INTEGRATING GEOSPATIAL AND ENVIRONMENTAL SCIENCES INTO EXPOSURE ASSESSMENT FOR EPIDEMIOLOGICAL RISK ANALYSIS

J.R. NUCKOLS, PhD

Emeritus Professor of Environmental Health
Colorado State University

Principal, JRN Environmental Health Sciences
North Besthesda, Maryland, USA

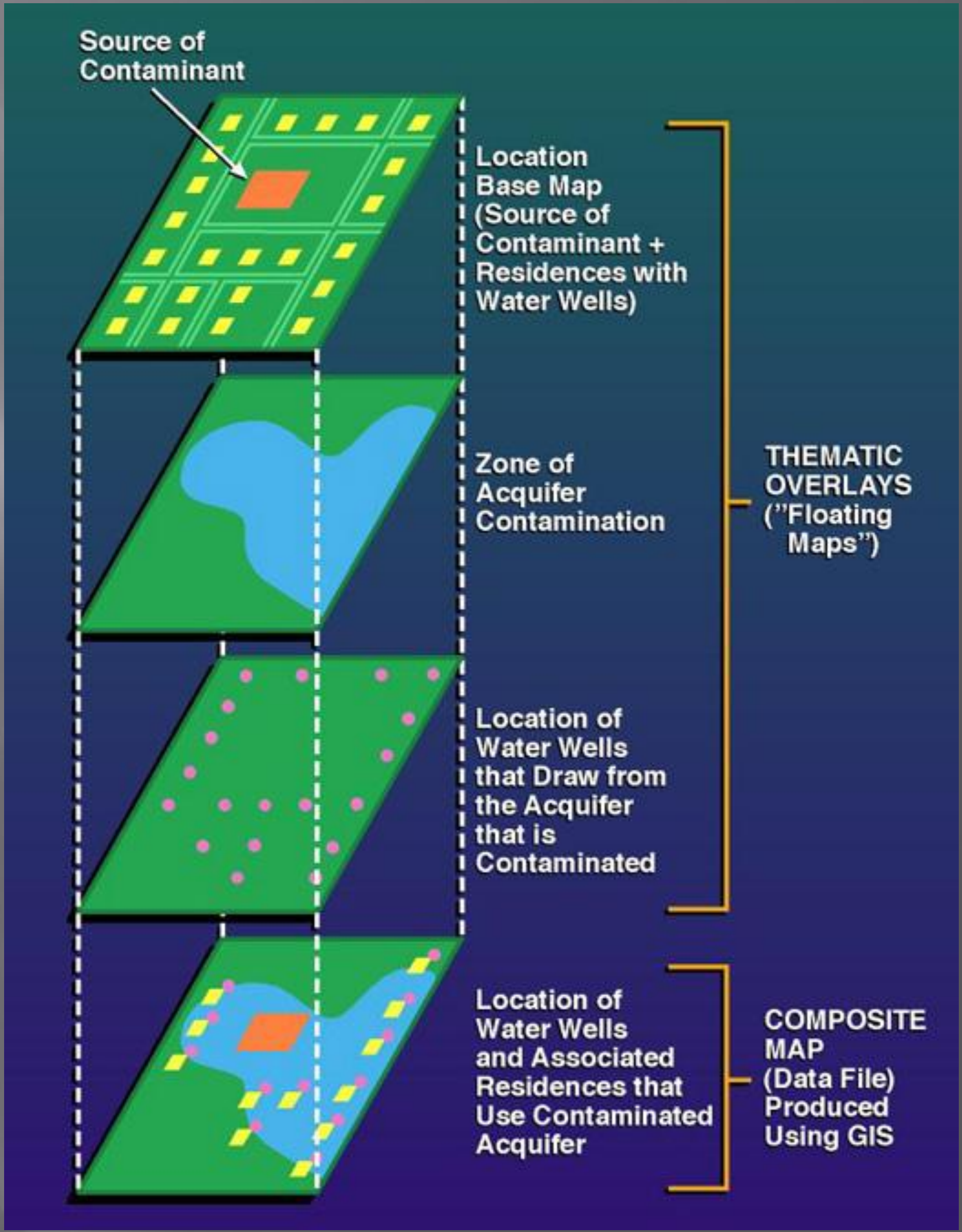
OUTLINE OF TALK

- **Fundamentals of GIS**

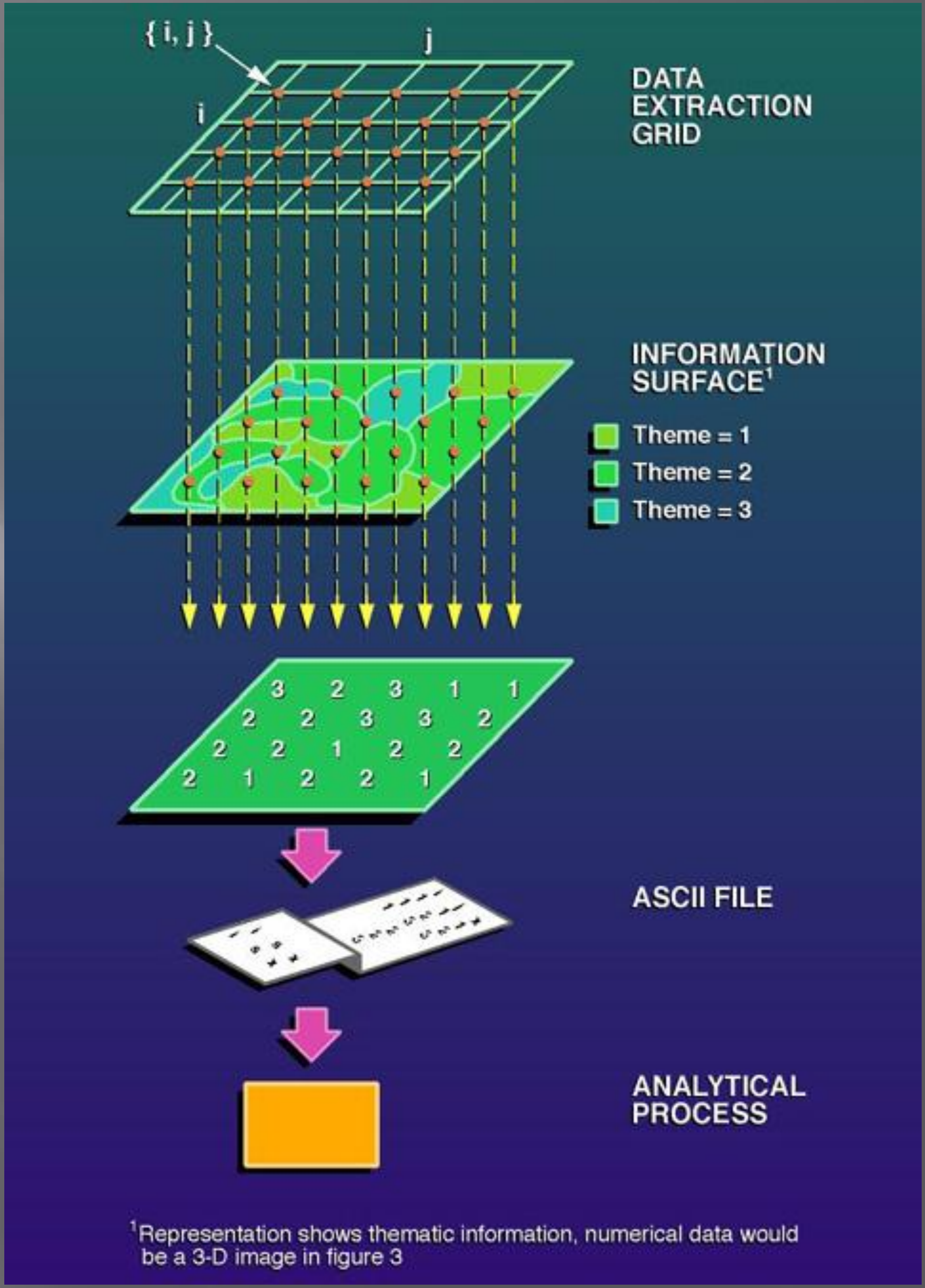
- **Applications to exposure assessment and environmental epidemiology**

- **Example - fugitive emissions of dioxin**

WHAT IS GIS?


Source of Contaminant
Location Base Map (Source of Contaminant + Residences with Water Wells)
Zone of Acquifer Contamination
Location of Water Wells that Draw from the Acquifer that is Contaminated
THEMATIC OVERLAYS ("Floating Maps")
Location of Water Wells and Associated Residences that Use Contaminated Acquifer
COMPOSITE MAP (Data File) Produced Using GIS

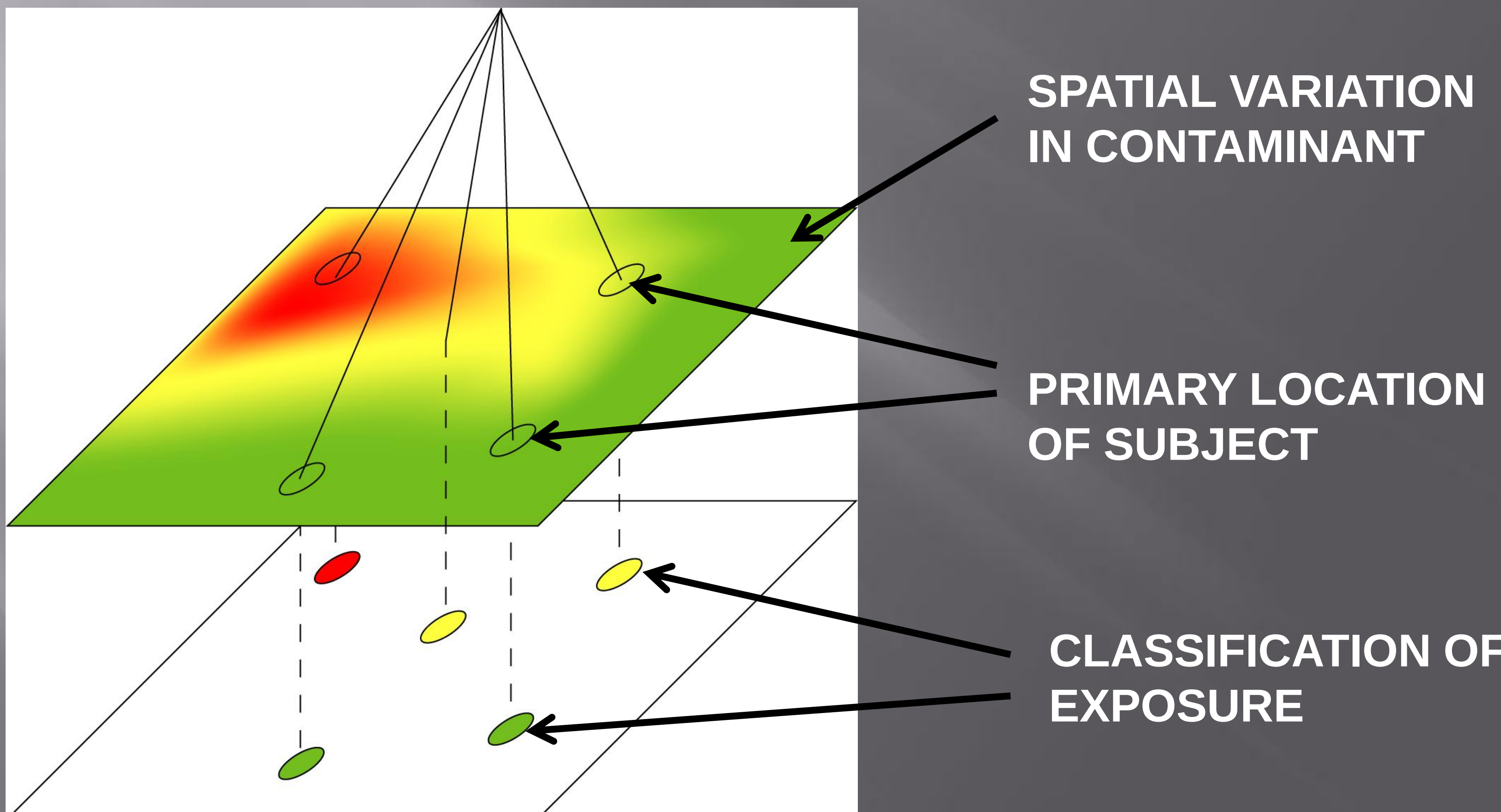
GENERAL FUNCTIONALITY OF A GIS



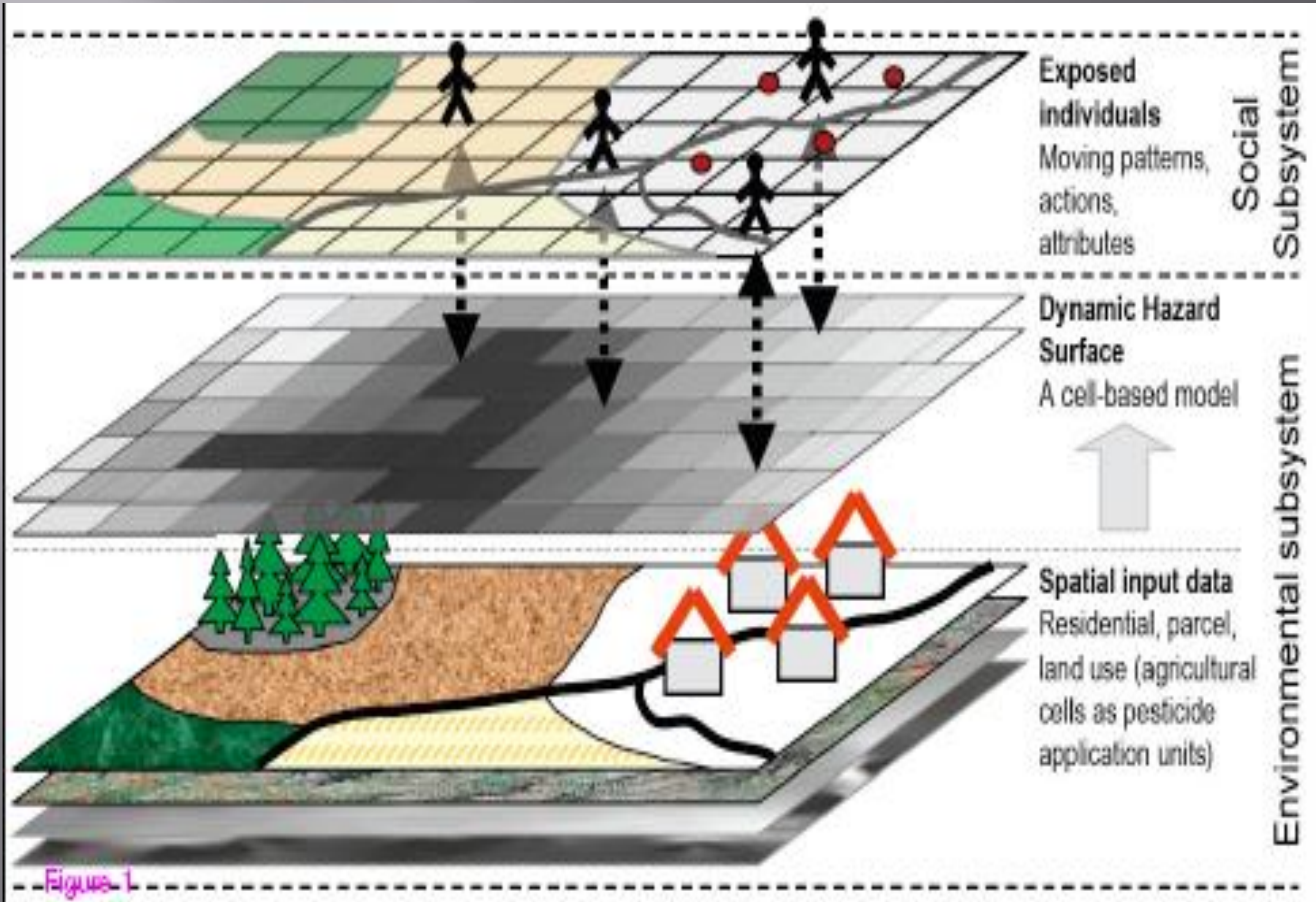
BASIC ROLE OF ENVIRONMENT IN EPIDEMIOLOGIC RISK ASSMT

BASIC GIS APPLICATION TO EPIDEMIOLOGY

CASE – CONTROL STUDY DESIGN



INCORPORATING TIME IN A GIS



Leyk S, Binder CR, Nuckols JR. 2009. : Intl J of Health Geog. 2009 Mar 30;8:17

EXPOSOME ASSESSMENT

Identify agent

Characterize exposure data

Identify and locate source

Identify potential route(s) of exposure

Define study population and system boundary

Define exposure groups

Design exposure metric

Estimate environmental levels

Validate estimates of environmental levels

Estimate personal exposures

Estimate personal dose

Genetic Susceptibility / Validate personal dose

EXTERNAL

INTERNAL

Nuckols, J.R., Ward, M.H., and Jarup, L. 2004. Using GIS for Exposure Assessment in Environmental Epidemiology Studies. Environmental Health Perspectives 112(9): 1007-1015.

CASE STUDY: DIOXINS

- Persistent organic pollutants associated with diseases known or suspected to be caused by environmental exposures
- Multiple sources primarily from combustion activities
- Amenable to GIS-based Exposure Assmt:
  - Proximity Analysis (Elliott 1996, Pronk 2013)
  - Dispersion models (Floret 2003, Viel 2008)
  - Geographic-based Emission Index (Pronk, 2013)
  - S/T Variation Blood biomarkers (De Roos 2005, Viel 2011)
  - S/T Variation Environ Samples (Dahlgren 2007, Hensley 2007, Garabrant 2009, Feng 2011, Deziel, 2012)

Determinants of dioxins and furans in carpet dust samples from four areas of the United States

2011. INTL SOC EXPOSURE SCIENCES. Nicole C. Deziel, Nuckols JR, Colt JC, Roos AJ, Pronk A, Gourley C, Severson RK, Cozen W, Cerhan JR, Morton LM, Ward MH

2012. Deziel NC, Nuckols JR, Colt JC, De Roos AJ, Pronk A, Gourley C, Severson RK, Cozen W, Cerhan JR, Hartge P, Ward MH. 2012. *Sci of the Total Environment*. 433. 516-522

Study Objective

- Better understand the contribution of an array of outdoor sources on house dust levels of dioxins and furans in the general U.S. population

Study Design

- Population: 40 participants of NCI-SEER NHL Study living in Iowa, Los Angeles County, Detroit, and Seattle
  - Selection captured range of proximities to various sources
- Study Period: 1998 to 2000
- Interview: demographics, residential characteristics, occupation, diet and lifestyle
- Dust Collection: participants provided vacuum bags
- Dust Analysis: sieved (150 um) and analyzed by HRGC/HRMS following EPA Method 8290

GIS Analysis–Proximity Determinants

- Traffic-related variables
  - Residential proximity (100 m & 400 m) to major roadways using Streetmap (TeleAtlas Dynamap Transportation 5.2)
  - Residential proximity to freight routes (100 m & 400 m) using Federal Highway Administration database (Freight Analysis Framework 2.2)
- Facility-related variables
  - EPA database (EPA/600/C-01/012)
  - Residential proximity (3 km and 5 km) to dioxin-emitting facilities
  - Dioxin emission index: annual inverse distance-squared weighted emission index for every facility within 5 km of the residence, up to 15 yr

Statistical Methods

- Multivariate regression models
  - Evaluate relationship between determinants and concentrations of dioxins and furans in carpet dust
  - Outcome variables: 17 EPA-designated toxic congeners and Toxic Equivalence (TEQ) (all log-transformed)
    - TEQ is a summed metric which weights congeners relative to the potency of TCDD
  - Determinants: proximity metrics, dioxin emission index, population density, when home built
  - Imputation procedure for measurements <LOD

Proximity Determinants

Proximity Metric	Number (%)	
	Within 100 m	**Within 400 m**
Freight route	**9 (23)**	**19 (48)**
Major roadway	**7 (18)**	**13 (33)**
	Within 3 km	**Within 5 km**
Cement kiln	**1 (3)**	**2 (5)**
Coal fired plant	0 (0)	**2 (5)**
Sewage incinerator	0 (0)	**2 (5)**
Medical waste incinerator	**9 (23)**	**18 (45)**
Emission index		
>0 (ng TEQ/yr)	**20 (50)**	

No residences within hazardous waste incinerators, solid waste incinerators, copper smelters, industrial boilers, or iron ore sintering plants.

Distributions of Dioxins and Furans in Carpet Dust

Congener	TEF	% Detected	Geometric Mean (ppt)	GSD (ppt)
Dioxins				
2,3,7,8-TCDD	1	83	0.51	1.9
1,2,3,7,8-PeCDD	1	93	1.8	1.9
1,2,3,4,7,8-HxCDD	0.1	90	3.7	2.6
1,2,3,6,7,8-HxCDD	0.1	100	23	2.8
1,2,3,7,8,9-HxCDD	0.1	100	14	2.3
1,2,3,4,6,7,8-HpCDD	0.01	100	790	2.9
OCDD	0.0003	100	6700	2.6
Furans				
2,3,7,8-TCDF	0.1	100	2.2	1.7
1,2,3,7,8-PeCDF	0.03	98	1.4	2.0
2,3,4,7,8-PeCDF	0.3	98	2.5	1.9
1,2,3,4,7,8-HxCDF	0.1	98	8.3	2.6
1,2,3,6,7,8-HxCDF	0.1	100	5.4	2.1
1,2,3,7,8,9-HxCDF	0.1	48	0.46	1.8
2,3,4,6,7,8-HxCDF	0.1	98	5.4	2.1
1,2,3,4,6,7,8-HpCDF	0.01	100	130	2.8
1,2,3,4,7,8,9-HpCDF	0.01	93	7.4	3.2
OCDF	0.003	100	300	2.6
TEQ			24	2.4

Proportional increase in dioxin concentrations with proximity to sources

Congener Determinants	exp(β) (95% Confidence Interval)
2,3,7,8-TCDD[a]	
Cement Kiln 5km	2.5 (1.1, 5.6)**
Sewage Incinerator 5km	2.4 (1.1, 5.5)**
1,2,3,4,7,8-HxCDD[a,b]	
Cement Kiln 3km	7.6 (1.2, 47)**
1,2,3,6,7,8-HxCDD[a]	
Cement Kiln 3km	6.7 (0.92, 49)*
1,2,3,7,8,9-HxCDD[a]	
Cement Kiln 3km	5.7 (1.2, 28)**
1,2,3,4,6,7,8-HpCDD	
Cement Kiln 3km	8.6 (1.1, 69)**

*$p<0.10$, **$p<0.05$, [a]model includes population density, [b]model includes gender

No significant determinants for 1,2,3,7,8-PeCDD or OCDD.

Proportional increase in furan concentrations & TEQ with proximity to sources

Congener Determinants	exp(β) (95% Confidence Interval)
2,3,7,8-TCDF	
Cement Kiln 5km	3.7 (1.9, 7.0)**
1,2,3,7,8-PeCDF[a]	
Cement Kiln 5km	4.1 (1.8, 9.5)**
Freight Route 400m	1.4 (0.98, 2.0)*
2,3,4,7,8-PeCDF	
Cement Kiln 5km	4.0 (2.0, 8.3)**
Freight Route 400m	1.7 (1.3, 2.4)**
1,2,3,4,7,8-HxCDF[a]	
Freight Route 400m	2.0 (1.1, 3.5)**
1,2,3,6,7,8-HxCDF[a]	
Cement Kiln 5km	2.9 (1.1, 7.8)**
Major Roadway 400m	1.9 (1.2, 3.0)**
2,3,4,6,7,8-HxCDF	
Cement Kiln 5km	2.9 (1.1, 7.7)**
Major Roadway 100m	1.9 (1.1, 3.3)**
Total Toxic Equivalence (TEQ)[a]	
Cement Kiln 3km	5.3 (1.0, 28)**

*p<0.10, **p<0.05, [a]model includes population density, [b]model includes gender

No significant determinants for 1,2,3,4,6,7,8-HpCDF, 1,2,3,4,7,8,9-HpCDF, OCDF.

Conclusions

- Dioxins and furans were universally detectable in carpet dust in 4 sites across the U.S.
- Higher concentrations of certain dioxins and furans near cement kilns, freight routes, and major roadways suggest that these outdoor sources are contributing to indoor exposures.
- Further study of the contribution of these sources to total dioxin and furan exposure is warranted.

ENVIRONMENTAL EXPOSURE TO DIOXINS FROM LIVING NEAR INDUSTRIAL COMBUSTION SOURCES AND RISK OF NON-HODGKIN LYMPHOMA

2011. Intl Society of Environmental Epidemiology. Anjoeka Pronk, John R. Nuckols, Dave Cleverly , Matthew Airola, Anneclaire J. De Roos, Joanne S. Colt, James R. Cerhan, Richard Severson, Aaron Blair, Mary H. Ward

2012. Pronk A, Nuckols JR, De Roos AJ, Airola M, Colt JS, Cerhan JR, Cozen W, Severson R, Blair A, Cleverly D, Ward MH. 2013. *Environmental Health* (On-line version avail)

NATIONAL CANCER INSTITUTE

NATIONAL INSTITUTES OF HEALTH

NCI-SEER NHL Study

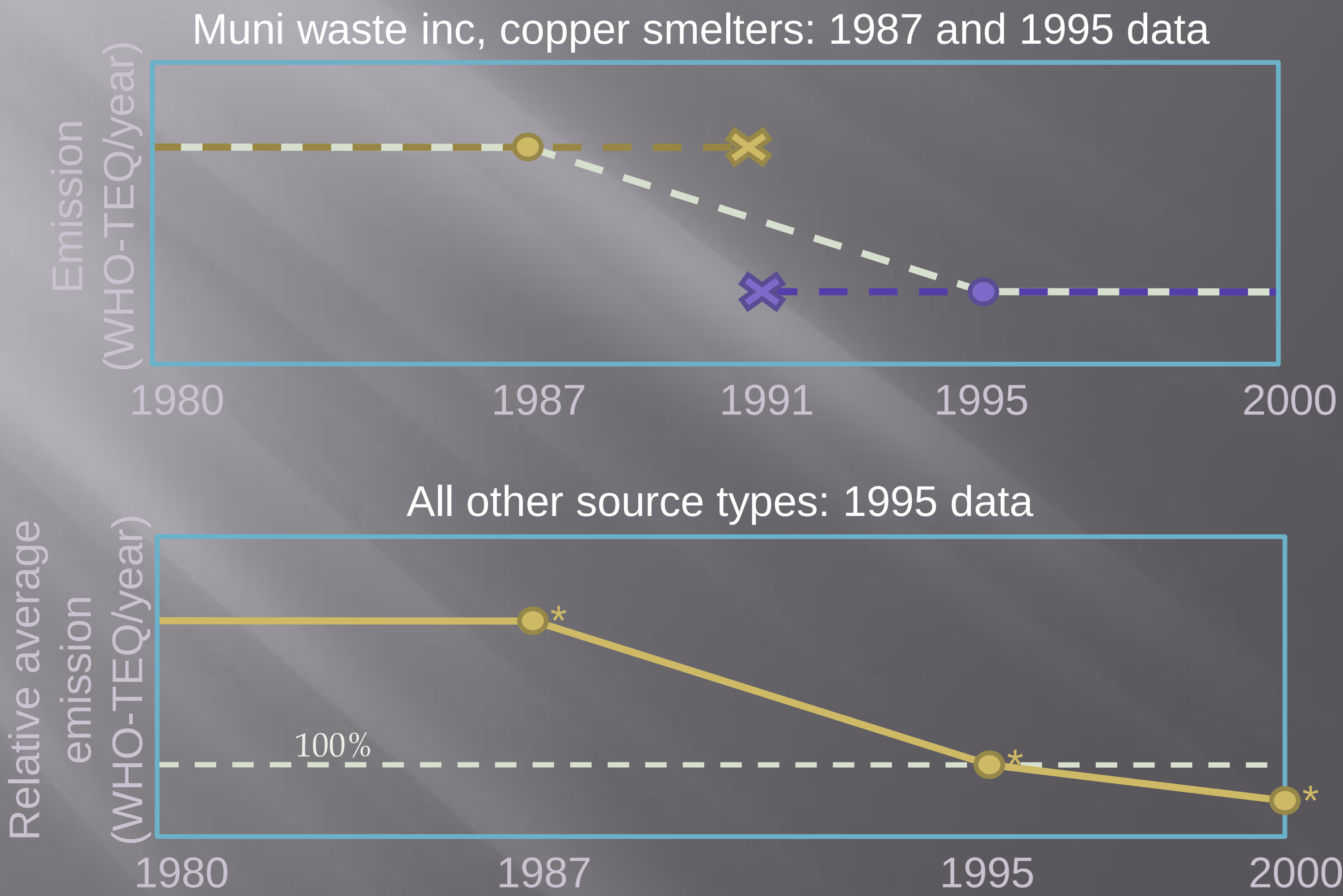
- Aim: To identify potential environmental causes of NHL
- Study design:
  - 1321 cases (diagnosed 1998-2000), 1057 controls
  - Surveillance, Epidemiology and End Results (SEER) cancer registries:

    Iowa, Los Angeles county, Detroit, Seattle
  - Collected data:
    - Questionnaire
    - Residential history
    - Blood sample (62% cases, 66% controls)
    - House dust sample (58% cases, 56% controls)

Geocoding

- Residential history: current , past 20 years
  - Only subjects with >70% of residences accurately geocoded (n=1,416)
- 8 major industrial sources 1995 (EPA database)
  - 73-100% verified (83% of total)

Temporal variation emissions



* Inventory of source releases of dioxin-like compounds in the US in 1987, 1995 and 2000 (EPA)

Exposure metrics

- Exposure period = 20 years
- Proximity metric
  - Ever within 5 km
  - Duration within 5 km
- Emissions metric
  - Distance weighted within 5km
  - Emission = throughput * facility specific emission factor
  - Summed over exposure period for each individual
  - Annual average over exposure period
  - Annual maximum

Data analyses

- Odds ratios and 95% confidence intervals
  - Quartiles for continuous variables
- Adjusted for other potential risk factors:
  - Age, gender, race, education level
  - Other dioxin sources:
    - Occupational exposure: occupational history SIC code
    - Traffic (diesel): major highways
    - Diet: Saturated fat
- Stratified by gender, study center, histology

RESULTS

- Proximity to any dioxin-emitting facility was not associated with NHL risk (3 km OR=1.0, 95% CI 0.8-1.3).
- Risk was elevated for residence near cement kilns (5 km OR=1.7, 95% CI 0.8-3.3; 3 km OR=3.8, 95% CI 1.1-14.0).
- The Geographic-based Emissions Index was not associated with risk of NHL overall.
- Risk for marginal zone lymphoma was increased for the highest versus lowest quartile (5 km OR=2.6, 95% CI 1.0-6.8; 3 km OR=3.0, 95% CI 1.1-8.3).

Conclusions

- Geospatial methods proved a valuable tool in exposure assessment of a large study population with a residential history and associated dioxin sources distributed over a very large geographic region
- Findings for high emissions and marginal zone lymphoma and for specific facility types and all NHL provide some evidence of an association and deserve future study.
- Because study population was not specific to study of dioxin emissions, statistical power for detecting risk was low for most facility types

Collaborators

- John R Nuckols, Colorado State University, Fort Collins, CO
- Nicole Deziel, National Cancer Institute, Bethesda, MD
- Joanne C Colt, National Cancer Institute, Bethesda, MD
- Anneclaire J De Roos, Fred Hutchinson Cancer Research Center, Seattle, WA
- Anoejka Pronk, National Cancer Institute, Bethesda, MD
- Chris Gourley, Southwest Research Institute, San Antonio, TX
- Richard K Severson, Karmanos Cancer Institute, Wayne State University, Detroit, MI
- Wendy Cozen, University of Southern California, Los Angeles, CA
- James R Cerhan, Mayo Clinic College of Medicine, Rochester, MN
- Lindsay M Morton, National Cancer Institute, Bethesda, MD
- Mary H Ward, National Cancer Institute, Bethesda, MD
- Lonn Irish, Information Management Services, Inc., Silver Spring, MD

These studies was supported by the Division of Cancer Epidemiology and Genetics, National Cancer Institute (NCI), Intramural Research Program of the National Institutes of Health

GEO3N PROJECT. IMPACT OF ENVIRONMENTAL DIOXIN EXPOSURES ON ENDOCRINE DISRUPTORS AND RISK OF BREAST CANCER IN THE E3N WOMEN'S COHORT

DOSSUS L[1,2] , ANZIVINO-VIRICEL L[3], FAURE E[3] , SALIZZONI P[4], NUCKOLS JR[5], CLAVEL-CHAPELON F[1,2], FERVERS B[3]

1. Inserm U1018, Centre for Research in Epidemiology and Population Health (CESP), Institut Gustave Roussy, Villejuif, France
2. Paris South University, Villejuif, France
3. Cancer and Environnement Unit, Centre Léon Bérard, Lyon, France
4. University of Lyon Ecole Centrale de Lyon, INSA Lyon
5. JRN Environmental Health Sciences, N. Bethesda, MD USA

Objectives

- Study of the association between environmental exposure to dioxins and the risk of breast cancer.
- Case-control study nested within the E3N cohort (Françoise Clavel-Chapelon, Nutrition, Hormones and team women's health ', Inserm U1018, www.e3n.net
- Evaluation of environmental exposures to dioxins through the use of a dispersion model coupled with a Geographic Information System (GIS)

Expected Results

- **Account for multi-source emissions**
  - **Combustion facilities**
  - **Power generation, Traffic**
- **Improve Exposure Classification**
  - **Account for uncertainties in contaminant levels**
  - **Account for residential history of each participant**
  - **Account for individual exposure factors in study population**
- **Study of the impact of the evolution of regulations and technologies**

Pilot Study in Rhône-Alpes

*** Feasibility and validation of a methodological approach for retrospective assessment of individual level environmental exposure to dioxins in the E3N population within R-A Region**

*** Evaluate transferability of the methodology to a National Study of the E3N cohort.**

Programme ONCOSTARTER

CLARA
CANCÉROPÔLE LYON AUVERGNE RHÔNE-ALPES
SPEEDING UP PROGRESS

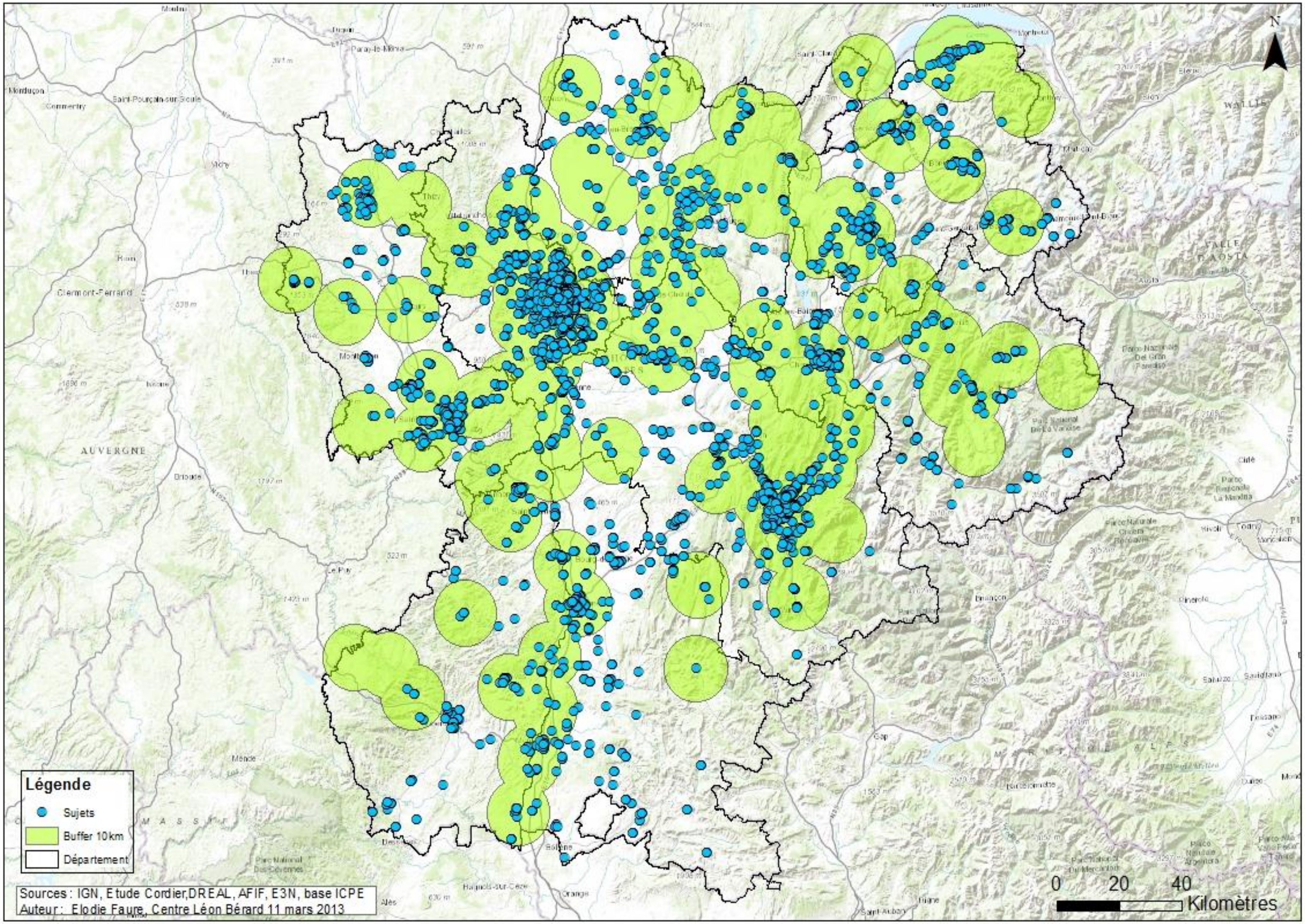
Région RhôneAlpes

Pilot Study in Rhône-Alpes

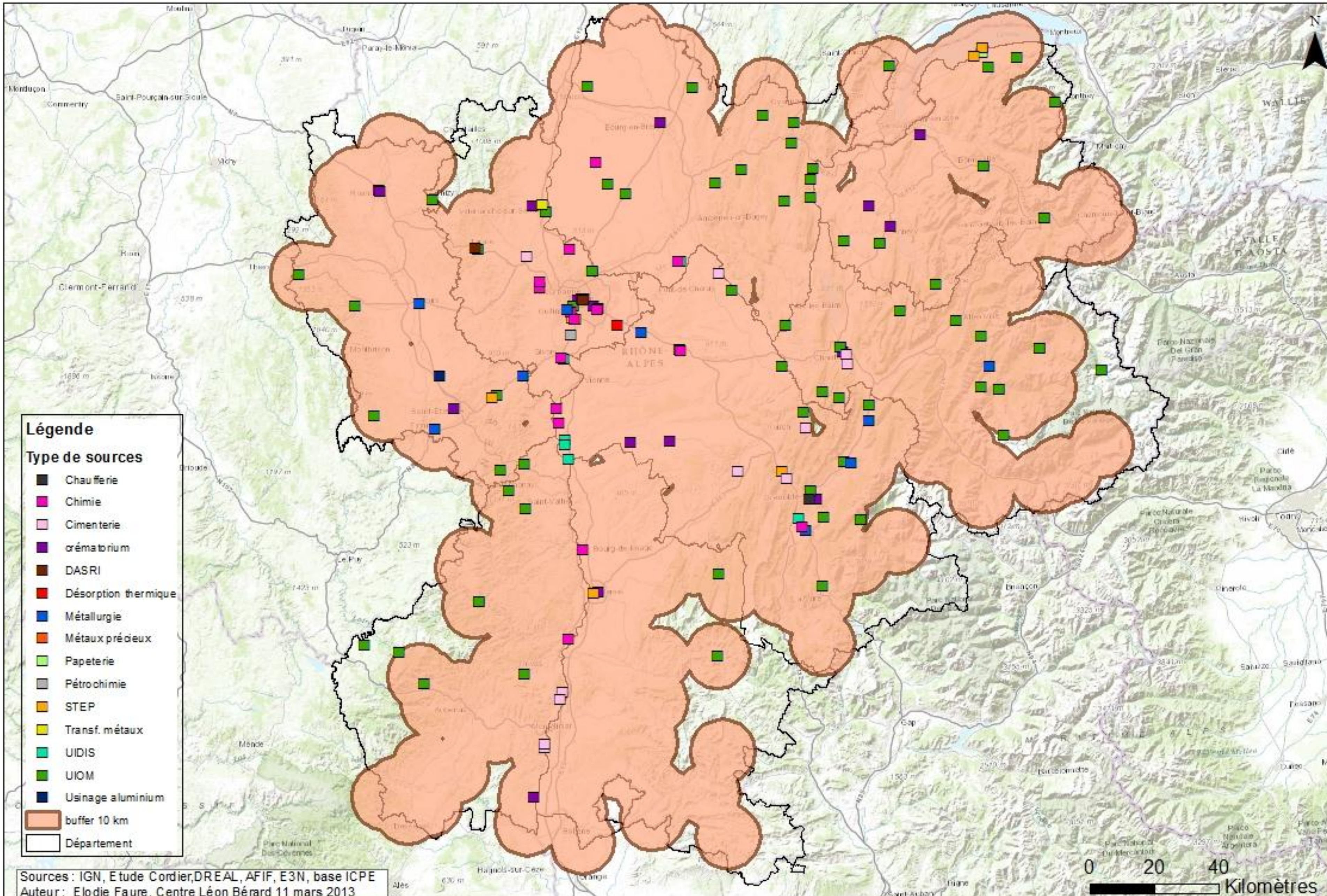
- 543 E3N cases + 2 controls from within cohort
- Validation of Information and Methods:
  - Sources of exposure
  - Indicators / Dispersion models
  - Geographic-based exposure metrics
  - Proportion of study population exposed

- Evaluate feasibility of extrapolaton to national project

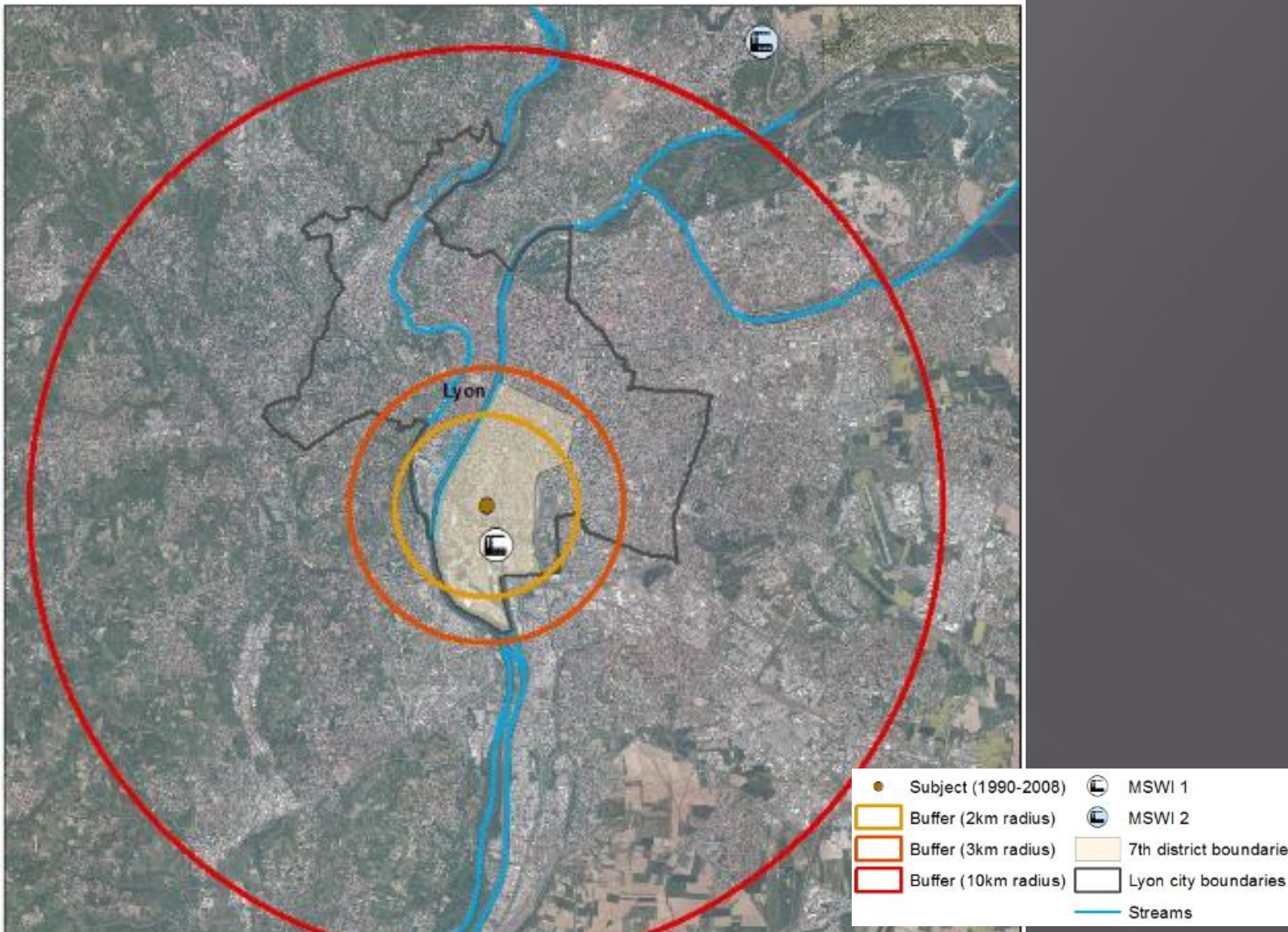
GEO3N : les sujets et les buffesr de 10 km autour des sources en Rhône-Alpes



GEO3N : les sources et buffer de 10 km autour des sujets en Rhône-Alpes



Example in the 7th district of Lyon
Location of the subject n°3 and proximity to waste incinerators



Author : Alice Denoyel, Leon Berard Center, Jean Moulin Lyon 3 University (2012)
Source : BD Ortho IGN, BD topo IGN, E3N (IGR)

J. R. Nuckols, PhD

Emeritus Professor Environmental Health Sciences
EHASL 1992-2007; NIHIPA 2002-2011; Wash, D.C. 2011-

INTEGRATION :
ENVIRONMENTAL AND GEOSPATIAL SCIENCES
HEALTH RISK ASSESSMENT

WATER / AIR RESOURCES

NON-OCCUPATIONAL CHEMICAL / BIO EXPOS

ENVIRONMENTAL EPIDEMIOLOGY

CONTACT: jnuckols@colostate.edu
SKYPE: jnuckols
Ph +1.970.218.4757