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with *B. fragilis*, *Lactobacillus*, or SFB did not affect colonic T_{reg} cells, and a cocktail of 16 *Bacteroides* species only marginally increased the number and frequency of colonic T_{reg} cells. Thus, *Clostridium* species appear to be specialized in their ability to promote T_{reg} cell accumulation and activity in the colon.

Unlike SFB that tightly adhere to the intestinal epithelium, Atarashi *et al.* observed that the *Clostridium* cocktail formed a non-adherent layer in the cecum and colon. Still, the *Clostridium* species promoted the release of transforming growth factor- β (TGF- β), a molecule that promotes T_{reg} cell differentiation and survival, by intestinal epithelial cells. Furthermore, colonic T_{reg} cell accumulation occurred normally in mice that lack intestinal lymphoid follicles and Peyer's patches, suggesting that T_{reg} cells accumulated as a result of a *Clostridium*-specific signal, rather than as a secondary consequence of the formation of lymphoid tissues in *Clostridium*-colonized mice. These signals could be transmitted to CD4⁺ T cells independently of each of the three major innate immune microbial-sensing pathways, suggesting either redundancy among sensors or an unknown mechanism. Additionally, T_{reg} and Tr1-like cells in the small intestine still produced IL-10 in germ-

free mice. Because human inflammatory bowel diseases often affect the small intestine (4), understanding whether dietary or other factors activate T_{reg} cells in this site is particularly important.

Atarashi *et al.* found that increasing the frequency and abundance of the cocktail of *Clostridium* species in mice with an otherwise normal immune system and microbiota also enhanced colonic T_{reg} cell accumulation. Such mice were more resistant to experimental models of allergy or intestinal inflammation. These findings suggest that either probiotic administration of human gut-resident *Clostridium* species or boosting the relative frequency of *Clostridium* species in the gut microbial ecosystem with antibiotics could reduce susceptibility to chronic disease. However, targeting defined *Clostridium* species that enhance T_{reg} cell activity should be done cautiously, because the closely related bacterial species SFB and *Clostridium difficile* can instead trigger or exacerbate inflammatory disease. Also, an individual with an altered microbiota containing an abundance of intestinal *Clostridium* species might become more susceptible to enteric infections (16). It may be that *Clostridium* and related Gram-positive gut-resident bacteria are among the

most potent modulators of T cell immunity in the normal microbiota. Understanding the molecular properties that make these bacteria immunostimulatory and either pro- or anti-inflammatory will be an important step toward manipulating the microbiota for therapeutic purposes.

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MATERIALS SCIENCE

Low-Loss Plasmonic Metamaterials

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Metamaterials (MMs) are artificial, engineered materials with rationally designed compositions and arrangements of nanostructured building blocks. These materials can be tailored for almost any application because of their extraordinary response to electromagnetic, acoustic, and thermal waves that transcends the properties of natural materials (1–3). The astonishing MM-based designs and demonstrations range from a negative index of refraction, focusing and imaging with sub-wavelength resolution, invisibility cloaks, and optical black holes to nanoscale optics, data processing, and quantum information applications (3). Metals have traditionally been the material of choice for the building blocks, but they suffer from high resistive

losses—even metals with the highest conductivities, silver and gold, exhibit excessive losses at optical frequencies that restrict the development of devices in this frequency range. The development of new materials for low-loss MM components and telecommunication devices is therefore required.

Metamaterials and plasmonics exploit another revolutionary field in photonics, whereby the features of photonics and electronics are combined by coupling the energy and momentum of a photon to a free electron gas in the form of surface plasmons. Surface plasmons propagate on the surface of the metal, and enable the routing and manipulation of light at the nanoscale (4). Plasmonic MMs face the challenge associated with overcoming the losses that dampen these sub-wavelength coupled excitations.

One solution would be to combine MMs with a gain medium to offset the metallic losses (5). However, even the highest gain provided by existing active materials is not

New materials are being developed that meet the requirements for nanoscale photonics.

enough to compensate the large losses. A different approach would be the discovery of better plasmonic materials that have a negative real part of dielectric permittivity. This search requires an investigation of previously overlooked elements, improving the optical properties of the existing metallic materials via doping, or alloying and careful band structure engineering (6–8).

The material losses are not the only consideration—the real part of the dielectric permittivity is critical because it determines the optical performance of the system (6). For example, although negative real permittivity is required for any plasmonic structure, an extremely negative value is not desirable for MM devices like hyperlenses or transformation optics (9, 10). Both the loss issue and the ability to tune the real part of the dielectric permittivity are factors to consider when searching for alternative plasmonic materials.

Materials can be classified on the basis of two important parameters that determine the

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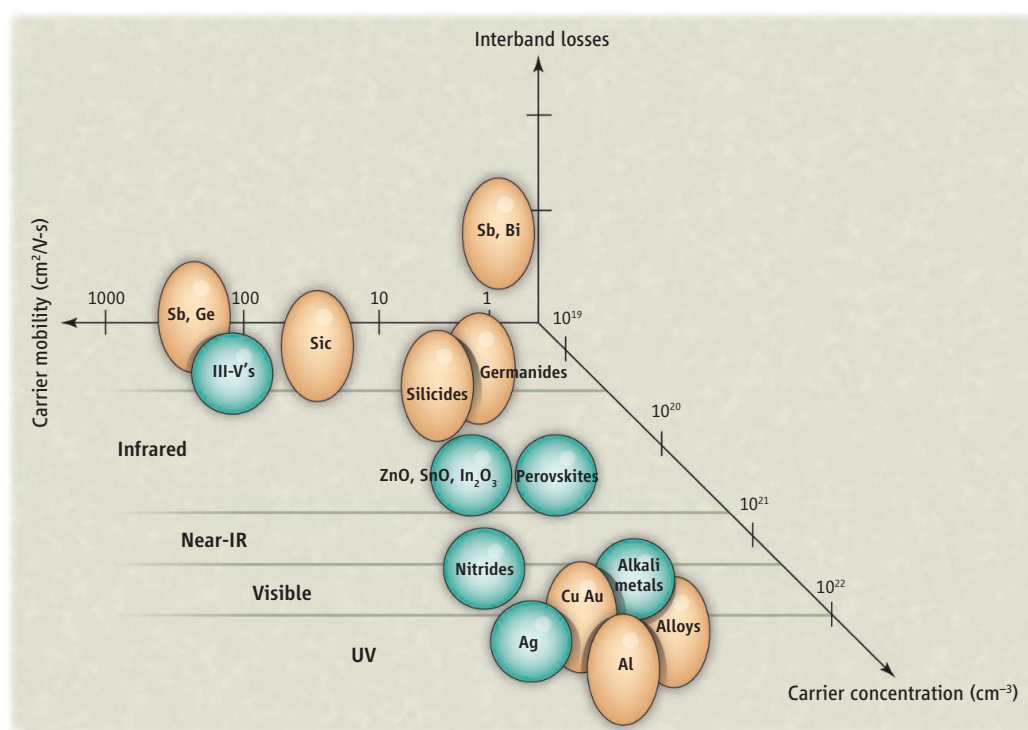
Metamaterials map. The important material parameters such as carrier concentration (maximum doping concentration for semiconductors), carrier mobility, and interband losses can be optimized for various applications. Spherical bubbles represent materials with low interband losses, and elliptical bubbles represent those with larger interband losses in the corresponding part of the electromagnetic spectrum.

optical properties of conducting materials: the carrier concentration and carrier mobility (see the figure). The carrier concentration has to be high enough to provide a negative real permittivity, but it also must be tunable so that larger negative values would be accessible with further increases in carrier concentration. Lower carrier mobilities translate to higher material losses. Additional losses due to interband transitions are highly undesirable and severely limit potential applications. The ideal material for plasmonics would lie at the left end of the plot on the horizontal plane where interband losses are zero. Such a loss-less metal remains elusive (11).

The potential candidates to replace silver and gold in plasmonic applications include alkali metals, intermetallics (7), various alloys (8), transparent conducting oxides (TCOs) (6), and graphene (12). In the visible-wavelength range, silver and gold and their alloys with slightly improved properties (8) are the best materials (6). Many other metals exhibit higher losses, whereas alkali metals have attractive properties but are ruled out by their extreme chemical reactivity.

The plasmonic properties of semiconductors are suitable for MM applications at near-infrared (NIR) and mid-infrared (MIR) wavelengths. Operation in the NIR requires heavy doping (10^{21} carriers cm^{-3}) that can be achieved in TCOs such as indium tin oxide, or zinc oxide doped with aluminum or gallium (6). In the MIR, silicon carbide, gallium arsenide, and other semiconductors have already been shown to be suitable for some MM applications (13, 14).

Because the losses associated with metals partly arise from free electron densities that are too large, an overall approach would be either to reduce the electron density in metals or increase it in semiconductors. Free electron gases at intermediate carrier concentrations in TCOs have enabled plasmonics in the NIR range. Plasmonics in the visible range with TCOs would require still higher doping



concentrations, which becomes increasingly difficult. Instead, we could reduce the carrier concentration in metals by mixing them with nonmetals and giving rise to intermetallics (silicides, germanides, borides, nitrides, oxides, and metallic alloys). For example, the optical properties of titanium nitride approach those of gold for plasmonic applications above 550 nm (15). In this way, the optical properties of silicides and germanides of tungsten and tantalum could be optimized to produce low-loss plasmonic materials in the NIR. Nonstoichiometric oxides such as vanadium, titanium, and aluminum oxides are good candidates in the NIR and visible ranges, as plasmonic materials and also as switchable optical materials.

These new intermediate carrier density materials offer the prospect of other exotic properties beyond lower losses. For example, heavily doped semiconductors and TCOs can provide extraordinary tuning and modulation of their complex refractive indices because their carrier concentrations can be changed by orders of magnitude by applying an electric field. Such materials can go from being metallic to dielectric, opening up exciting possibilities for novel device concepts (16). Along with "phase change" materials like chalcogenide glasses and transition metal oxides that are prime agents for switching and memory storage applications, TCOs and graphene (17) are promising candidates for adding electro optical capabilities to plasmonic and MM devices.

With their high dielectric constants, plasmonic semiconductors might also contribute to the further development and improvement of solar cells and light-harvesting devices (18). The development of new plasmonic materials should lead to tremendous progress in the technology of MMs, providing low-loss and tunable materials suitable for use in the electronics industry.

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