additional pathways should be targeted for more efficient antilymphangiogenic therapies. Unwanted side effects also have to be considered because lymphangiogenesis is induced after wounding, and the inhibition of lymphangiogenesis may interfere with tissue regeneration.

Furthermore, some preclinical studies have aimed at promoting lymphangiogenesis in order to cure lymphedema. Lymphedema is most commonly caused by the removal or damage of lymph nodes, and it is one of the most common side effects of breast cancer treatments. There is no cure available to treat lymphedema. However, the overexpression of VEGF-C or VEGF-D in preclinical animal models of lymphedema leads to the formation of new lymphatic capillaries and reduced edema. These results look encouraging, and the process could decrease the discomfort resulting from lymph node resection. To date, lymph node transplantations have been performed following breast cancer surgery, but the transplanted lymph nodes are incorporated into the existing lymphatic vasculature at low frequency. In a mouse model, the overexpression of VEGF-C in lymph nodes improves the success rate of the lymph node transplantation. However, it is important to remember that VEGF-C promotes the lymphatic metastasis of tumor cells, and an overexpression of VEGF-C can lead to an increase of metastasis if some tumor cells are still present.

Despite recent advances in the understanding of lymphangiogenic processes, few factors (except those involved in the VEGF-C/VEGF-D/VEGFR-3 signaling system) have been identified. Identification of new factors involved in the growth and development of the lymphatic vasculature is mandatory to delineate more approaches for the molecular manipulation of lymphatic vessels. Regarding lymphatic vessels as a therapeutic target, important questions remain to be answered, especially in terms of treatment efficacy and patient safety.

For background information see CANCER (MEDICINE); CLINICAL IMMUNOLOGY; DISEASE; EDEMA; GROWTH FACTOR; IMMUNOLOGY; INFLAMMATION; LYMPHATIC SYSTEM; NEUTRALIZING ANTIBODY; TRANSPLANTATION BIOLOGY; VASCULAR DISORDERS in the McGraw-Hill Encyclopedia of Science & Technology. 

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**Manipulation of heat flow**

Artificial materials engineered to exhibit properties that do not typically exist in nature are often called metamaterials, and these unique materials have attracted a significant amount of scientific interest in recent years. Just as conventional materials owe their properties to the average response from an ensemble of atoms and molecules, in “artificial” materials, each structural unit plays the role of an atom. The material properties are controlled not only by what elements are used and their individual properties, but also by the way they are arranged collectively in lattice-like geometrical patterns with prescribed spatial variations. This immense flexibility is one of the main reasons why material engineering has become such an explosive catalyst in so many scientific disciplines. For example, metamaterials applied to the manipulation of electromagnetic waves have demonstrated some counterintuitive concepts such as a negative index of refraction, which allows light to bend at the interface of materials in a direction opposite to what you would observe from any ordinary materials. The concept of artificial material engineering has extended beyond conventional material science and it has now started to be applied to the manipulation of heat flow.

**Heat conduction.** Heat current is everywhere. Heat flows wherever there is a temperature difference, and as we are very much aware from our daily lives, it flows from hot to cold. Heat conduction is a diffusive energy flow and is not a wave phenomenon governed by the so-called wave equation. In that sense, heat conduction differs significantly from energy propagation in the form of waves exemplified by light and sound. However, some clear analogies and common properties exist among these disparate physical phenomena. One such example is that it is possible to manipulate their flow path with anisotropic material properties. An anisotropic property here refers to a physical property that has a different value when measured in a different direction. To control heat flux in unconventional manners, for example, one needs to prescribe various structural elements that play the role of atoms and design overall structures that exhibit different thermal conductivities at the same point in space if measured in different directions. Thermal conductivity has to be not only spatially varying, but also direction dependent. Mathematically that means that the conductivity of the material needs to be a tensor, not a scalar.

**Heat flux manipulation.** Anisotropic materials do exist in nature. For example, quartz and graphite can exhibit direction-dependent thermal conductivities due to their inherent internal structures. It would...
be ideal to be able to build up materials with such anisotropy from the ground up, tailored to our specific needs to force the heat flux to follow the paths of our interest. That is easier said than done. Even with the recent technological advances in nanofabrication and characterization, we still lack the ability to build materials one atom at a time and scale things up to a macroscopic size. One therefore needs a different approach: a practical one that approximates the same end result. One such approach is to construct a layered composite. If one looks at a set of stairs from very far away, it appears to be a smooth continuous slope. By stacking discrete layers of materials characterized by constant but individually different thermal conductivities, we can mimic materials with a smooth gradient in their conductivity profiles. What is important here, again, is the arrangement. For example, if one constructs a material by alternating elements characterized by high and low thermal conductivities, just as in the case with electric current in resistor networks, heat would prefer to flow in the parallel direction rather than in the series direction. That is a bit oversimplified, as more complicated heat-flow patterns can appear depending on the exact geometry of the material placement and the configurations of externally applied heat flux. However, the principle is clear. By using only isotropic materials that exist in nature, one can design and construct anisotropic materials with uniquely engineered thermal conduction properties.

**Recipe.** There is a wide parameter space that one can explore for determining the exact spatial distribution of thermal conductivities. It turns out that it is so wide that, given a particular heat flux manipulation of interest, the process of figuring out the exact elements required along with the specific patterns and configurations to place those elements in can be quite daunting. To make that process more efficient, a recipe called coordinate transformation can be used. The conduction equation is mathematically form invariant when one moves from one coordinate system to another. One can then view the bending of heat current as a mere coordinate transformation, or more precisely a distortion of space from such transformation. Once the adequate coordinate transformation that achieves the required heat flux distortion is found, formulations in linear algebra allow the same transformation to be used to transform the thermal conductivities to the values necessary for such distortion. Since the mathematical transformation that achieves a particular operation is generally not unique, it makes the most sense to choose the one that gives the conductivity profiles that can easily be assembled; for example, a layered configuration. The parameter space that needs to be explored becomes a bit narrower, and this provides researchers with an appropriate starting point for designing and assembling composites. The coordinate transformation approach was initially discussed in the context of electrical impedance tomography where, given current-voltage measurements on a sample, its electrical conductivity profile cannot be uniquely determined. The same principle was developed further and applied to more recent metamaterial work such as cloaking a spatial region from electromagnetic waves.

**Local heat current inversion.** An interesting example of heat flux manipulation using thermal metamaterial is the local inversion of heat current. A hollow cylindrical material with artificial thermal properties is embedded in a block of ordinary material (Fig. 1). In this case the engineered material consists of approximately 100 layers of polyurethane and copper in a spiral configuration designed with the aid of coordinate transformation discussed above. A heat source and a sink are applied at the two ends of the block to externally force the heat to flow from left to right. Simulations reveal the designed functionality of this material (Fig. 2). The temperature profile rotates within the composite to invert the temperature gradient in the inner region. The heat flux lines become distorted within the artificial material in such a way that it forces heat to flow from right to left in the inner region to be able to get out to the heat sink. Such local inversion of heat flux has been experimentally observed (Fig. 3). Even with the direction of heat flow strictly imposed from outside, it is possible to design material properties such that heat current becomes manipulated passively and it flows backwards in a targeted region.

**Outlook.** Heat current manipulation using thermal metamaterials is a step toward a more robust control of heat flux. Thermodynamics is a well-established discipline in science and the concept of heat has
conductivities could potentially lead to new types of thermoelectric materials. It is not clear at the moment how small one can make these thermal metamaterials, and that is a topic that will require further investigation along with the thermal responses in the transient regime. What is exciting is that, with further advancement in material growth, synthesis, and fabrication, more complicated structures should become feasible to assemble. Not restricted by the layered structures, truly graded materials tailored with multi-functionalities could be experimentally investigated and applied to various scientific frontiers in the future.

For background information see COMPOSITE MATERIALS; CONDUCTION (HEAT); COPPER; HEAT TRANSFER; MATERIALS SCIENCE AND ENGINEERING; POLYURETHANE RESINS; THERMAL CONDUCTION IN SOLIDS in the McGraw-Hill Encyclopedia of Science & Technology.

Yuki Sato


Fig. 2. Simulations of thermal responses. (a) When the metamaterial is embedded in a host medium (agar-water block) and subjected to an external thermal gradient, the temperature profile rotates to invert the gradient in the inner region, while making minimum perturbation to the outside. (b) Heat-flux lines are distorted and forced to flow from right to left in the inner region, while they continue to flow from left to right in the exterior region.

Fig. 3. Experimentally observed temperature profile showing the inversion of the thermal gradient in the inner region with respect to the outside. Dotted lines outline the inner and outer diameters of the metamaterial.

been known for a long time. That often makes us forget how difficult it really is to manipulate heat current. Compared to the field of electrical conduction, which is armed with nonlinear solid-state devices, the field of thermal conduction is still in its infancy. Given that temperature differences exist everywhere and the resultant heat flow is often just wasted, it is worthwhile to consider various possible means to manipulate, control, and more speculatively process heat current. With engineered thermal functionalities available, one property that seems within reach is the ability to switch on and off those functionalities. For example, with materials that exhibit temperature-dependent thermal conductivities, particular functionalities can be turned on and off with a temperature change in the environment. Such nonlinear thermal materials may pave the way for more sophisticated thermal management. Simultaneous manipulations of thermal and electrical

Mars Science Laboratory

The Mars Science Laboratory is an advanced, instrumented roving vehicle designed to assess whether its landing site on Mars contains evidence of past or present habitable environments. Named Curiosity, the rover landed inside Gale crater on August 6, 2012, with the intention of exploring a tall central mound of layered sediments within the crater.

Spacecraft characteristics. NASA’s Mars Science Laboratory represents the most advanced spacecraft ever sent to the surface of another planet (Fig. 1). The space agency sponsored an essay contest in 2009 to choose the rover’s name. The winning entry, Curiosity, was submitted by Clara Ma, who at the time was a sixth-grade student.

Curiosity utilizes a six-wheeled design, as have previous Martian rovers, which provides the ability to traverse uneven terrain and some degree of redundancy should any of the individual wheels fail. Roughly the size of a Mini Cooper automobile, the rover has an overall length of 9.8 ft (3.0 m), a width