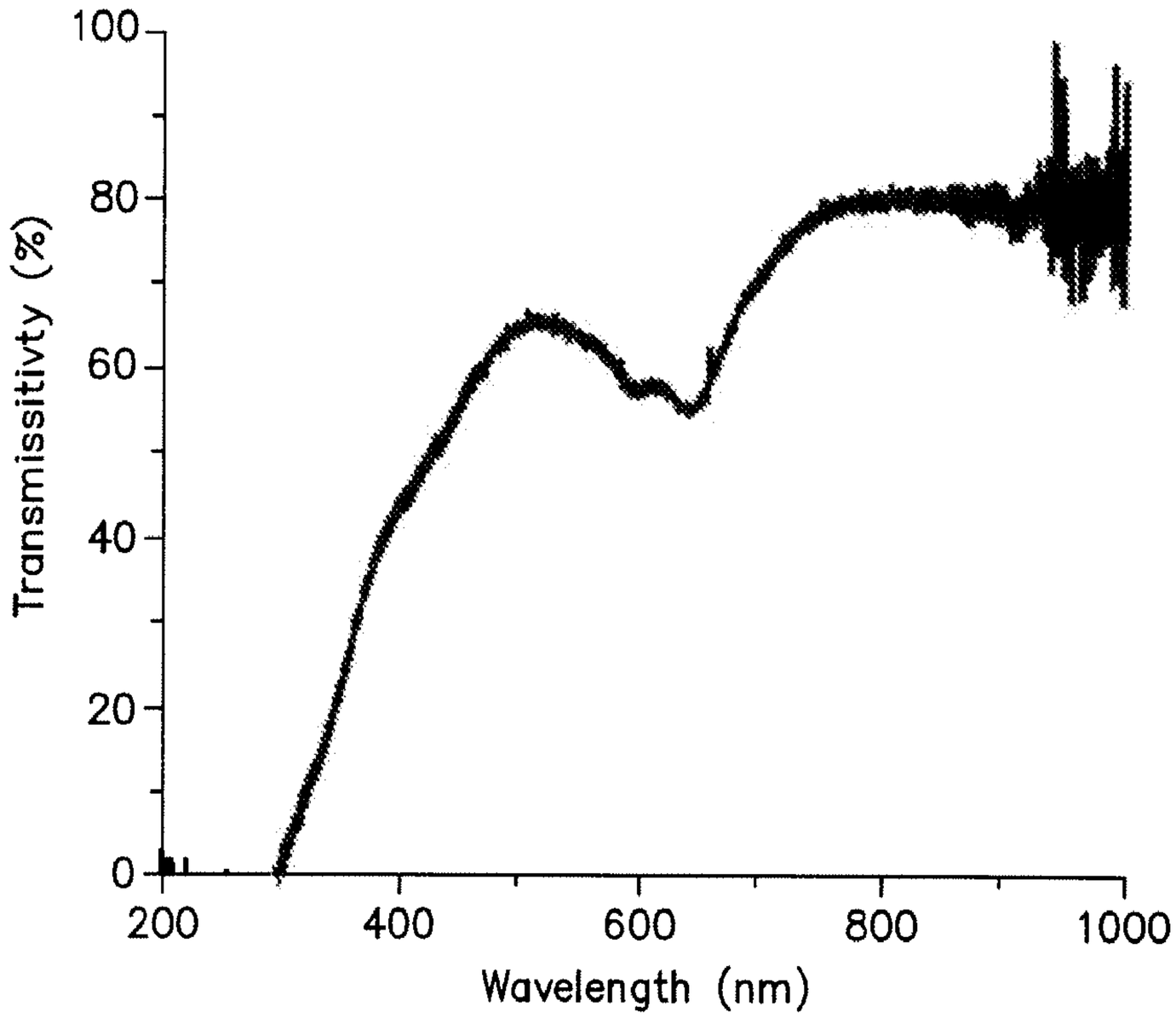


FIG. 11A

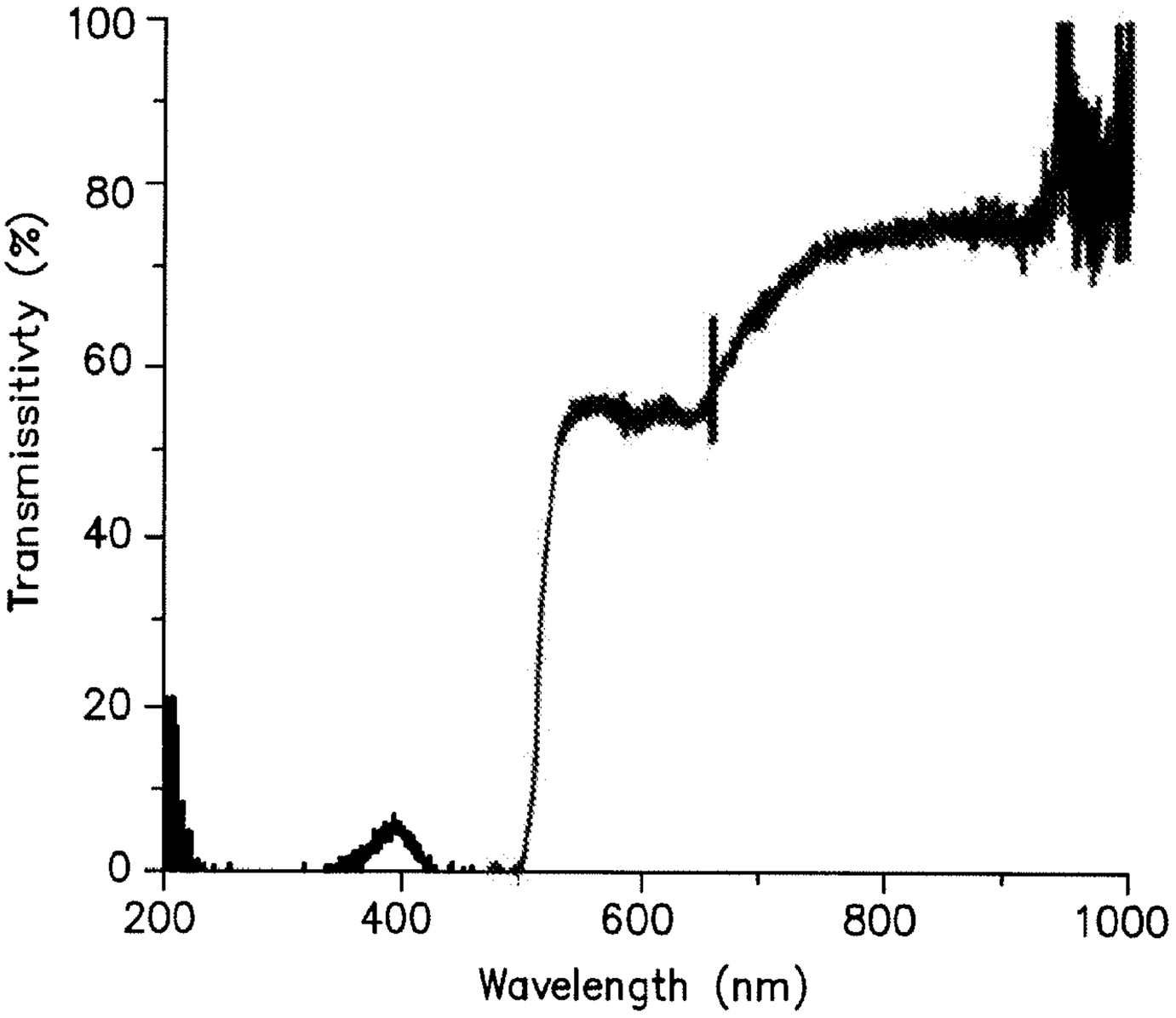


FIG. 11B

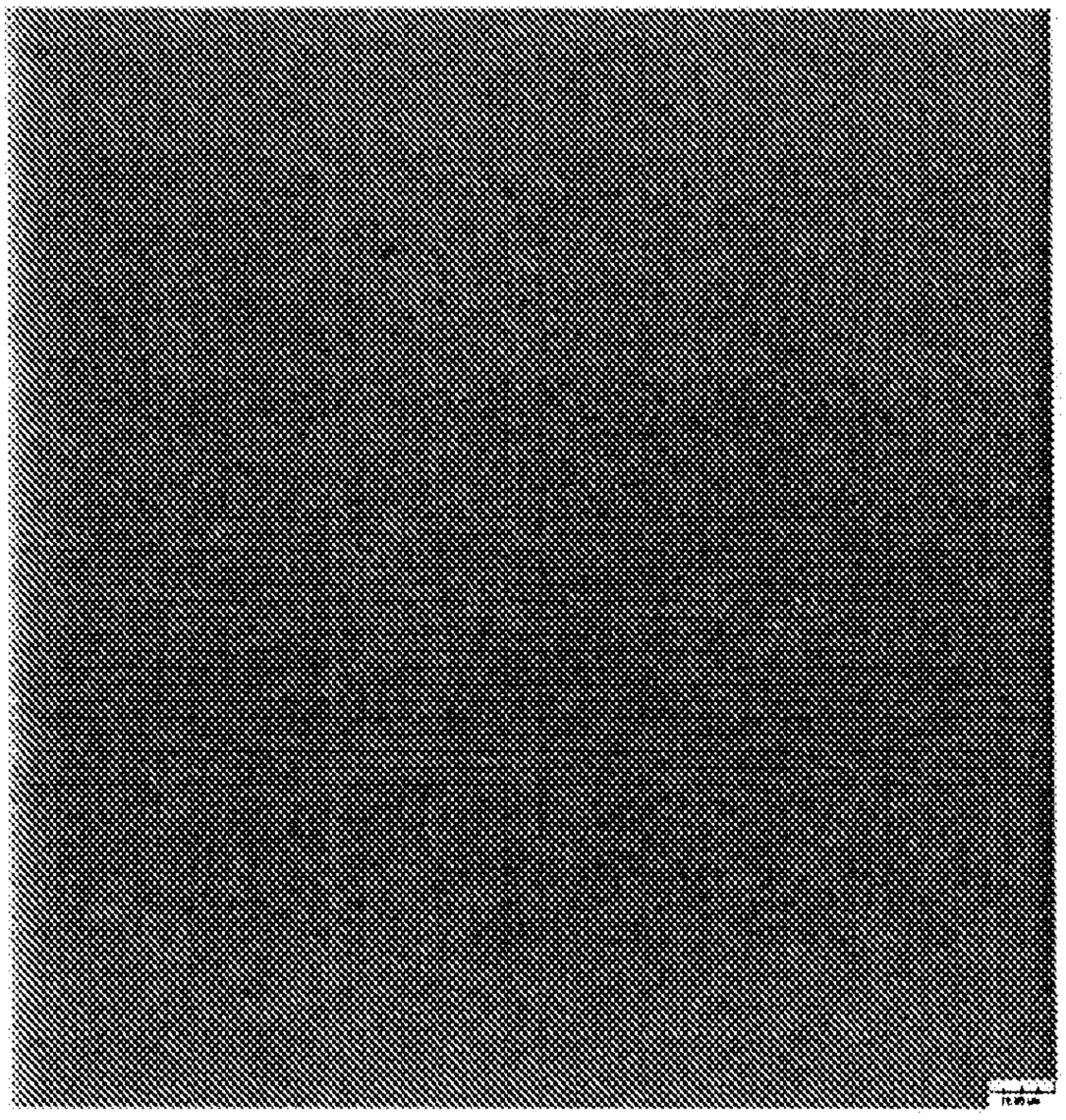


Figure 12A

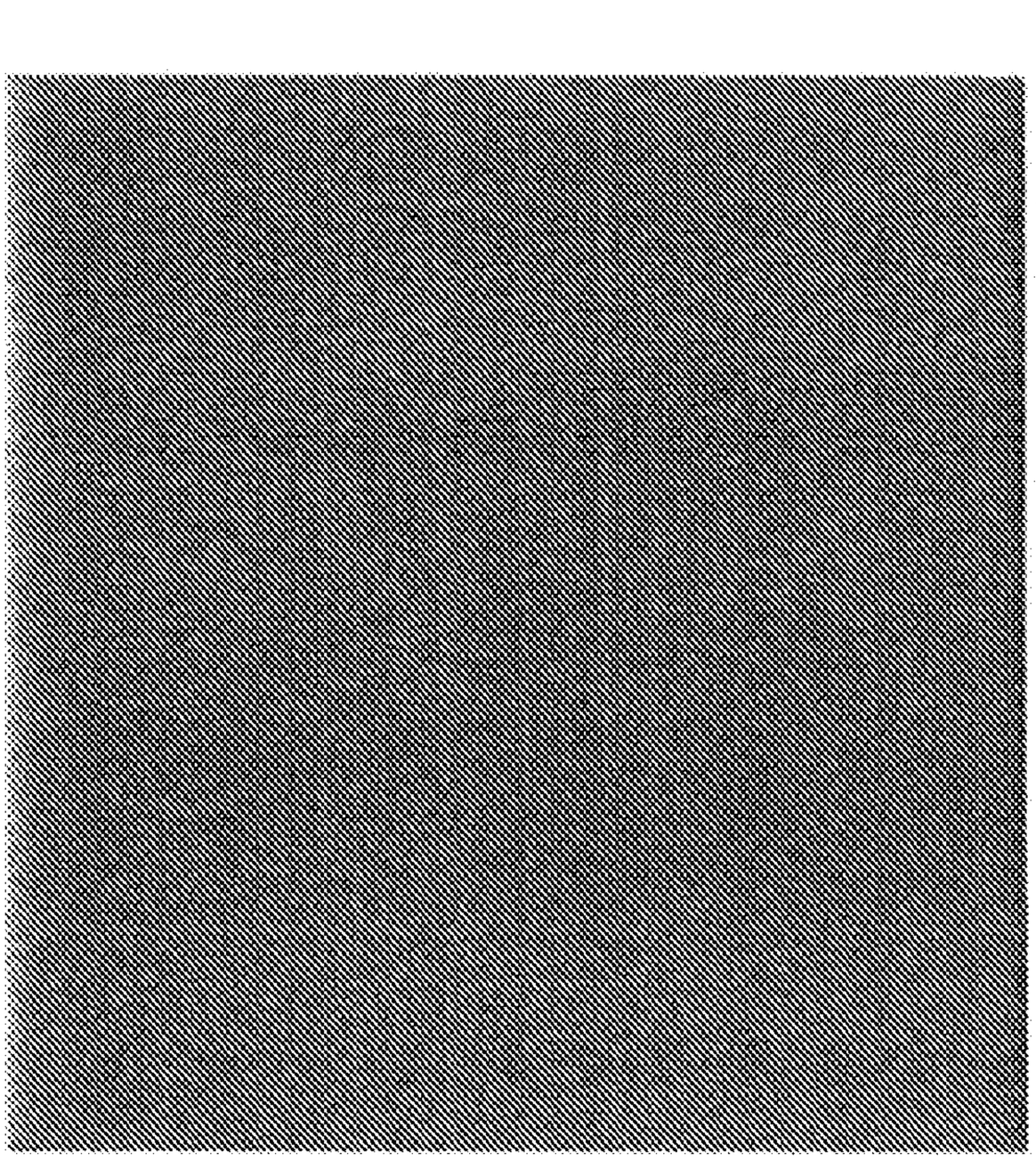


Figure 12B

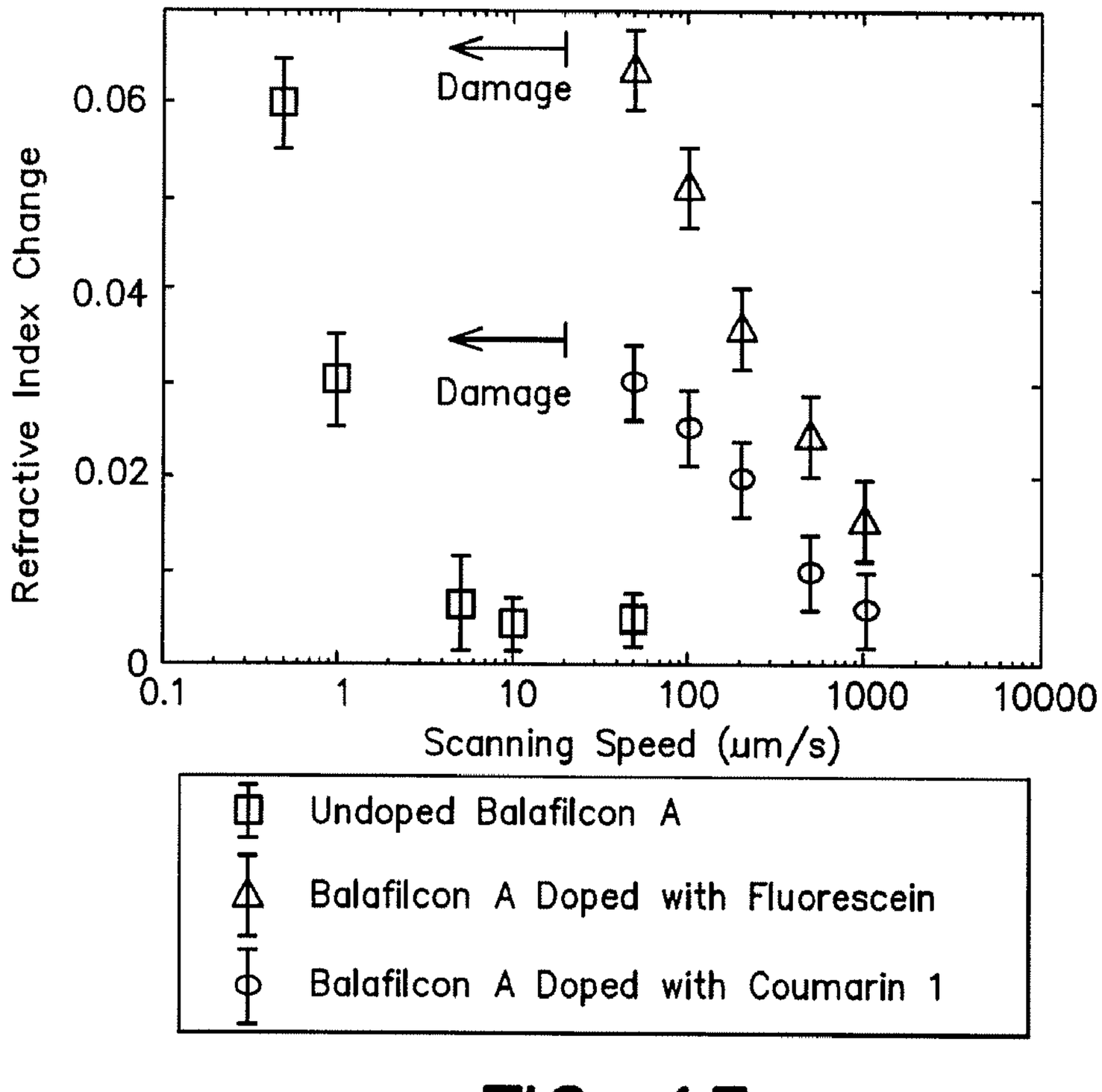

Refractive Index Change
0.06
0.04
0.02
0
Damage
Damage
0.1
1
10
100
1000
10000
Scanning Speed (μm/s)
Undoped Balafilcon A
Balafilcon A Doped with Fluorescein
Balafilcon A Doped with Coumarin 1

FIG. 13

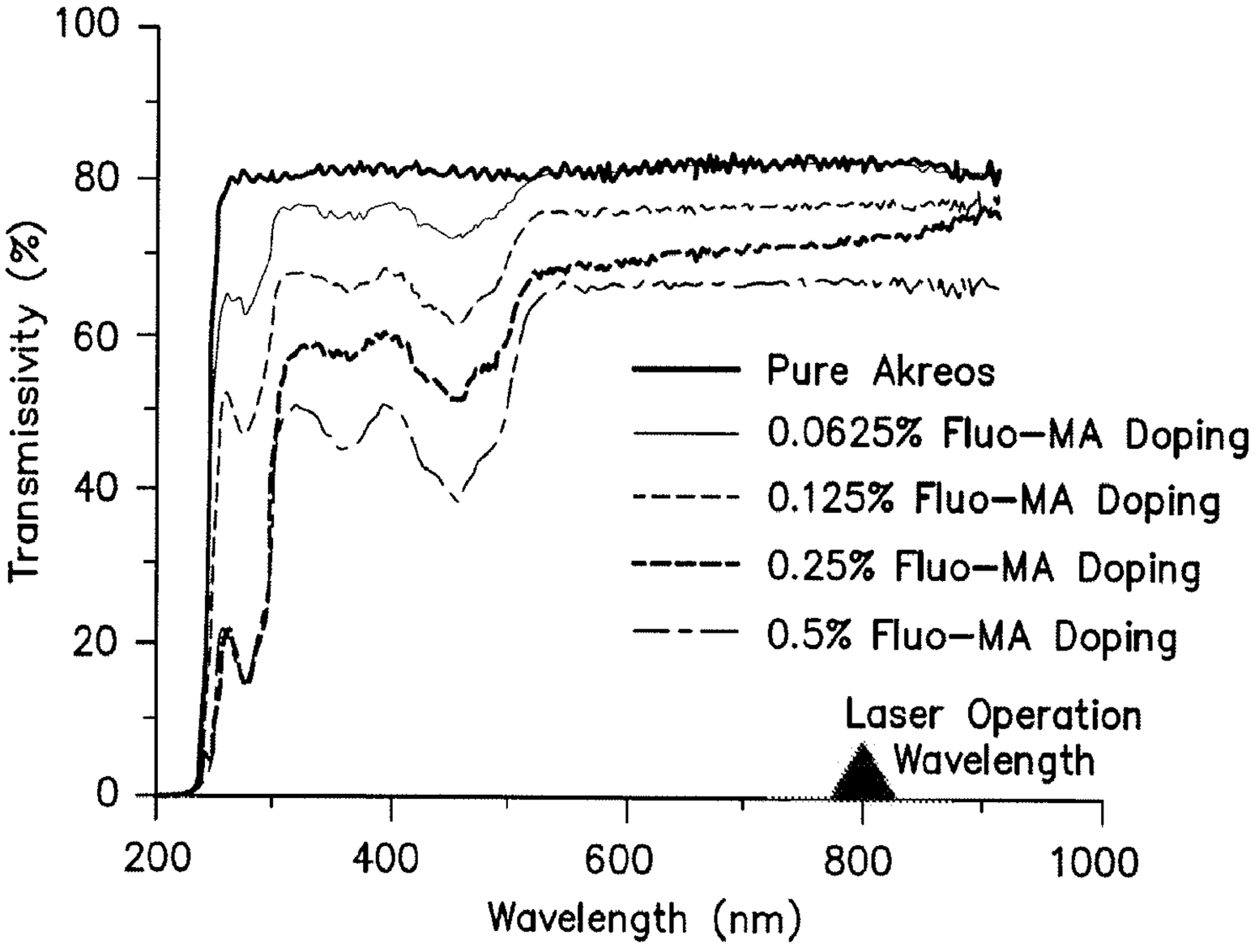

Transmissivity (%)
100
80
60
40
20
0
200
400
600
800
1000
Wavelength (nm)
Pure Akreos
0.0625% Fluo-MA Doping
0.125% Fluo-MA Doping
0.25% Fluo-MA Doping
0.5% Fluo-MA Doping
Laser Operation Wavelength

FIG. 14

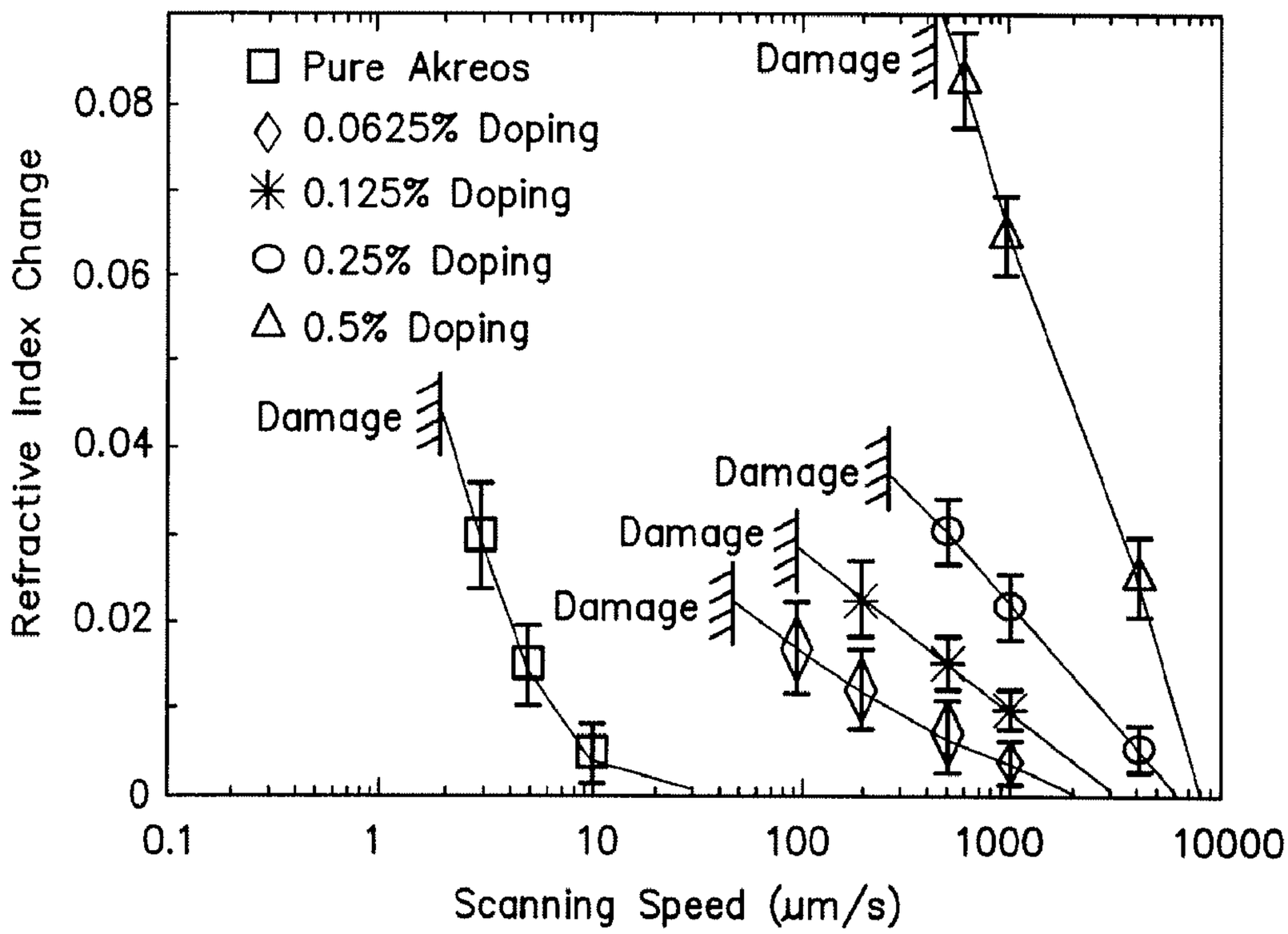

Pure Akreos
0.0625% Doping
0.125% Doping
0.25% Doping
0.5% Doping
Damage
Damage
Damage
Damage
Damage
Refractive Index Change
0.08
0.06
0.04
0.02
0
0.1
1
10
100
1000
10000
Scanning Speed (μm/s)

FIG. 15

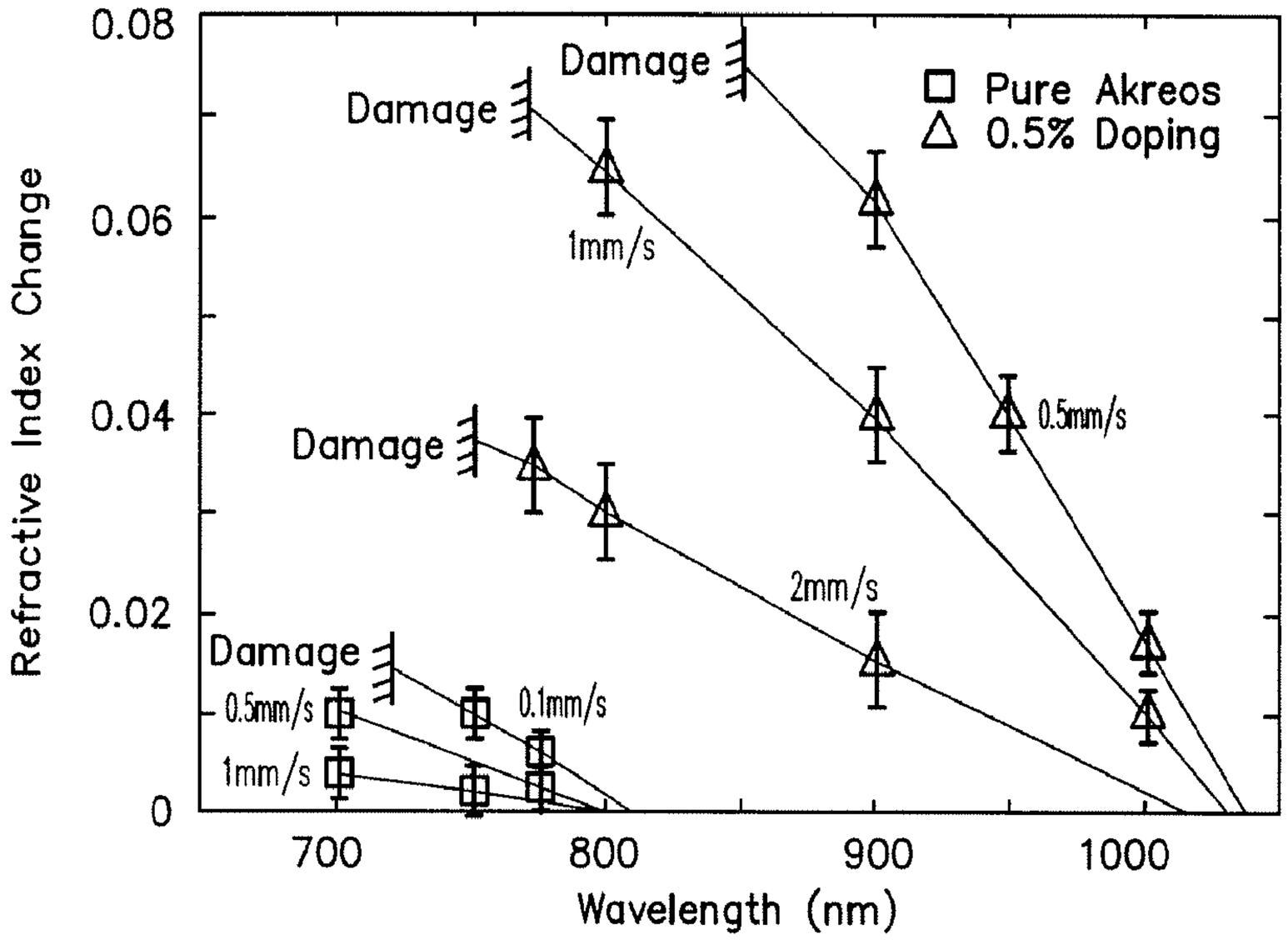


FIG. 16A

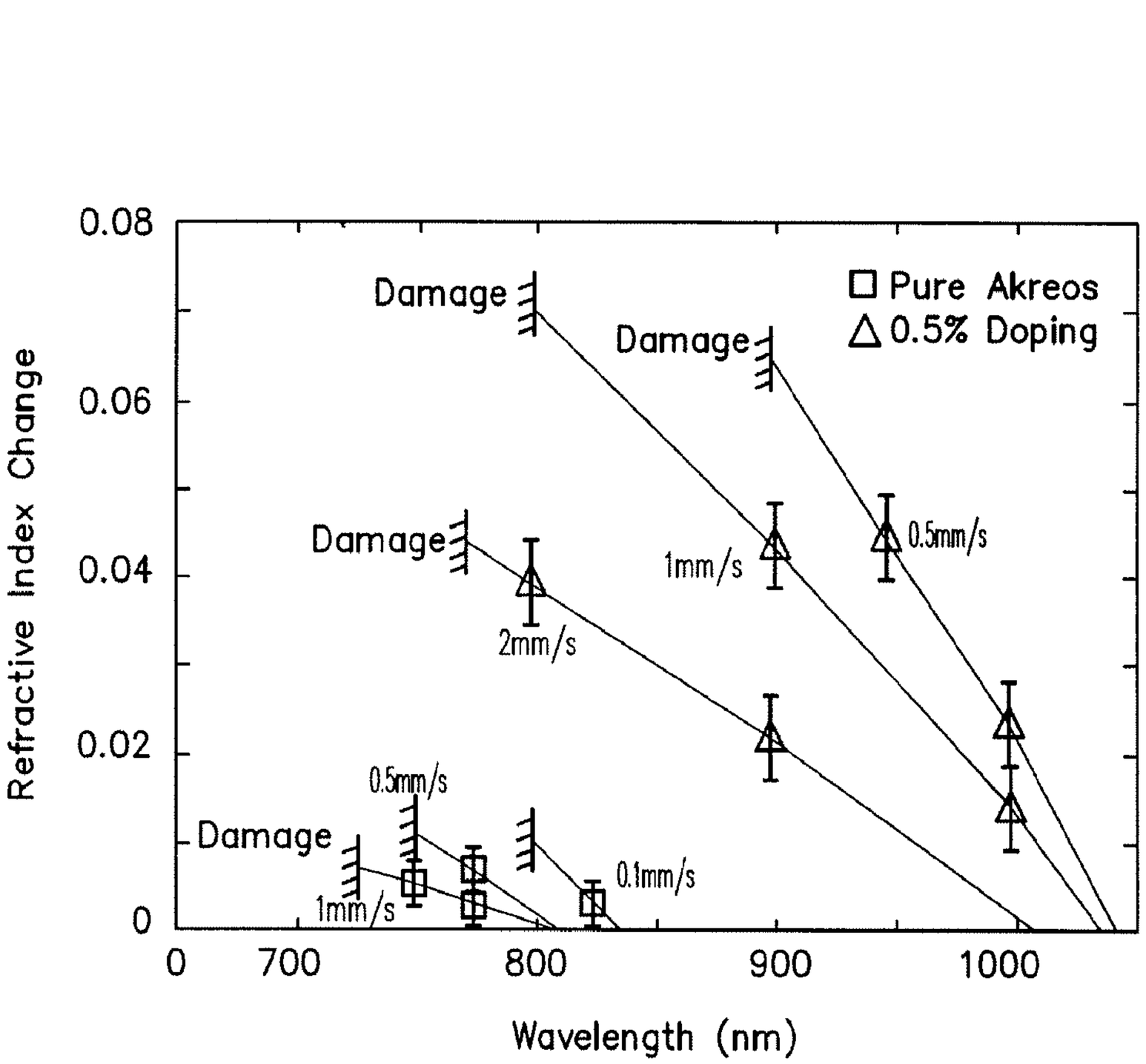


FIG. 16B

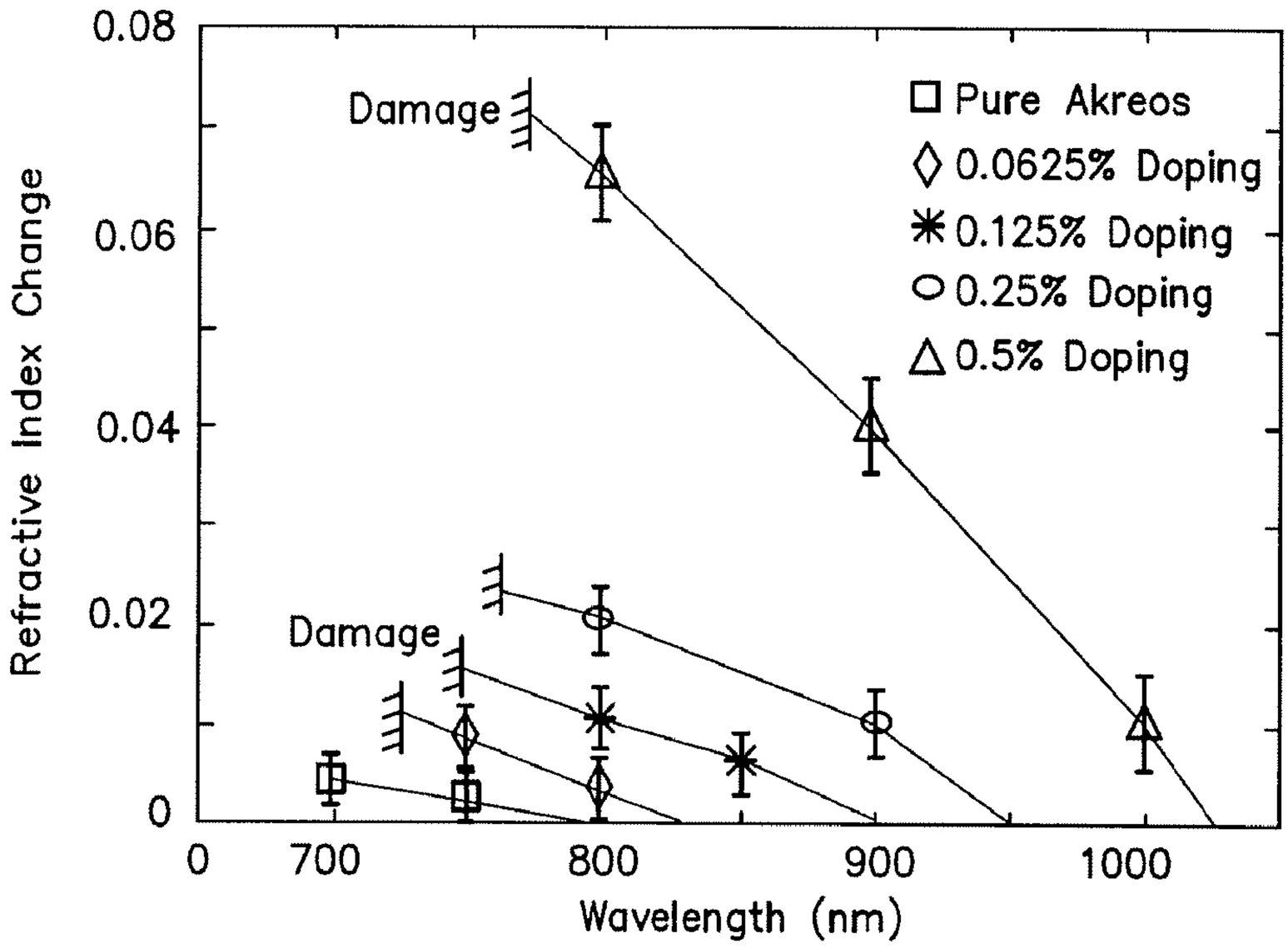

0.08
0.06
0.04
0.02
0
Refractive Index Change
Damage
Damage
Pure Akreos
0.0625% Doping
0.125% Doping
0.25% Doping
0.5% Doping
0
700
800
900
1000
Wavelength (nm)

FIG. 17

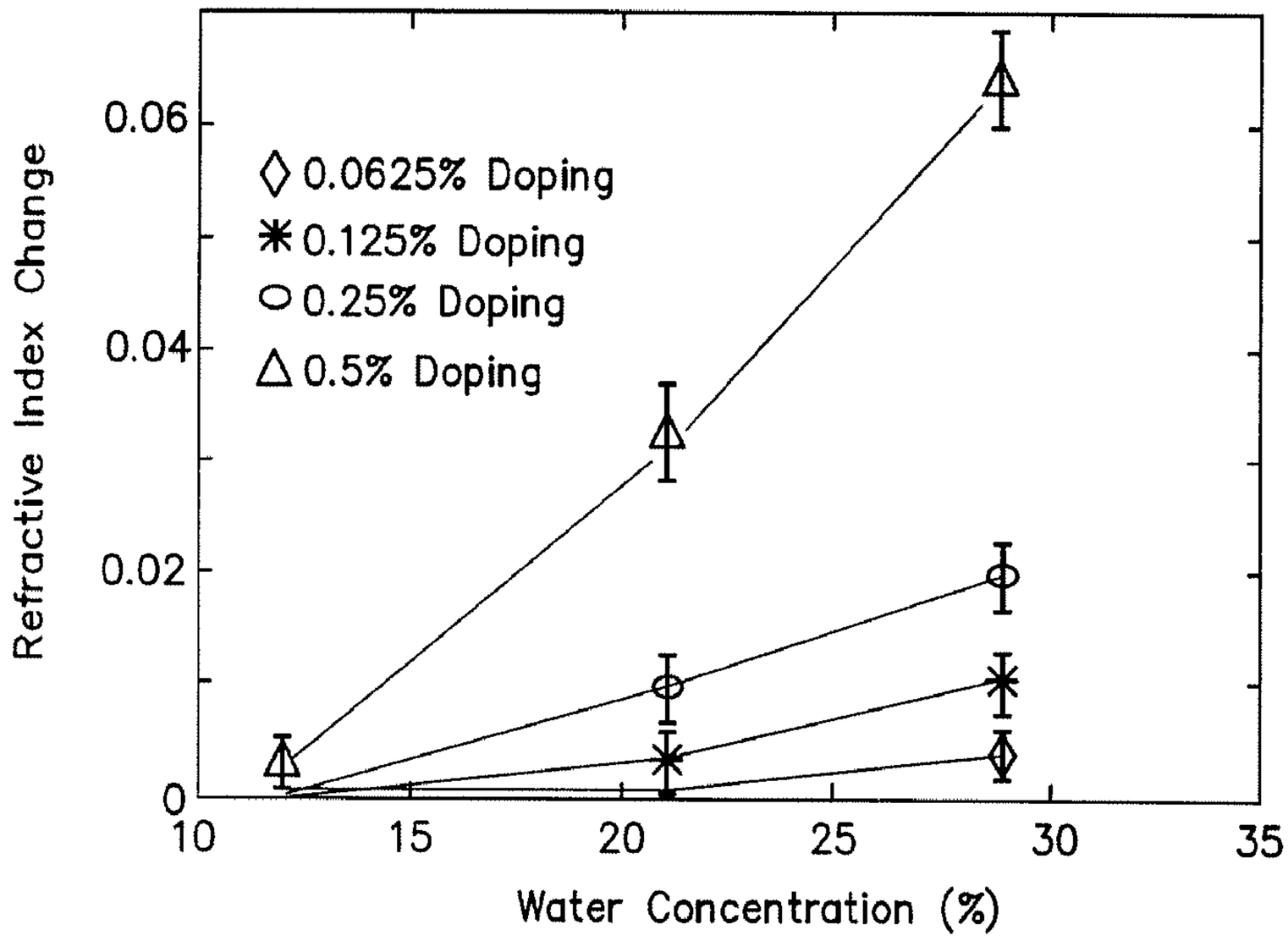
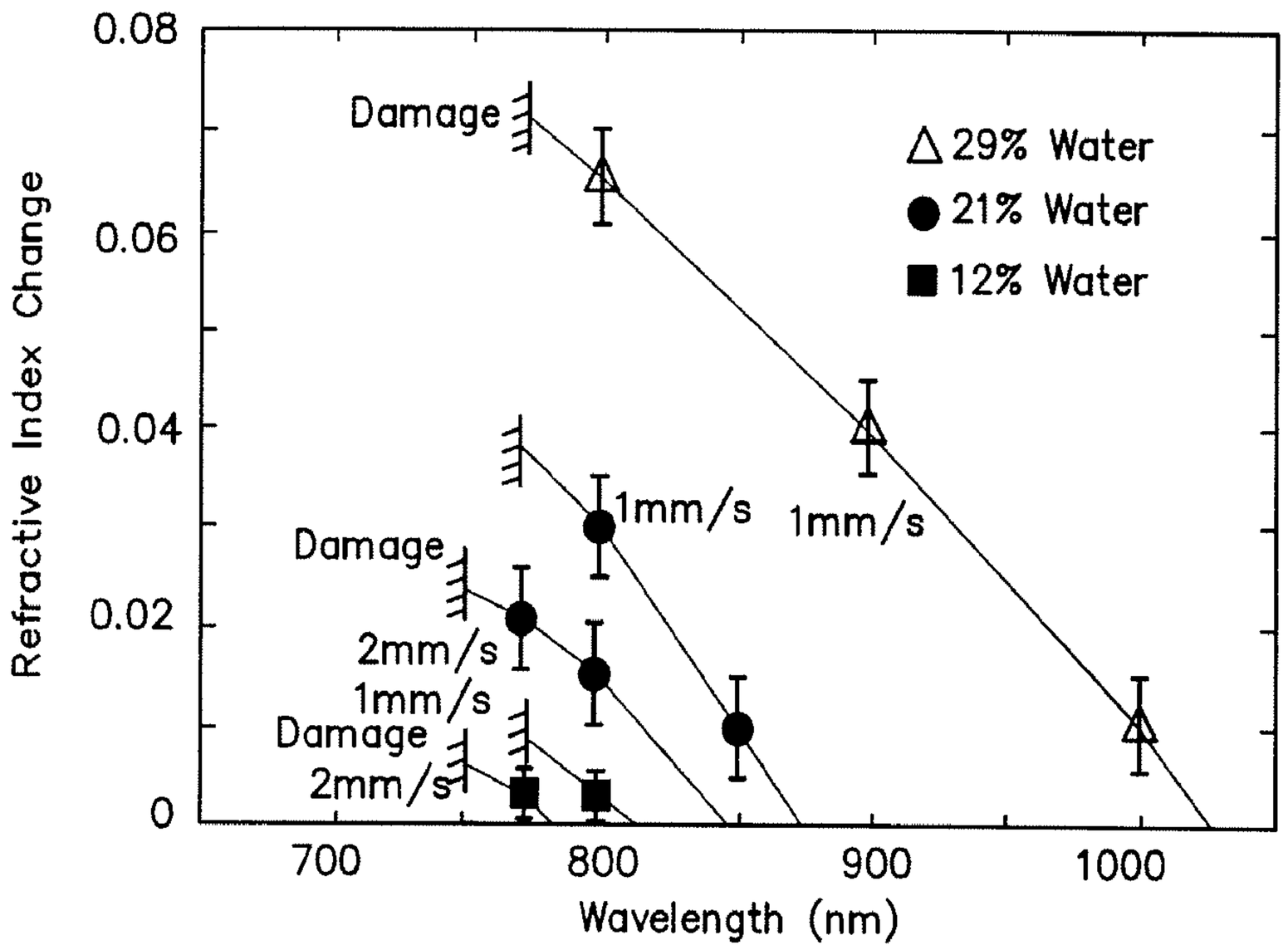

0.06
0.04
0.02
0
Refractive Index Change
0.0625% Doping
0.125% Doping
0.25% Doping
0.5% Doping
10
15
20
25
30
35
Water Concentration (%)

FIG. 18


0.08
0.06
0.04
0.02
0
Refractive Index Change
700
800
900
1000
Wavelength (nm)
Damage
1mm/s
29% Water
21% Water
12% Water
Damage
2mm/s
1mm/s
Damage
2mm/s
1mm/s

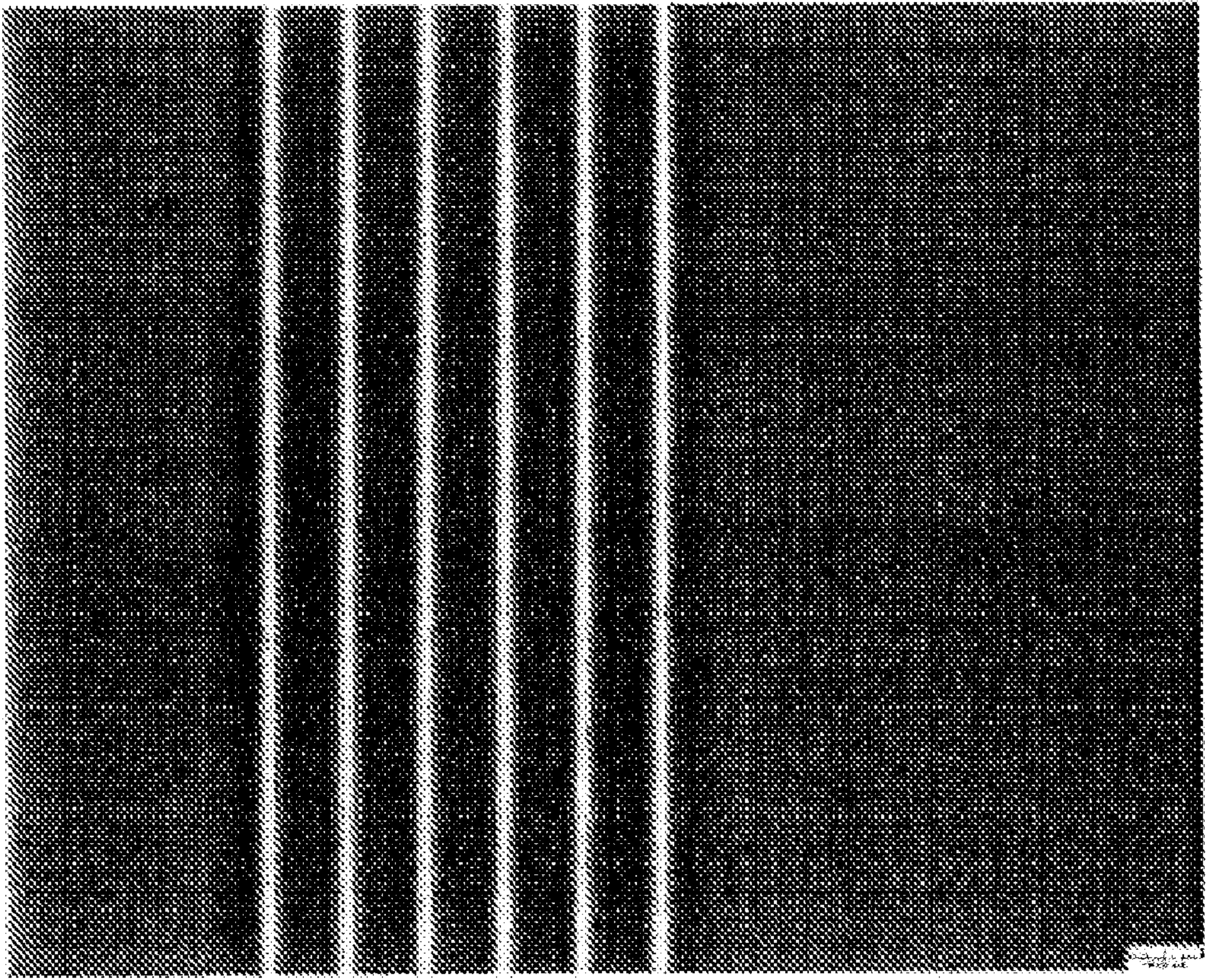



FIG. 19