McGRAW-HILL YEARBOOK OF Science & Technology

2001

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to be targeted to their specific locations. Blobel's research has substantially increased understanding of the molecular mechanisms governing these processes.

In the future the knowledge about protein trafficking may be applied to different parts of the cell which may contribute to the development of new drugs. The ability to alter cellular instructions in a specific way may also be applied to cell and gene therapy.

For background information *see* CELL MEMBRANES; CELL ORGANIZATION; ENDOPLASMIC RETICULUM in the McGraw-Hill Encyclopedia of Science & Technology.

Nonpoint source pollution

The subsurface migration of hazardous wastes from point sources has caught the public's attention with well-publicized case histories such as Love Canal and Woburn. In the United States there have been tremendous advances in the last 25 years related to point source pollution. For example, cleaning up the aquatic environment by controlling pollution from industries, and remediating the legacies associated with failed hazardous waste landfills are well-established practices in today's environmentally conscious society. Nonpoint source pollution, with all the implications of scale and variability (both spatial and temporal), can pose even greater environmental problems than those from point sources. Nonpoint source pollution occurs when rainfall, snowmelt, or irrigation water runs over land or through the ground, picks up pollutants, and deposits them into rivers, lakes, and coastal water or introduces them into ground water. Nonpoint source pollutants are spread over large areas, as opposed to point source pollutants that are located at a single site. Nonpoint source pollutants can be diffuse and intermittent and are influenced by changes in climate, geology, hydrology, land use, topography, and vegetation at regional scales. Obviously, nonpoint source pollution can be a much more difficult problem to control than point source pollution. The Environmental Protection Agency has identified nonpoint source pollution as the nation's largest water quality problem. Due in large part to nonpoint source pollution, approximately 40% of the surveyed rivers, lakes, and estuaries in the United States are not clean enough to meet basic uses such as fishing or swimming.

During the 1990s, significant headway was made in addressing nonpoint source pollution in the United States. Nonpoint sources are regulated under Section 319 of the 1972 Clean Water Act, by amendments approved by Congress in 1987 (Nonpoint Source Pollution Management Program). States are required to identify the major sources of nonpoint source pollution and draft plans (Best Management Programs, or BMPs) to rectify the problems. Also, the Coastal Nonpoint Pollution Program (for states and territories with approved Coastal Zone Management Programs), established in the 1990 Coastal Zone Act Reauthorization Amendments, has helped to reduce nonpoint source pollution impacts. The cost of remediation for nonpoint source pollution at the regional scales associated with, for example, modern agricultural and forestry practices can be staggering. Therefore, input reduction is the cheapest way to reduce nonpoint source pollution.

Types. Nonpoint source pollution is widespread because it can occur any time that activities disturb the land or water. Major sources are (1) air pollution fallout, (2) agriculture, (3) construction, (4) forestry, (5) mining, and (6) urban areas. Other sources include grazing, septic systems, recreational boating, urban runoff, physical changes to stream channels, and habitat degradation.

Acid rain is the result of air pollution fallout. Runoff from agriculture can result in, for example, agrochemicals and topsoil washing into streams or other water bodies, and agrochemicals leaching through

Relative importance of pollutant concentrations*

Nonpoint source category	Suspended solids/ sediments	Nutrients	Pesticides	Toxic metals	Salinity	Pathogens	Acids
Air pollution fallout	M	L-M	L-M	L-H	N	N-L	L-M
Agriculture							
Nonirrigated crop production	H	H	H	N-L	N	N-L	N
Irrigated crop production	L	H	M-H	N-L	H	N	N
Pasture and range	L-M	H	N	N	N-L	N-L	N
Construction	H	L	N	N-L	N	N	N
Forestry							
Growing	N	L	L	N	N	N-L	N
Harvesting	M-H	L-M	L	N	N	N	N
Urban storm runoff	M	L	L	H	M	H	N

*N = negligible; L = low; M = moderate; H = high.
SOURCE: After J. J. Peirce et al., *Environmental Pollution and Control*, 4th ed., Butterworth-Heinemann, Boston, 1998.

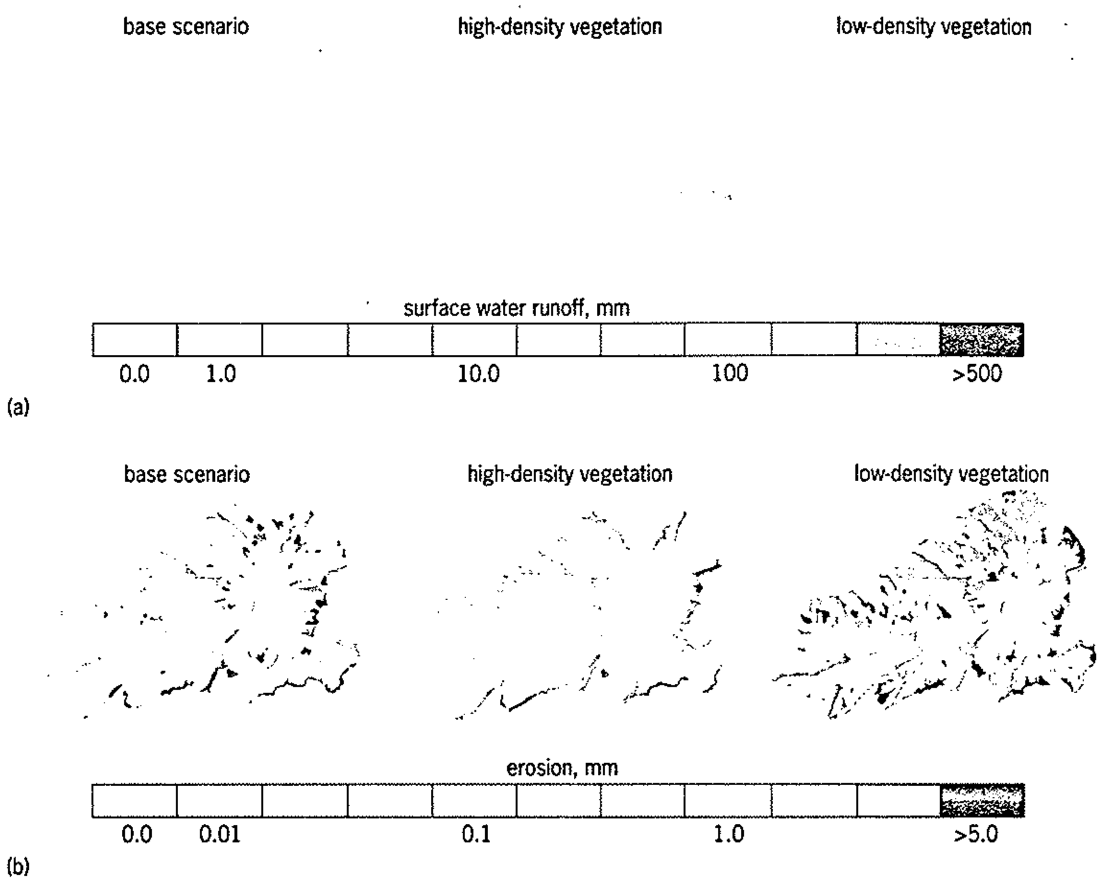

Fig. 1. Impact of vegetation on (a) surface runoff and (b) nonpoint source erosion for Kaho'olawe. (*After E. Wahlstrom, K. Loague, and P. Kyriakidis, Hydrologic response: Kaho'olawe, Hawaii, J. Environ. Qual., 28:481–492, 1999*)

the near-surface vadose zone to ground water. Runoff in areas of construction can result in accelerated rates of erosion and high sediment loading into streams, rivers, lakes, and estuaries. Runoff from forested hillslopes, where the near surface has been disturbed by logging and timber operations, can result in sediment loading to streams, and slope instability and landslide-type events. Water seeping through large mined areas can result in acid drainage. Urban storm runoff (including water off buildings and streets) can transport oil, grease, trash, salts, and other pollutants into surface water bodies depending upon the type of sewerage (separate or combined). The different types of nonpoint source pollutants include acids, nutrients, pathogens, pesticides, toxic metals, salts, and suspended solids/sediments. The **table** summarizes the relative importance of pollutant concentrations for the different nonpoint source categories.

Nonpoint source pollution impacts from agriculture can be minimized, in part, by properly managing the use of agrochemicals and irrigation. Nonpoint source pollution impacts from forestry can be managed by minimizing detrimental timber harvesting, establishing restricted streamside areas, proper road construction, and efficient replanting. Nonpoint source pollution impacts from urban runoff can be minimized by reducing pollutant loads for both existing and new developments (residential, commercial, and industrial).

Assessing impacts. The information age has resulted in global awareness of complex environmental problems that do not respect political or physical boundaries, such as climatic change, ozone layer depletion, deforestation, desertification, and nonpoint source pollution. Scientists working on nonpoint source pollution problems are concerned with the public policy aspects of their efforts. The difficulties associated with the enormous amount of information required (such as climate, geology, hydrology, land use, topography, and vegetation) for the assessment of regional-scale nonpoint source pollution impacts can often be facilitated by remote sensing and geographic information system (GIS) technologies. The ability to simulate spatially and temporally variable environmental impacts via mathematical modeling is a necessity; simulation provides the ability to ask and answer "what if" questions that can be used to guide decision-making strategies.

In general, nonpoint source vulnerability assessments rest upon data that are extremely sparse and therefore contain considerable uncertainty. Uncertainty in simulated assessments is unavoidable and sometimes even undetectable in environmental modeling. Quantification of accuracy and uncertainty in environmental modeling establishes the extent to which simulated results are reliable predictions of observed truth. Uncertainty can be due to model errors (produced from oversimplification of process complexities) or data errors (resulting from errors in the input data or lack of information). Intrinsic model and data uncertainties have significant practical implications, either affirming or negating the use of predictive outputs from environmental models for guidance in a decision-making process. There are obvious questions: What reductions in uncertainty could be made in nonpoint source vulnerability assessments if the data used to drive the models were themselves less uncertain? How much additional information is required to realize the reductions in data uncertainty? How much would this supplemental information cost?

Kaho'olawe. Erosion resulting from surface runoff has historically been a major nonpoint source pollution problem for Kaho'olawe, the eighth largest (117 km^2) island in the Hawaiian chain. Land-use practices (overgrazing and military activities) over the last 150 years have resulted in a dramatic loss of vegetation and (subsequently) soil across Kaho'olawe, causing substantial damage to the island's ecosystem. In 1999, near-surface hydrologic response simulations were reported that were designed to evaluate the impact of landscape remediation on Kaho'olawe. Based upon the event-based simulations in this report, landscape restoration via the introduction of vegetation, which is a strong control on runoff and erosion, was shown to be an effective means of significantly reducing erosion across Kaho'olawe. **Figure 1**, abstracted from the report, shows the impact on runoff generation and erosion from the introduction or removal of vegetation across the entire island, as compared to the base (current) scenario. Large portions of the island that experienced significant erosion under the base scenario had erosion reduced by nearly an order of magnitude with the introduction of vegetation. The removal of all vegetation, however, shows that the rate of soil removal from the island would be significantly accelerated.

Tenerife. The nonpoint source ground-water contamination problem is especially important for insular systems. As in most insular systems, the ground-water resources on the Canary island of Tenerife are in the form of an easily impacted lens of fresh water floating on top of a saltwater body. Tenerife is the largest (2038 km^2) island of the Canary Archipelago; it has a triangle-based pyramid shape with generally steep relief except in the coastal agricultural areas. Agriculture in Tenerife is dependent upon pesticides; therefore, precious ground-water resources are vulnerable to contamination from leaching pesticides. In 1999, researchers combined soil, climatic, and chemical data in a GIS framework with simple pesticide leaching indices to generate ground-water vulnerability assessments for all the agricultural areas across Tenerife for the most important agrochemicals currently in use. A major focus in the efforts was to characterize the uncertainty in the Tenerife ground-water vulnerability assessments resulting from data uncertainties. The vulnerability maps of

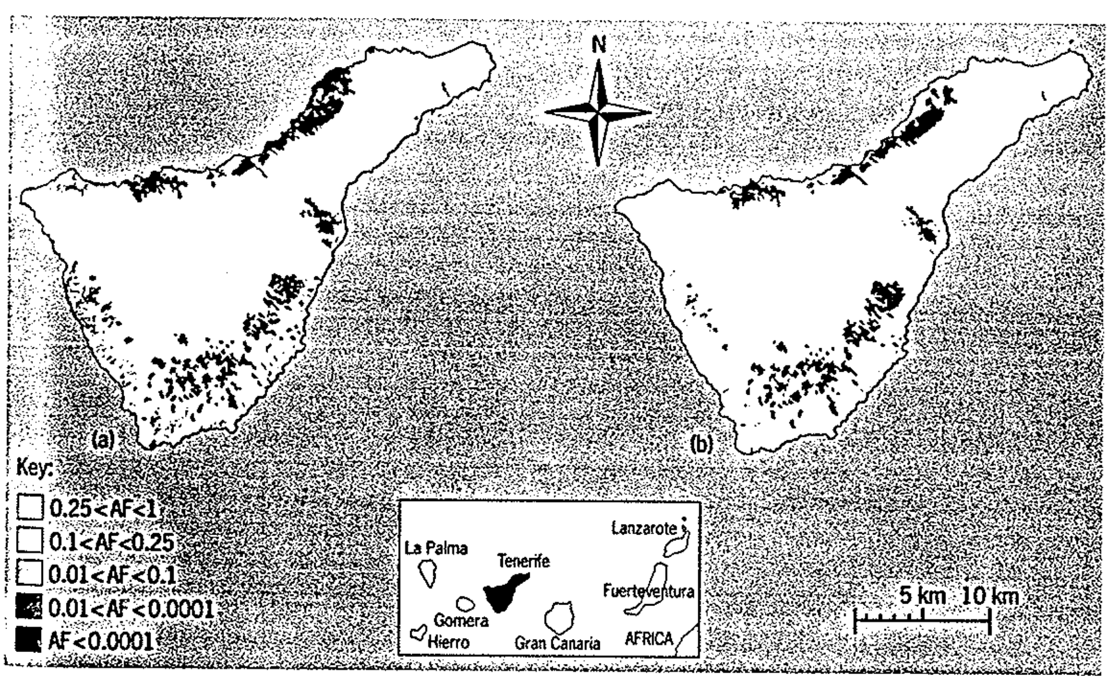

Fig. 2. Example of the results of a GIS-driven assessment of regional-scale nonpoint source ground-water vulnerability for Tenerife. (*a*) Estimates of pesticide (Ethoprophos) leaching, were made for the agricultural areas with the AF (attenuation factor) index. (*b*) Uncertainty (AF + S_{AF}) in the estimates of pesticide leaching are indicated, where S_{AF} is one standard deviation in the AF estimate. When the value of AF is 0.0 the leaching classification is "very unlikely," and when the value of AF is 1.0 the leaching classification is "very likely." (*Adapted from R. Diaz-Diaz and K. Loague, Regional-scale leaching assessments for Tenerife: Impact of data uncertainties, J. Environ. Qual., 29:835–847, 2000; R. Diaz-Diaz, K. Loague, and J. S. Notario, An assessment of agrochemical leaching potentials for Tenerife, J. Contam. Hydrol., 36:1–30, 1999*)

pesticide leaching that were produced identified locations where ground-water contamination was a potential problem, as well as areas of limited information (Fig. 2).

Regional-scale vulnerability maps of nonpoint source pollution and their associated uncertainty maps (of the type shown in Fig. 2) have tremendous potential, when used together, as management tools for identifying which pesticides are the least likely to result in ground-water contamination in the future, and for targeting the most efficient data collection strategies.

For background information *see* ACID RAIN; AIR POLLUTION; EROSION; GEOGRAPHIC INFORMATION SYSTEMS; HAZARDOUS WASTE in the McGraw-Hill Encyclopedia of Science & Technology. Keith Loague

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Notch signaling

Notch signaling is an evolutionarily conserved developmental pathway utilized during the differentiation of a plethora of tissue types, in organisms as diverse as nematodes and humans. Neurogenesis, hematopoiesis, apoptosis, formation of somites, and limb development are just a few of the cellular differentiation events which rely upon cell-to-cell communication mediated by the Notch signaling mechanism. The *Notch* gene, which was first discovered in the fruit fly, *Drosophila melanogaster*, and was named for the presence of "notches" in the wings of mutant animals, encodes a cell-surface receptor molecule. The fruit fly has only a single identified Notch-like gene in its genome, nematodes have two Notch-like genes, while at least four homologs have been identified in mammals. Given this diversification of Notch and its widespread use during development, it is not surprising that mutations in components of the Notch system are associated with human diseases. The Notch mutation TAN-1 is a truncated form of human Notch1 that may be constitutively active and is associated with neoplastic lymphomas. Mutations in human Notch3 are associated with a disorder known as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) which affects vascular integrity. Finally, mutations of a human activating ligand, Jagged1, are associated with the dominant disorder Alagille syndrome, resulting in childhood chronic liver disease and heart, eye, facial, and skeletal disorders.

Function. As one might expect with such a widely used signaling system, the pathway is highly regulated at many levels. Components of the Notch pathway fall into general categories common to many signaling pathways. These are activators (ligands), the receptor itself, effectors (CSL proteins, which are DNA-binding proteins), and transcriptional target genes.

The best-studied Notch signaling event is neurogenesis in flies. In this ectodermal differentiation process, proneural clusters of cells express transcription factors initiating the neuronal program. All cells of the cluster begin with equivalent potential and express both a ligand and the Notch receptor. As a result of a feedback mechanism, small differences in the expression levels of ligand and receptor are amplified and reinforced such that ultimately a single cell expresses ligand while the surrounding cells express the Notch receptor. The ligand-expressing cell will become the neuroblast, while those receiving the Notch signal delay differentiation. In the absence of Notch function, all cells of the proneural cluster follow the neuronal differentiation pathway, resulting in overspecification of neuronal tissue at the expense of other ectodermally derived structures. In the case just described, Notch is used in a lateral inhibition mechanism to limit the number of cells following the neuronal differentiation pathway. Mesodermal and endodermal tissues also require Notch-based decisions during development, and some of these decisions can utilize Notch in more inductive roles. However, for the most part, the mechanism of signal transduction is generally thought to be the same for both processes.

Notch-ligand interactions. In flies, the Notch molecule spans the cell membrane and has a large extracellular domain consisting of 36 epidermal growth factor (EGF)-like repeats and three cysteine-rich Notch/lin-12 repeats (see **illus.**). Intracellularly, Notch has six tandem CDC10/ankyrin repeats, a glutamine-rich stretch (called opa), and a PEST (proline, glutamate, serine, and threonine) sequence which may regulate stability of the molecule. Studies of known Notch mutations and a variety of expression investigations indicate that the function of the extracellular domain is to regulate the signal transducing intracellular domain. When one examines Notch-like molecules from other organisms,